Uveitis Society (India)

NEWSLETTER

EDITION-08 | VOLUME-1 | APRIL 2025

From Haze to Hope: Paediatric Uveitis

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Dear Friends,

A heartfelt thanks to the incredible responses to our previous newsletters. Your feedback and continued interest have helped shape the content we share and we are excited to keep bringing you even more value and insight in the editions to come.

The 8th edition of the USI Newsletter features “Paediatric Uveitis”. Paediatric uveitis is a rare and potentially sight threatening condition. This rarity, presents an unmet need in our understanding of this entity in children, in terms of the robust immune system they have, the need for early recognition, accurate diagnosis and appropriate treatment. These pose unique challenges and has implications for ophthalmologists.

Dr.Abhilasha and the editorial team have compiled interesting articles and challenging cases contributed by our members in this newsletter. A Paediatric rheumatologist’s perspective on “what an ophthalmologist should know” will be very informative for our clinical practice. I hope through this edition, we can convey that “Children are not little adults” and handling uveitis in them is not the same as that in adults.

On behalf of the USI, I thank all the authors, the editorial team and team hallmark for their coordinated efforts in bringing this interesting issue. We do hope this issue will be well received by our readers as our previous editions.

Regards,
Dr. Kalpana Babu

Secretary
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Dear Members,

I'm really excited to share this special issue of the Uveitis Society of India Newsletter, thoughtfully put together by our Editor, Dr. Abhilasha Baharani.

This edition focuses on Pediatric Uveitis, the one that really tugs at the heart. It can be tough to catch early, and if missed, it can deeply affect a child's vision and quality of life. As clinicians, that's something we all care deeply about.

What I love about this issue is the rich mix of insights from colleagues across the country.

You'll find practical tips, real world experiences, and the latest research—all shared with the goal of helping us do better for our young uveitic kids

All this is possible only because of Dr. Abhilasha - a heartfelt thanks to her for pulling this together so seamlessly, And a big 'thank you" to all the contributors for bringing attention to such an important topic.

Whether you're just starting your journey in uveitis or have seen it all, there's something in here for everyone

Let's keep learning, sharing and supporting each other as we work to give every child the best possible care.

Warm regards,
Dr. Sudharshan S

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Every child is a little David with immense potential to slain the most formidable Goliath. As uveitis specialists we need to hand them the right diagnosis (the sling) and timely treatment (five smooth stones) to defeat the Goliath (uveitis) in their lives and come out as little champions.

The current issue of the US(I) Newsletter titled, "From Haze to Hope" on paediatric uveitis aims to inspire and update uveitis specialists on various clinical, diagnostic and management aspects of common intraocular inflammatory diseases affecting children. We have often heard in our clinical postings that children are not small adults and they need to be treated meticulously with specific, tailored investigation protocols and treatment guidelines. With this in mind, the Newsletter attempts to incorporate the challenges we face in the clinics, our brilliant authors showing us the way.

The Newsletter opens with "Top systemic signs in paediatric uveitis that an ophthalmologist should know", a very systematically written article by pediatric rheumatologist, Dr. Archana Khan. She has taken a step-wise approach and described all the important signs in a generously illustrated write up.

The next three articles on top ten pearls in the management of pediatric uveitis are written by our coveted stalwarts. Prof. Amod Gupta focuses on surgical interventions, Prof. Jyotirmay Biswas on non-infectious uveitis and Prof. S.R. Rathinam (with co-authors, Dr. Lisa and Dr. Rajashree) on infectious uveitis. The articles written in points compile their wisdom and experience to guide us in the clinic.

Dr. Rakshita, Dr. Mahesh and Dr. Parthopratim in their article on juvenile idiopathic arthritis describe the most challenging paediatric uveitis entity with considerable impact on a child's vision and quality of life. The write-up is commendable in that the authors have kept the Indian perspective in mind. It contains as many as six important tables that will serve as ready reckoners.

Dr. Ranju Kharel has contributed not one but two worthy articles for the current issue. The one on sarcoidosis-associated uveitis in children is written lucidly covering

all the important aspects with the latest references in literature. She is an authority on Seasonal Hyperacute Panuveitis (SHAPU) and has contributed an intriguing case report, on request. This serious, blinding disease of children needs more awareness and attention from researchers and Dr. Ranju's contribution is one of the foremost in this field.

Dr. Rishika Rathore and Dr. Simar Rajan Singh's article on Blau syndrome associated uveitis is concise and precise.

"Sunset glow in young eyes: Insights into paediatric Vogt-Koyanagi-Harada (VKH) syndrome" by Dr. Hrishikesh Kaza, Dr. Mudit Tyagi, Dr. Soumyava Basu and Prof. Dr. S. R. Rathinam is a detailed, well-researched article on the subject. It also highlights the differences in clinical presentation and management of the paediatric and the adult form of the disease.

Tubulointerstitial nephritis and uveitis is an uncommon and may be underdiagnosed entity that should be kept in the differentials. Dr. Yogish Kamath with co-author Dr. Aishwarya Kulkarni, have described the clinical features, management as well as mechanisms of TINU in a very well-structured article.

Trematode Granuloma by Dr. Vedhanayaki Rajesh is a brief account of the disease that needs to be actively looked for and careful history taking is the key.

I'm grateful to Dr. Subhav (with coauthors, Dr. Santosh Honavar, Dr. Kaustubh Mulay and Dr. Vijay Anand P. Reddy) a busy orbit, oncology, oculoplastic surgeon for sharing a challenging case of retinoblastoma masquerading as panuveitis. Retinoblastoma is the commonest primary intraocular malignancy of childhood. A high index of suspicion is needed to make an accurate diagnosis.

Last but definitely not the least is the article on imaging by Dr. Padmamalini and her team from Narayana Nethralaya, Bengaluru. It is likely the most detailed article you will find on imaging in paediatric uveitis which is also generously illustrated with case examples.

Every issue of the Newsletter attempts to encourage participation from all members. EyeOpener: paediatric uveitis case contest was conducted for US(I) members. The jury consisted of Prof. Amod Gupta, Dr. Manisha Agarwal and Dr. Alok Sen. Five winning cases emerged for publication, Dr. Bhavik Panchal getting the top spot, Dr. Saloni Desai came second and the third place was a tie between Dr. Fathima Fahima, Dr. Neethu Latiff and Dr. Kasturi Chavan. I immensely thank all the participants and the esteemed jury in making this endeavour a success.

The final section titled, "Get on board" is a directory of uveitis fellowship opportunities in India, Nepal and Singapore. It is aimed to increase and strengthen our tribe so that patients with uveitis can get expert care in their city/ town.

I sincerely thank the President, Dr. Kalpana Babu Murthy, Secretary, Dr. Sudharshan Sridharan, Vice President Dr. Padmamalini, Joint Secretary Dr. Soumyava Basu and Treasurer Dr. Parthopratim Dutta Majumdar for their support and guidance.

Thanks to the Hallmark Team, especially, Mr. Sampath for his efforts in designing the Newsletter, Mrs. Veidhehi and Mrs. Pramila for their help in the EyeOpener case contest, and compiling the "Get on board" section on uveitis fellowship opportunities.

I would also like to thank my son Akshaj Manraj for his colour pencil art for the cover page.

The Newsletter is from the members and for the members and without them, it wouldn't have been possible. I thank each one who has given ideas, last minute help and sometimes moral support. Special mention for Prof. Amod Gupta, Dr. Parthopratim Dutta Majumder, Dr. Aniruddha Agarwal, Prof. Yogish Kamath, Prof. Vishali Gupta and Dr. Atul Arora.

The current issue is a sincere effort to help all of us in tackling the challenges of pediatric uveitis. I hope members will benefit from the efforts of our authors. Kindly reach out to me for suggestions and ideas for the future.

Sincerely,
Abhilasha

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Top Systemic Signs in Paediatric Uveitis that an Ophthalmologist should know:A Stepwise Diagnostic Approach

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Paediatric uveitis accounts for 5–10% of all uveitis cases and may not be merely an ocular issue. Approximately every third child with uveitis harbours a systemic disease, placing them at a heightened risk for ophthalmic complications such as cataract, band keratopathy, glaucoma, cystoid macular edema, and severe vision loss (25–30%). Moreover, the diagnosis is often delayed because uveitis in these cases is commonly asymptomatic.

Paediatric uveitis thus often serves as a sentinel for an underlying systemic disease, underscoring the importance of a meticulous stepwise approach. Early recognition and management is thus imperative to avoid ophthalmic complications and to mitigate systemic morbidity.

Ophthalmologists are often uniquely positioned to detect early systemic involvement since uveitis may either precede, parallel, or even be the only initial manifestation of a systemic disease.

Key Message for Ophthalmologists
When paediatric uveitis is encountered, think beyond the eye. A thorough history, systemic examination, and close collaboration with other paediatric subspecialties, especially rheumatology could be both vision-saving and life-saving.

Epidemiology and Patterns of Paediatric Uveitis
Recent multi-centre data reveal the following breakdown of paediatric uveitis (Figure 1A,B).

Anterior uveitis: 59.7%

Panuveitis: 30.6%

Intermediate uveitis: 7.5%

Posterior uveitis: 2.2%

28.4% of paediatric uveitis has a documented systemic rheumatic association, with **Juvenile Idiopathic Arthritis (JIA)** being the single most common entity (14.8% of all pediatric uveitis cases). Across different regions, the prevalence of JIA in paediatric uveitis can range from 11% to 30%.

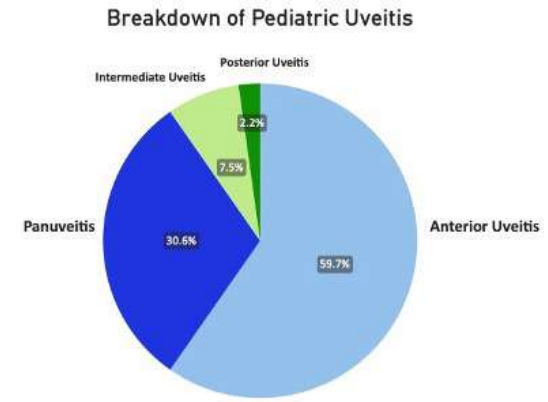


Figure 1A

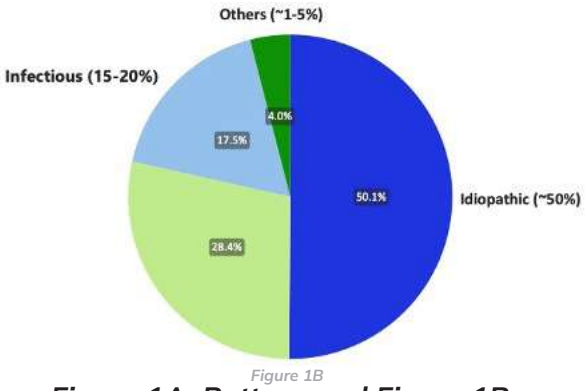


Figure 1B

Figure 1A Pattern and Figure 1B Causes of Paediatric Uveitis

Stepwise Approach to Decipher Systemic Involvement

Step 1: Characterize the Uveitis

A detailed ocular examination is crucial to classify uveitis, guide further investigations and zero down to a clinical diagnosis. Key aspects include

Anatomic Location: Anterior, intermediate, posterior, or panuveitis.

Onset: Sudden/acute (painful, photophobic, red) vs. insidious/chronic (often asymptomatic until complications arise).

Laterality: Unilateral vs. bilateral. Bilateral uveitis frequently points to systemic associations.

Presence of Granulomatous Features: Mutton-fat keratic precipitates suggest sarcoidosis, tuberculosis, Blau syndrome, or Vogt-Koyanagi-Harada (VKH).

Practical pointer:

- When both eyes are inflamed, it's usually more than just bad luck; think systemic.
- Some auto-inflammatory and autoimmune conditions can cause primary inflammatory conjunctivitis; think systemic if chronic or recurrent!

Ocular Clues Pointing to Systemic Disease: A Comparative Table

Feature	Systemic Etiology	Local or Idiopathic Etiology
Granulomatous Inflammation	Sarcoidosis, TB, Blau Syndrome	Fuchs Heterochromic Iridocyclitis (mild KPs)
Bilateral Uveitis	Systemic disease (JIA, Bechet's, Sarcoid)	Uncommon for purely local causes
Hypopyon	Bechet's (sterile)	Infectious endophthalmitis (bacterial/fungal)
Retinal Vasculitis	Sarcoidosis (candle-wax drippings), VKH, tuberculosis	Idiopathic peripheral vasculitis (rare), tuberculosis
Sectoral Iris Atrophy	Herpetic (HSV, VZV) uveitis (can be recurrent)	Fuchs Heterochromic Iridocyclitis (diffuse atrophy)

Step 2: Elicit Systemic Signs & Symptoms

A thorough history and clinical examination is critical to uncover potential systemic disease. Below are the top systemic associations and their hallmark features:

Ten Key Questions for patients to narrow down systemic causes:

1. Does the child have joint pains, swelling, or morning stiffness in joints?
2. Does he suffer from fevers, fatigue, rashes, or unexplained weight loss?
3. Is there a history of oral or genital ulcers or skin lesions or pathergy?
4. Are there gastrointestinal complaints like bloody diarrhoea or chronic abdominal pain?
5. Any neurological symptoms such as headaches, neck stiffness, or hearing changes?
6. Are there symptoms of hair loss, change in hair colour, or alopecia?
7. Is there any family history of HLA-B27 or autoimmune diseases?
8. Is there history of recurrent infections, otorrhoea, oral thrush?
9. Any lymph node enlargements, hepatosplenomegaly, or night sweats?
10. Is the child's growth appropriate for their age, or is there failure to thrive?

Joint/s Involvement

1. Juvenile Idiopathic Arthritis (JIA):

Approximately 10–25% of children with JIA develop uveitis. Among these, 30–40% may experience complications like cataracts or glaucoma if not promptly treated.

JIA is the leading cause of chronic anterior uveitis in children.

Typically presents with joint swelling (Figure 2A,2B), redness and warmth often worse in the morning or after rest.

Elevated ESR/CRP (inflammatory markers) ANA positivity is common in the oligoarticular (less than 5 joints involved) subtype.

Practical pointer:

Presence of ANA positivity increases the propensity of uveitis in children. Uveitis may not also correlate with active joint disease

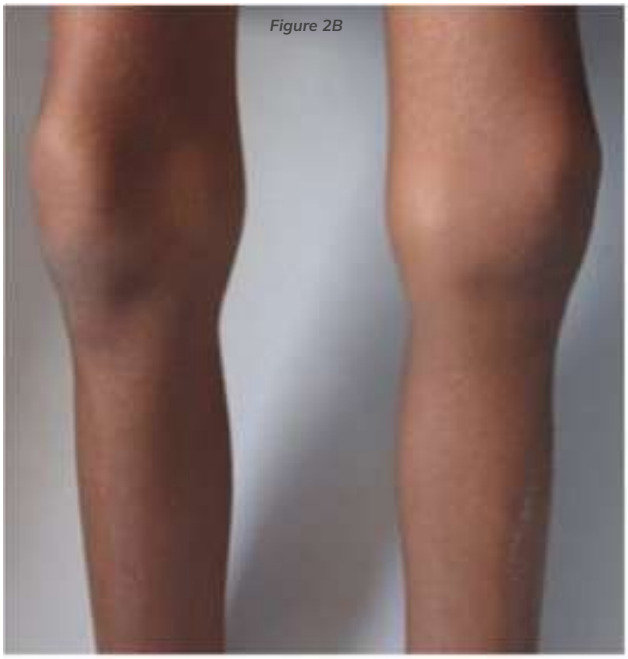


Figure 2: Swelling over wrist and knee joints in JIA

and can be "silent disease in a white eye." Thus in children with ANA positivity, monitoring for ocular inflammation and uveitis is required more frequently and long after joint disease is 'controlled'.

Spondylarthritis (e.g., HLA-B27–related arthritis):

Includes psoriatic arthritis, ankylosing spondylitis, enthesitis related arthritis (ERA), reactive arthritis and Inflammatory Bowel Disease (IBD) related arthritis

Sacroiliac /hip / large lower limb joint arthritis and/or tarsitis may be predominant features.

Entheseal points pain especially in insertion of patellar ligament at the inferior patella, plantar fascia at the calcaneus, and Achilles' tendon could be elicited.

Sudden acute red eye is characteristically seen and can rapidly lead to visual compromise if not recognised and treated early.

Family history of HLA-B27 positivity should raise suspicion.

2. Fever and Rash

Infectious causes like chicken pox and herpes will have vesicular rashes (Figure 3).

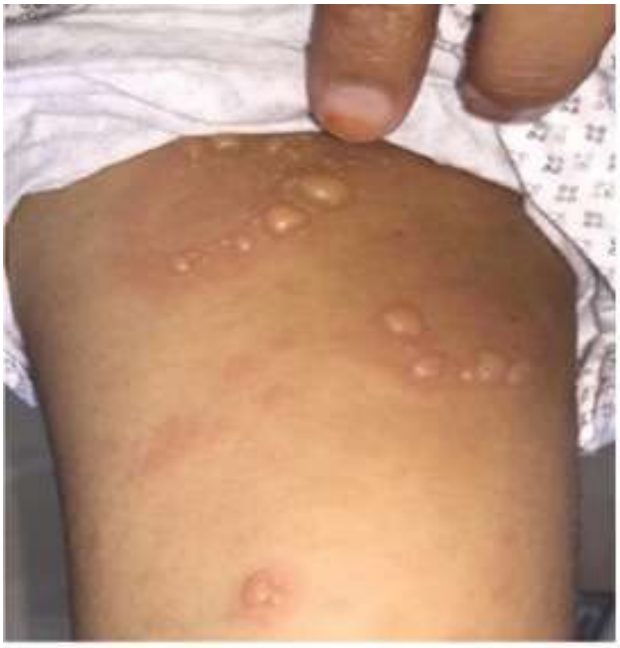


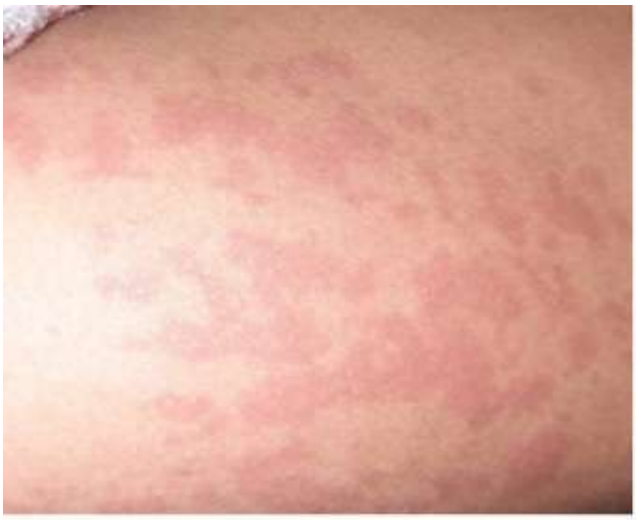
Figure 3: *Vesicular rash in Herpes Simplex*

Eye finding is generally unilateral non-granulomatous in acute cases and granulomatous in chronic cases. Acute retinal necrosis is also a complication.

Differential of autoinflammatory diseases should be considered if associated with consanguinity, early onset, persistent or recurrent rashes (Figure 4A,B) and failure to thrive.

Systemic Lupus Erythematosus (SLE) and Other Connective Tissue Diseases

Malar or discoid rash, photosensitivity, and painless oral palatal ulcers are classic (Figure 5A,B).



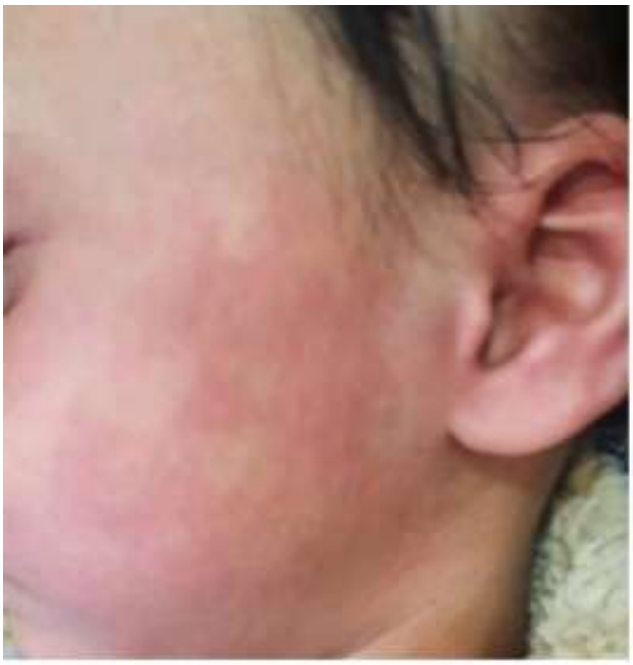


Figure 4A,B: *Rashes in autoinflammatory disease*

Figure 5A: *Malar photosensitive rash*

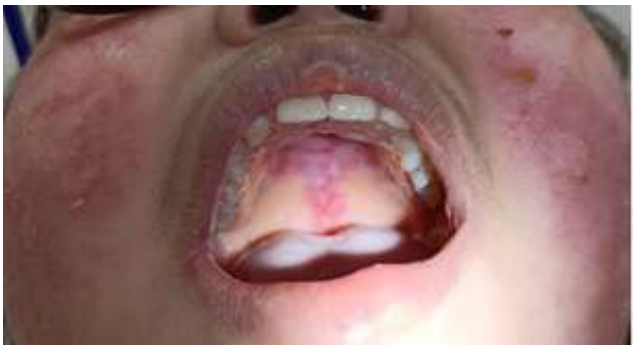


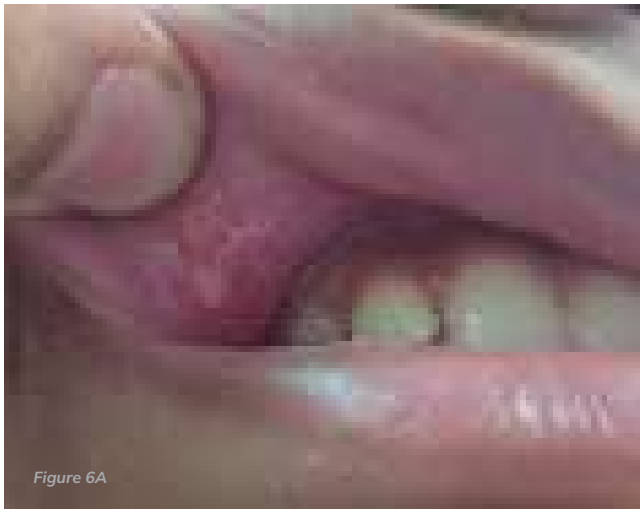
Figure 5B: *Palatal Rash*

Ophthalmic manifestations can include keratoconjunctivitis sicca, scleritis, episcl eritis, lupus retinopathy, choroidopathy, and optic neuropathy.

3. Oral and Genital Ulcers:

Bechet's Disease

Recurrent, painful oral ulcers (Figure 6A) ± genital involvement (Figure 6B); erythema nodosum-like lesions, pathergy positivity.



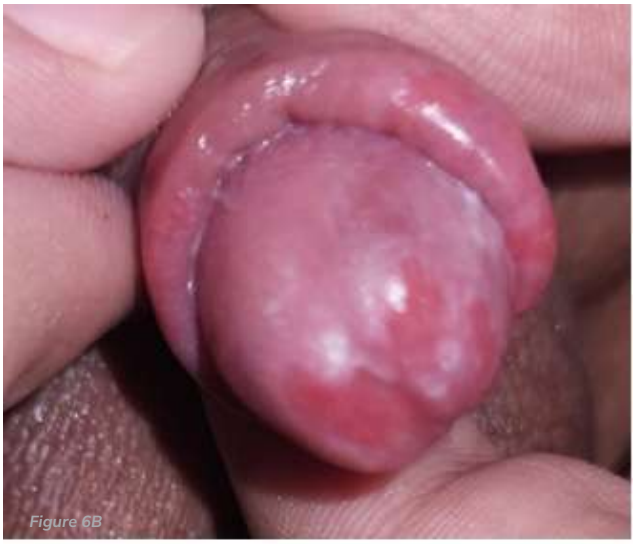


Figure 6A: *Oral and* ***Figure 6B:*** *genital ulcers characteristic of Bechet's disease*

Eye involvement: Scleritis, chorioretinitis, retinal vasculitis, recurrent anterior chamber hypopyon.

Secondary glaucoma can occur due to recurrent inflammation.

4. Gastrointestinal Symptoms

Inflammatory Bowel Disease (IBD): Crohn's Disease, Ulcerative Colitis

Chronic abdominal pain, bloody diarrhoea, growth failure.

Maybe associated with spondyloarth ropathy

Ocular manifestations: scleritis, uveitis (anterior, posterior, or panuveitis).

5. Skin Lesions

Psoriatic Arthritis: Scaly plaques (Figure 7) more commonly on nape of neck, scalp, elbows and trunk, nail pitting (Figure 8)

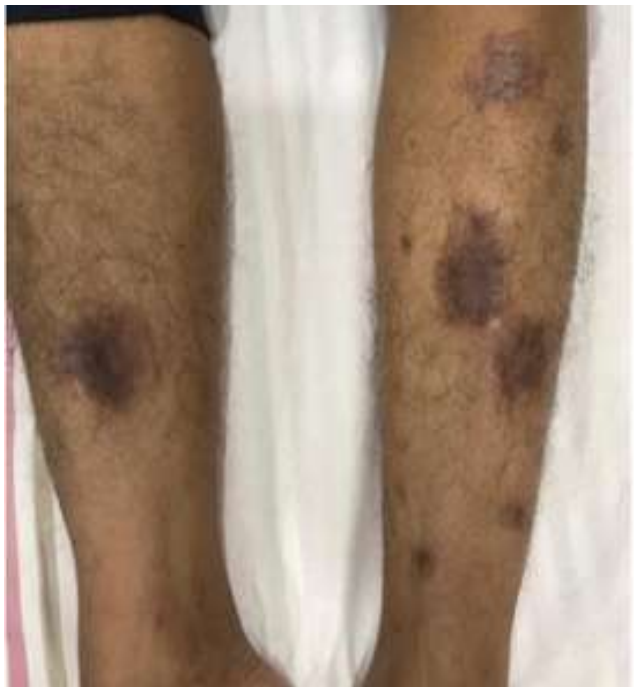


Figure 7: *Psoriatic dry scaly rashes on lower legs*

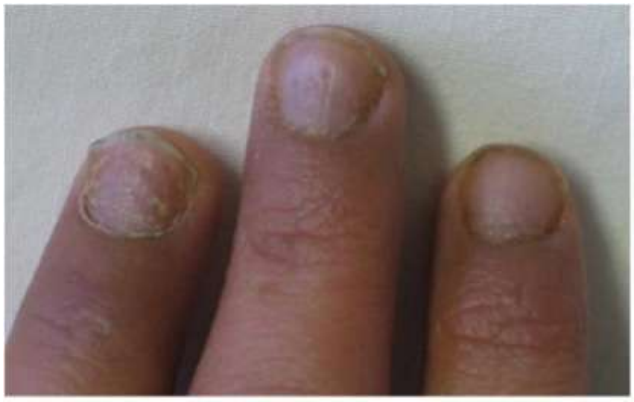


Figure 8: *Nail pitting*

Ocular manifestations: keratoconjunctivitis sicca, blepharitis, redness, light sensitivity, uveitis.

Dermatomyositis:

Heliotrope rash (violaceous discoloration of the eyelids) (Figure 9A,B), Gottron's papules (Figure 10) and calcinotic nodules (Figure 11).

Ocular manifestation: conjunctival edema, ptosis, chemosis, exophthalmos, iritis, conjunctival pseudo polyposis, and in rare cases retinopathy

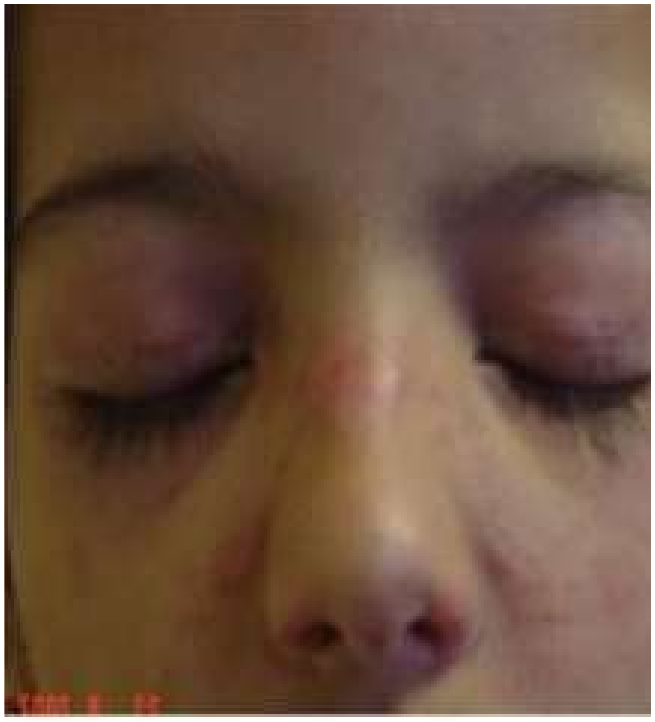


Figure 9A: *Heliotrope rash*

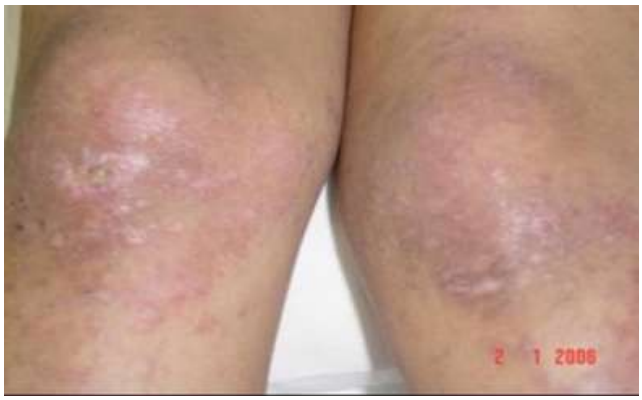


Figure 9B: *rash over knees*

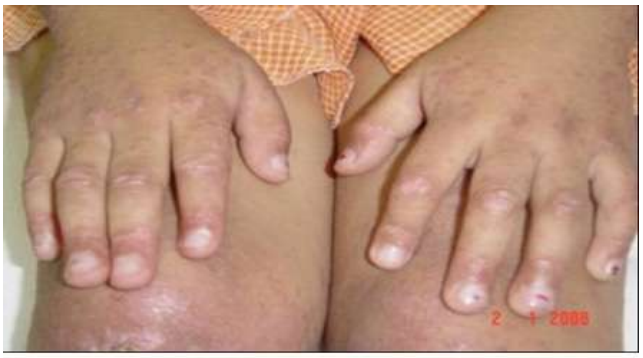


Figure 10: *Gottrons papules over dorsum of hands*

Figure 11: *Calcinosis over the index finger*

Sarcoidosis / Blau Syndrome (monogenic early onset sarcoidosis):

Triad of uveitis (mostly anterior), arthritis (mostly boggy knee and wrist), and skin lesions (granulomatous dermatitis) (Figure 12A-C).

Figure 12A: *Sago like granular rash on the back*

Figure 12B: *Boggy joints*

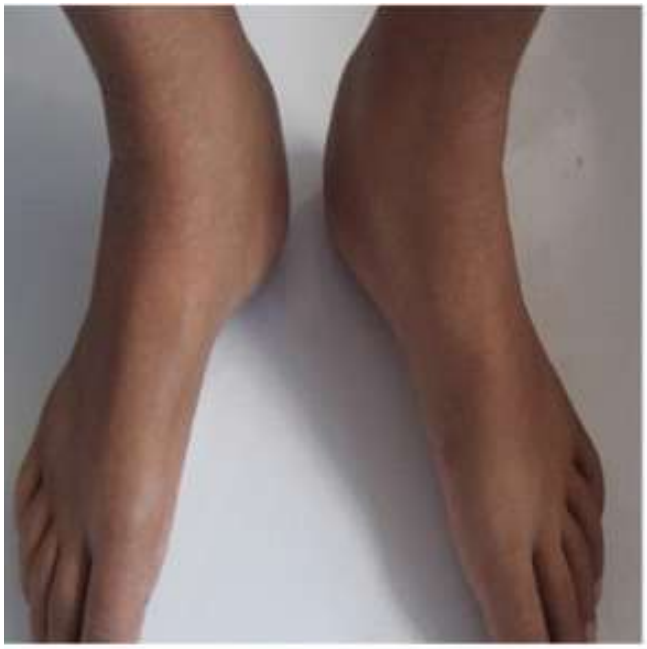


Figure 12C: *Boggy joints*

Neurological Symptoms

Vogt-Koyanagi-Harada (VKH): Headache, neck stiffness, tinnitus, poliosis, alopecia, typically bilateral granulomatous uveitis.

Neuro-Bechet's: Meningoencephalitis, cranial nerve palsies, or behavioural changes.

6. Growth Retardation / Failure to Thrive

Chronic Inflammatory Conditions (e.g., IBD, Blau syndrome, Sarcoidosis): Ongoing inflammation can stunt growth if untreated.

7.Lymphadenopathy,Hepatosplenomegaly and/or joints involvement

Sarcoidosis, Tuberculosis, SLE: May present with these systemic findings. In endemic areas, tuberculosis may account for 5–15% of paediatric uveitis.

8. Recurrent Infections

Primary Immunodeficiencies (e.g., Chronic Granulomatous Disease, CVID): Patients may present with atypical or opportunistic infections plus uveitis.

9. Constitutional Symptoms

Fatigue, weight loss, night sweats suggest possible malignancies (leukemia, lymphoma), granulomatous disease, or chronic infections.

Practical Pointer:
Never ignore a rash, fever, or joint complaint in a child with uveitis. It's often a text message from the immune system!

Step 3: Directed Investigations
Basic Laboratory Tests

CBC, ESR, CRP: - inflammatory markers.
Fecal calprotectin (suspected IBD)

ANA by immunofluorescence, RF: Helpful in JIA, Connective tissue/ lupus spectrum disorders.

Urinalysis: Screen for Tubulointerstitial Nephritis and Uveitis (TINU).
Imaging

Chest X-ray / HRCT Chest: For suspected sarcoidosis or tuberculosis.

MRI Brain: Evaluate VKH, neuro-Behçet's, CNS involvement.

Specific Serologies
HLA-B27 (PCR): Enthesitis-related arthritis, acute anterior uveitis.
HLA B51(Suspected Bechet's)
IGRA / Tuberculin Skin Test: Rule out latent or active TB
Bartonella henselae: Cat-scratch disease
Toxoplasma IgG/IgM: Toxoplasmosis

Practical Pointer:
Tubulointerstitial Nephritis and Uveitis (TINU) may practically have no systemic signs. There may be multiple recurrences of uveitis before the condition is diagnosed. It must be ruled out before labelling the child as 'Idiopathic' uveitis.

Key Learning Points
High Clinical Suspicion
Chronic anterior uveitis may be asymptomatic. Routine screening is crucial, especially in children at high risk (e.g. JIA) and children with ANA positivity.

Tailored Investigations
A systematic, symptom-driven approach is both cost-effective feasible.

Non-Correlation of Eye and Joint Disease
In JIA-associated uveitis, ocular flares can occur even if joints are quiescent.

Early Intervention
Corticosteroids, immunomodulatory therapies, and biologics can prevent severe ocular complications and systemic damage. Delay is the biggest culprit in poor prognosis.

Multidisciplinary Collaboration
Early involvement of rheumatology, infectious disease, and other specialties leads to prompt, accurate diagnosis and better outcomes.

Risk Factors:
More in children with female gender, age under 7years at onset, oligoarticular subtype, and ANA>15U/ml (10-20U/ml is equal to1/80-1/160).

Final Take-Home Message:
In paediatric uveitis, always "think systemic" and collaborate early. The patient's overall health and vision may depend on it.

Suggested Reading:

1. *Chhabra M, Sivakumar M, Gupta V, et al. Spectrum of pediatric uveitis and its impact on vision. Ocul Immunol Inflamm. 2018;26(4):575–582.*
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Top 10 Pearls in the Management of Paediatric Uveitis:

Focus on Surgical interventions, Cataract and Vitrectomy

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1. **Band-shaped Keratopathy (BSK)** is one of the most frequent complications of paediatric uveitis, especially the insidious-onset JIA-associated anterior uveitis. BSK should be scrapped after chelating the calcium with ethylenediaminetetraacetic acid (EDTA) to improve the cornea's clarity and visual acuity. Allow at least two weeks for re-epithelialization of the cornea. Use a bandage contact lens to facilitate it. Phototherapeutic keratectomy is a good alternative for the more precise removal of BSK.

2. **Intravitreal Ozurdex implant:** Administering intravitreal Ozurdex to control intraocular inflammation, especially in paediatric intermediate and posterior uveitis, should be done cautiously. Children have low scleral rigidity, and the scleral track may not close spontaneously, as in adults, resulting in hypotony and cilio-choroidal detachment. Ozurdex implants may lead to the progression of cataracts and a rise in intraocular pressure. Ozurdex implants are contraindicated in eyes that have undergone lensectomy as the implant may migrate into the anterior chamber and damage the cornea. Removal of an Ozurdex implant from the anterior chamber is a herculean task.

3. **Intraocular inflammation** and associated systemic disease must be controlled for at least three months before any surgical procedure in paediatric uveitis. All attempts must be made to make the anterior chamber cell-free. It isn't easy to make the vitreous cavity completely cell-free. The interval before surgery can be shortened if there is no CME or a rapid response or increased if there is a slow response.

4. **Drugs** used to obtain preoperative quiescence can vary from topical corticosteroid drops four times a day in isolated anterior uveitis or Fuchs uveitis starting a week before the surgery to oral corticosteroids for children who have JIA-associated uveitis, intermediate uveitis, panuveitis or granulomatous uveitis. Continue with the immunomodulatory therapy. Some may need intravitreal or periocular corticosteroids. In herpetic uveitis-associated cataracts requiring surgery, antiviral treatment should be started a week before surgery and continued for at least 4 weeks. The use of biological therapy does not seem to have better outcomes than immunosuppressive therapy following cataract surgery.

5. **UBM** is the most critical ancillary investigation in paediatric uveitis-associated cataracts. It will reveal whether the ciliary processes are atrophic, the ciliary body is tractionally detached, or there is a cyclitic membrane, which would rule out phacoemulsification as a procedure of choice.

6. **Intraocular pressure:** Preoperatively, whether the eye is hypotonic or suffering from glaucoma must be determined. Hypotony due to inflammation must be aggressively addressed. Cataract in a quiescent hypotonic eye rules out phacoemulsification.

7. **Severity of Posterior Synechiae:** Phacoemulsification can be done in eyes with minimum or filiform synechiae. The choice of surgery should depend upon the status of IOP and whether there are 360° ring synechiae or broad-based posterior synechiae.

8. **Lensectomy-vitrectomy** is the preferred surgical procedure if there is tractional ciliary detachment, cyclitic membrane or hypotony with ciliary atrophy. Use 5000 cs silicone oil to prevent early emulsification, especially in eyes with ciliary atrophy. Vitrectomy with capsulectomy may be required for fibrotic posterior capsular opacification in eyes having undergone PCIOL implantation.

9. **PC IOL** carries better visual outcomes in eyes with controlled inflammation. Use acrylic hydrophobic IOL for better biocompatibility.

10. **Meticulous and long-term postoperative follow-up** is needed in paediatric uveitis patients undergoing intraocular surgery. Be on the lookout for CME and posterior capsular opacification. Nepafenac and difluprednate use are encouraged to prevent CME and manage postoperative hypotony. There is a high incidence of glaucoma/high IOP in the postoperative period, and it may require a glaucoma surgical procedure. A fibrotic capsular opacification may lead to contraction of the capsular bag with decentration or even displacement of the IOL into the anterior chamber.

Top 10 Pearls in the Management of Paediatric Uveitis: Focus on Non-infectious Uveitis

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1 I feel that in any children with anterior uveitis Juvenile idiopathic arthritis (JIA) associated uveitis should be kept in mind as it is the most common cause of anterior uveitis in children.

2. We all should take a good history of joint swelling, pain, and fever in children with uveitis. Sometimes joint pain may be absent. Pauciarticular types is most commonly associated with Juvenile idiopathic arthritis associated uveitis.

3. One should remember that non-infectious intermediate uveitis, is also common in children. Therefore, examination of anterior vitreous cells, peripheral fundus examination for parsplana exudates and snow banking should be done with scleral depression.

4. Though relatively uncommon in children with non-infectious uveitis Tubulointerstitial Nephritis and Uveitis (TINU) and BLAU syndrome should be kept in mind. We have several cases of TINU in recent years. Urinary beta 2 microglobulin should be estimated in such cases. Blau syndrome should be recognized as they after need biologic therapy. (References. Naik AU, Annamalai R, Biswas J. Uveitis in sporadic Blau syndrome: Long-term follow-up of a refractory case treated successfully with adalimumab. Indian J Ophthalmol 2018; 66:1483-5.

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5. I feel it is quite mandatory in JIA associated uveitis to consult pediatric rheumatologist to find out the systemic association, systemic status and to manage with immunomodulator and biologic agents whenever required.

6. I almost always use Immunomodulators in Juvenile idiopathic arthritis (JIA)-associated uveitis. In non-responsive cases biologic agents like injection adalimumab subcutaneously or infliximab intravenously can be given. Adalimumab is often chosen for convenience for use and is quite effective. We are seeing less cataract, less band shaped keratopathy following usage of injection of Adalimumab.

7. Do not forget to examine the fundus in a case of pediatric uveitis even they are present with anterior uveitis like Juvenile idiopathic arthritis associated uveitis. If necessary optical coherence tomography should be done as cystoid macular edema is quite common in JIA associated uveitis and we have seen few cases of choroidal neovascular membrane formation in JIA associated uveitis.

8. Intraocular lens implantation in JIA associated uveitis is controversial. I have seen patients doing well with lensectomy and vitrectomy and seen several cases of patients with JIA associated uveitis has gone to several complications like secondary glaucoma, phthisis bulbi, and gross hypotony.

9. Please do Rheumatoid factor and antinuclear antibody testing and HLA B27 testing in pediatric non-infectious uveitis. HLA B27 testing is required in cases of Juvenile onset spondyloarthropathy.

10. If you see a hypopyon in a quiet eye rule out diffuse infiltrating retinoblastoma by doing ultrasound biomicroscropy and Bscan ultrasound.

Top 10 Pearls in the Management of Paediatric Uveitis:
Focus on Infectious Uveitis

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Paediatric uveitis cases account for 5-10 % of total uveitis cases, and out of these, the majority are non-infectious. Infectious uveitis accounts for only 25-30 % of paediatric cases.[1]

Eliciting history and clinical examination might be difficult in preverbal and young children. They often present very late, after the uveitic sequelae such as complicated cataract has set in and are usually noted by the parents. It is important to identify these cases early, and manage them appropriately before they cause structural damage.

Infectious uveitis may be of bacterial, viral, parasitic or fungal etiology. It may be a congenitally or postnatally acquired infection.

Unilateral posterior uveitis is the most common presentation in infectious paediatric uveitis.[1]

In studies of paediatric uveitis in India by Babu et al[2] (2024), and Murthy et al[3] (2021), Tuberculosis and Toxoplasmosis were the most common causes of infectious uveitis.

Outlined below are the manifestations and management of few of the common causes of infectious paediatric uveitis.

1.Ocular tuberculosis

Mycobacterium tuberculosis can affect any part of the eye. Similar to adults, posterior uveitis with choroidal involvement is the most common presentation in paediatric ocular tuberculosis. Mycobacterial tuberculosis being an obligate aerobic bacteria prefer highly oxygenated tissues such as the vascular choroid (Figure 1).

It can also present as anterior, intermediate, panuveitis or retinal vasculitis (Figure 2)

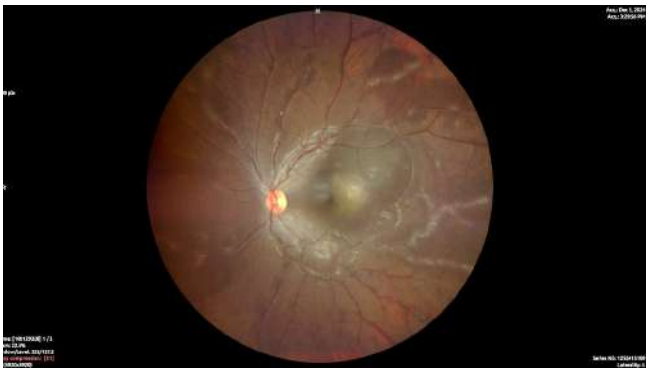

Figure 1. *Choroidal granuloma with associated subretinal fluid in a case of presumed ocular TB*

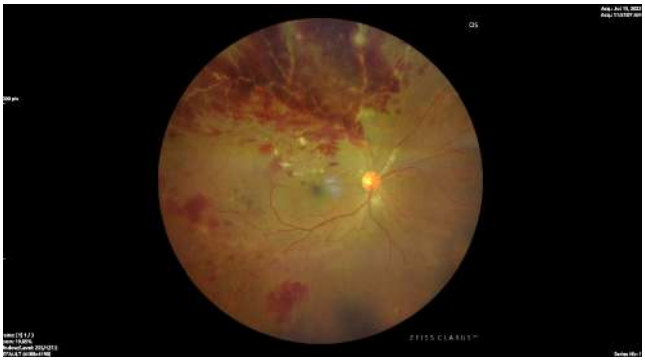

Figure 2*. TB retinal vasculitis*

In developing countries, TB can also present in children as anterior uveitis with BSK mimicking JIA related uveitis. It is important to keep a high index of suspicion and make an etiological differentiation, as treatment is vastly different for the two entities. Mutton fat keratic precipitates, Koeppe's and Busacca's nodules and broad based posterior synechiae are more in favour of a tuberculous uveitis.

Orbital TB is also more common in children compared to adults. Clinical features include painful proptosis with lid swelling, mechanical ptosis or a draining sinus with low grade fever.[4]

Investigations required are Mantoux testing along with chest radiography, preferably CT chest to look for evidence of active / old TB as well as routine testing including complete blood count, VDRL (Venereal Disease Research Laboratory), TPHA (Treponema Pallidum Haemagglutination Assay) and HIV.

Look for evidence of healed cold abscesses on the body, which mostly represents healed TB lymphadenopathy. Proper history should also be elicited from the parents about any prominent lumps / swellings which they might have noticed on the body of the child (Figure 3 A-C).

Figure 3A. *Cervical cold abscess in a patient with ocular TB with*

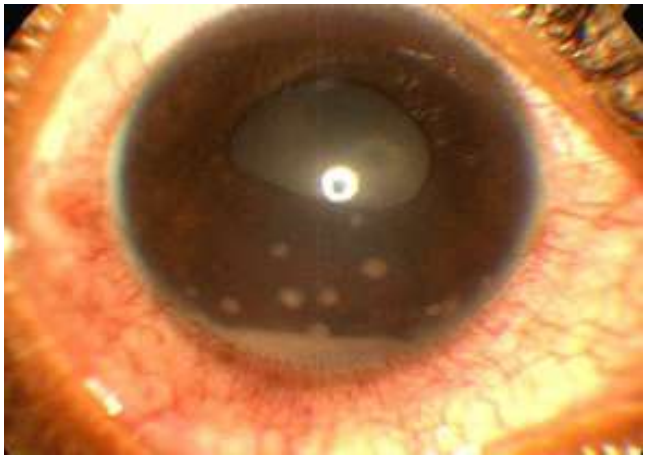

Figure 3B*. granulomatous KPs and pigmented hypopyon*

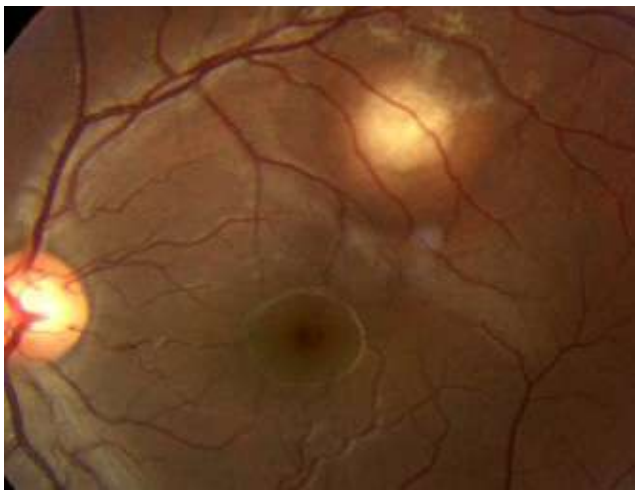

***Figure 3C**. choroidal granuloma*

Treatment- comprises of antituberculous treatment (ATT), as per body weight for 6-9 months, along with oral steroids. In children, inflammatory response may be more severe and adequate suppression with oral steroids or occasionally immunosuppressants may be required in few cases.

2. Ocular Toxoplasmosis

Toxoplasmosis in children can be either congenitally acquired (transplacental transmission) or acquired postnatally (due to contact with contaminated soil containing cat faeces with infective oocysts).

Disease acquired during first trimester will have more severe manifestations[5] including systemic features, which can present with the classic triad of retinochoroiditis lesion, cerebral calcification and seizures, and even result in intrauterine growth retardation or spontaneous abortion. Congenital toxoplasmosis mostly is seen as an atrophic hyperpigmented scar at the macula, with a "wagon wheel" appearance. Children infected during the third trimester often have minimal symptoms, but 80% develop ocular sequelae during their second or third decades of life, when the tissue cysts rupture and release bradyzoites and tachyzoites.

The typical toxoplasmosis lesion appears as a focal necrotising retinochoroiditis with associated dense vitritis, mostly adjacent to a chorioretinal scar (Figure 4). Absence of scarring suggests acquired disease. The retinochoroiditis lesion may also be accompanied by neuroretinitis, papillitis and retinal vasculitis.

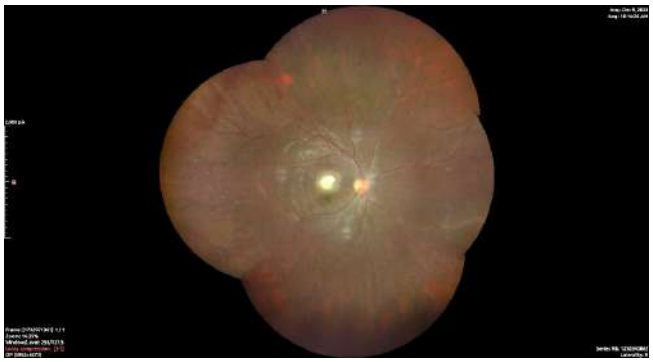

***Figure 4**. Ocular toxoplasmosis- focal necrotising retinochoroiditis lesion adjacent to a chorioretinal scar*

Anterior chamber spillover can occur in severe cases with granulomatous anterior uveitis which can be associated with high intraocular pressure.

Management: Diagnosis is mostly clinical and indications for treatment are same as in adults and include optic nerve head involvement, posterior pole involvement, immunocompromised patients, dense vitreous opacities, or lesions larger than 3-disc diameters. The combination of trimethoprim and sulfamethoxazole is effective in preventing recurrences. Azithromycin is effective against both tachyzoites and dormant tissue cysts. Triple therapy with Trimethoprim-Sulfamethoxazole, Azithromycin along with oral steroids is ideal for treating ocular toxoplasmosis.

3. Viral

Herpes simplex and Varicella zoster virus are the common etiologies of viral uveitis in children. Paediatric herpetic uveitis can often present with atypical features like hypopyon in white eye, apart from their usual presentation of keratouveitis and granulomatous uveitis.[6] Acute retinal necrosis is a very severe form of viral uveitis which can affect healthy as well as immunocompromised children, due to reactivation of neonatal herpes infection predominantly HSV -2. Patients will present with necrotizing retinitis lesion in the periphery, occlusive vasculopathy and vitritis.

Cytomegalovirus (CMV) affects immunocom promised children and could be transmitted congenitally or postnatally. Microcephaly, sensorineural hearing loss, thrombocytopenic purpura and hepatosplenomegaly are some of the other features of systemic CMV infection.[1]

PCR analysis of aqueous or vitreous sample is very useful in diagnosing the pathogen. Topical steroids, topical 0.15 % ganciclovir with oral valacyclovir in the dosage of 20mg/kg thrice daily is advised and slowly tapered until complete resolution of the infection.

Frosted branch angiitis is a type of immune mediated reaction characterized by diffuse retinal vasculitis with perivascular exudation and are often associated with infections like CMV, HSV, HZV, Epstein-Barr virus and rubella. These children require systemic corticosteroid treatment along with antimicrobial agents. We should also rule out other non-infectious etiologies for the same which includes SLE, Behcet's, sarcoidosis and masquerade.

Dengue and Chikungunya are some of the other etiologies of viral uveitis reported to have caused anterior uveitis in children. Intraocular steroids are generally avoided in any case of a suspected viral uveitis.

4. Endogenous endophthalmitis

The incidence of Endogenous endoph thalmitis in paediatric population in our country has been reported to be 28%, owing to generalized malnutrition and are often missed because of late presentation and absence of systemic features like fever or diarrhoea[7]. Sudden painful loss of vision associated with lid edema, chemosis, severe anterior segment inflammation, vitreous exudates, and increased retinochoroidal thickness in ultrasound should raise suspicion towards endophthalmitis. Blood cultures could be negative in most of the cases because of excessive use of antibiotics. Fungal etiology is suspected in severely immunocompromised children like prematurity, neutropenia, children who are on immunosuppressive treatment and post organ transplantation surgery. *Pseudomonas aeruginosa, Neisseria meningitides* and Gram-positive bacteria like Streptococcus are the most common etiologies of bacterial endophthalmitis. Candida and Aspergillus are the usual fungal infections reported. Patients can present with white fluffy retinal lesions with vitreous snow ball like lesions. Early recognition, intravenous antibiotics, intravitreal antibiotics followed by vitrectomy with or without lensectomy has been helpful in recovering useful visual outcomes. Vitrectomy also helps in removing the pathogen and its toxins along with better penetration of antibiotics. Vancomycin, Ceftazidime and Voriconazole are the preferred intravitreal antimicrobial agents.

5. Ocular toxocariasis

Ocular toxocariasis can be caused due to *Toxocara canis* or *Toxocara cati*, and usually affects children between 5-10 years of age, who are infected by ingestion of infective eggs while playing in the soil or from contact with affected animals, especially puppies.

The 3 major ocular presentations include posterior pole granuloma, peripheral granuloma and a diffuse endophthalmitis like picture. The ocular symptoms include unilateral blurred vision, squint, leukocoria and red eye.

Management: Diagnosis is again clinical, and treatment includes antihelminthics like albendazole along with oral steroids. B scan ultrasonography can be used to rule out calcifications and differentiate a Toxocara granuloma from a more ominous retinoblastoma lesion.[8]

6.Diffuse unilateral subacute neuroretinitis (DUSN)

DUSN is mostly caused by mobile nematodes such as *Baylisascaris procyonis* and *Ancylostoma caninum*. It can affect healthy children and young adults. It is mostly unilateral and presents with multiple yellowish or grayish white retinal lesions with associated vitritis, papillitis and retinal vasculitis (Figure 5). The worm may or may not be clinically seen.

Figure 5. *Diffuse unilateral subacute neuroretinitis*

Late-stage features include optic disc atrophy, vessel attenuation and subretinal tracks and has a poor prognosis

Management-Diagnosis is based on either visualisation of the worm or on the typical clinical picture. If the worm is visible, direct laser photocoagulation can be done. Otherwise, anthelminthics (such as albendazole) along with high dose oral steroids (for anti inflammatory effect) is the mainstay of treatment.

7. Trematode granuloma

Trematode granuloma is a parasitic infection caused by the worm Procerovum Varium which are inhabitants of conjuctival sac of herons, with the snail being the intermediate host and humans, an accidental host. Children get infected when they swim in cercariae infested water which are generally released in large number by snails. The granulomatous reaction could be due to direct inoculation of the parasite or secondary to inflammatory reaction.[9]

The clinical features include anterior chamber (Figure 6) or subconjunctival granuloma, retrocorneal membrane, granulomatous anterior uveitis, chalazion-like lesion in the eyelid, peripheral anterior synechiae and cataract. Systemic manifestations include inflamed buccal and genital mucosa.

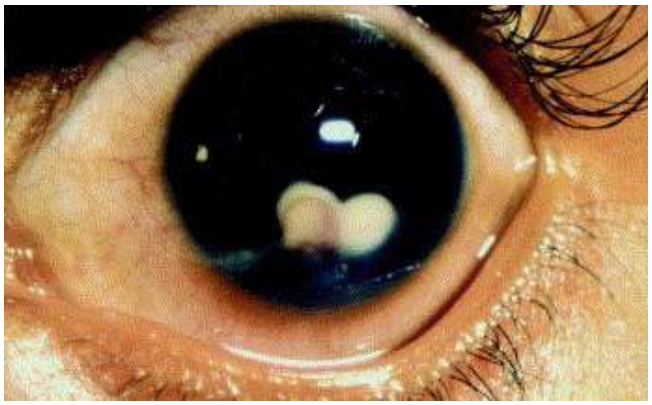

***Figure 6**. Anterior chamber granuloma secondary to trematode infestation*

Ultrasound biomicroscopy is a useful diagnostic tool to assess the extent of the lesion. Lesions less than 3mm in size are treated with topical and oral steroids. Greater than 3mm lesions are excised in toto and are sent for histopathological examination and real-time PCR/molecular diagnostics. Histopathology reveals fragments of the parasite, macrophages, neutrophils, multinucleated giant cells and eosinophilic infiltration. Public health awareness in and around the areas of contaminated water bodies goes a long way in preventing trematode infections.

8. Ocular cysticercosis

Cysticercosis is caused by *Cysticercus cellulosae*, the larva of porcine Taenia Solium. Ocular symptoms can be seen in up to 46 percent patients.

Clinical presentation varies depending on the location of the cyst. It is most commonly situated in the orbital region, causing altered ocular movements, diplopia or squint. In case of a subretinal or vitreous cyst, patient can manifest with a panuveitis like picture with associated retinal detachment and vitreous haemorrhage[10].

Management- Surgical removal of the cyst unruptured is preferred compared to antiparasitic drugs, as death of the parasite can trigger a severe inflammatory reaction resulting in severe visual morbidity.

9. Ocular syphilis

In children, ocular syphilis is mostly congenitally acquired, caused by transplacental transmission during pregnancy or, less commonly, by contact with infected maternal skin lesions during birth. In congenital syphilis, choroiditis with a salt and pepper fundus, bilateral cataract and granulomatous uveitis have been described. Interstitial keratitis has also been reported with congenital syphilis.

Management- Diagnosis is using Treponemal (TPHA-Treponema Pallidum Haemagglutination Assay) and non-treponemal (VDRL-Venereal Disease Research Laboratory) tests and as in adults requires treatment with intravenous penicillin.

10. Monitoring children with infectious uveitis

Children with infectious uveitis must be frequently monitored till resolution of the lesion and thereafter at much longer intervals, to look for any recurrence of infection, especially in immunocompromised children. As children are mostly not cooperative for a detailed fundus examination using indirect ophthalmoscopy, wide field fundus photography can be utilised to visualise the posterior segment. Intraocular pressure must be recorded at each visit, as children are more prone to develop steroid induced glaucoma.

Compliance to treatment, both topical and oral medication should be stressed to the parents every visit, especially in cases requiring long term antimicrobial regimen as ocular TB.

When required, a paediatrician opinion may be sought to rule out extraocular manifestations of the ocular infection.

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Juvenile Idiopathic Arthritis (JIA): A Snapshot

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Paediatric uveitis accounts for 5–10% of all uveitis cases, but its management remains extremely challenging.[1] Despite the seemingly smaller proportion, the visual impact of uveitis in this group is significant and probably underestimated. JIA is the most significant non-infectious cause of uveitis in children. It encompasses a group of idiopathic arthritides that manifest before the age of 16 years and persist for at least six weeks. JIA-associated uveitis often follows a chronic course with minimal conjunctival congestion or overt symptoms, leading to frequent misdiagnosis or delayed recognition. In many cases, it is erroneously treated as allergic conjunctivitis, only to present later with significant visual impairment. Due to its subtle symptoms, chronic nature and potential for severe vision loss, JIA-associated uveitis can be considered the 'silent thief of vision'. This short write-up provides a concise overview of the clinical phenotypes, systemic features, with a particular focus on recent advancements in its treatment. Our literature review is summarized through multiple tables, offering a quick and accessible reference on the topic.

Epidemiology

While there are several clinical studies on JIA have been published from India, studies aiming to estimate incidence or prevalence of the condition is rare. One study estimated the prevalence of JIA in Indian children to be 48 per 100,000.[2] Among the subtypes of JIA, enthesitis-related arthritis (ERA) is the most common JIA subtype in India.[3] One study indicated that ERA comprised 35.7% of JIA cases. Another study found ERA to be the predominant subtype (65.5%), followed by systemic-onset JIA (11.7%).[4]

Various case series have reported the prevalence of JIA among paediatric uveitis cases, along with the proportion of anterior uveitis in these patients

Table 1: Prevalence of Juvenile Idiopathic Arthritis in Various Retrospective Case Series from India

Author name	% of Total Cases of Uveitis	% of Total Cases of Anterior Uveitis
Venkatesh et al (2015)	6.66%	42.14%
Das et al (2009)	NA	47.07
Biswas et al (1996)	2%	39%
Das et al (1995)	1.50%	36.50%
Singh et at (2004)	3.30%	49.23%
Pandurangan et al (2022)	0.70%	23.40%
Tyagi et al (2022)	NA	38.14%
Rathinam and Namperumalsamy (2007)	1.80%	57.40%
Dogra et al (2016)	3.03%	43.04%
Sabhapandit et al (2016)	0.50%	47.28%
Biswas et al (2018)	NA	35.22%
Borde et al (2020)	2.85%	47.14%

However, most of these studies originate from tertiary eye care centers, reflecting a referral-based pattern rather than a true representation of JIA prevalence at the community level in a vast country like India. Consequently, an accurate estimate of JIA-associated uveitis in the general population remains uncertain. Over time, there has been a noticeable increase in the reported cases of JIA-associated uveitis, reflecting relatively improved awareness and diagnostic capabilities with better ophthalmologist-rheumatologist coordination. Earlier studies from the 1990s reported that JIA accounted for 2% of total uveitis cases, contributing to 39% of anterior uveitis cases..[5] Rathinam et al. found that JIA constituted 1.8% of all uveitis cases, with JIA responsible for 57.4% of anterior uveitis cases.[6] More recent studies indicate an upward trend in the proportion of JIA-related uveitis. Venkatesh et al. reported that JIA made up 6.6% of total uveitis cases, with JIA contributing to 42.1% of anterior uveitis cases.[7] Singh et al. found that JIA accounted for 3.3% of total uveitis cases, with the highest proportion of anterior uveitis cases at 49.23%.[8] Dogra et al. reported that JIA constituted 3.03% of total uveitis cases, with 43.04% of anterior uveitis cases attributed to JIA in their case series.[9] Meanwhile, Sabhapandit et al. observed the lowest proportion, with JIA comprising 0.5% of total uveitis cases, while still contributing to 47.28% of anterior uveitis cases.[10]

Clinical Features

Ocular involvement in JIA is typically bilateral, though one eye may be affected earlier, making asymmetric presentation common in these children. These patients are often asymptomatic, especially in the early stages of ocular involvement.

Uveitis in JIA is usually chronic, non-granulomatous anterior uveitis. (Figure 1A) A mild to moderate degree of fine anterior chamber cellular reaction can be observed, with or without fine non-granulomatous keratic precipitates (Figure 1C). In contrast, children with ERA, who usually test positive for HLA-B27, present with acute anterior uveitis and symptomatic, painful red eyes, along with a moderate to severe anterior chamber reaction, with or without hypopyon (Figure 1D). In the majority of cases, presentation is delayed and often associated with ocular complications of JIA-associated uveitis, such as extensive posterior synechiae, band-shaped keratopathy, complicated cataract (Figure 1B), or secondary glaucoma.

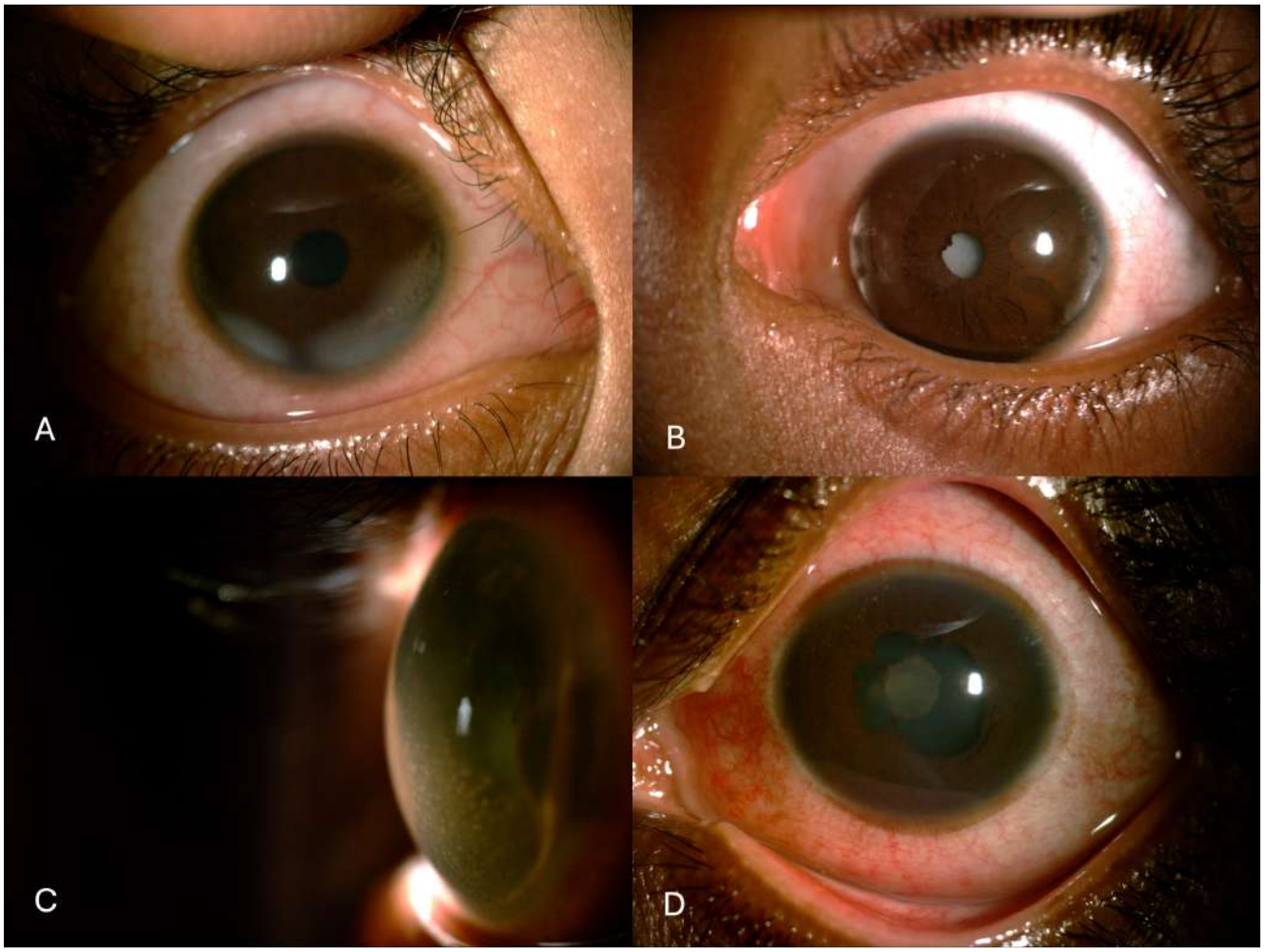

Figure 1A. *Uveitis in Juvenile Idiopathic Arthritis is usually chronic, non-granulomatous anterior uveitis, often presenting with band shaped keratopathy.*

Figure 1B. *Often the child present late with complications such as cataract*

Figure 1C*. A mild to moderate degree of fine anterior chamber cellular reaction can be observed, with fine non-granulomatous keratic precipitates.*

Figure 1D. *Children with Enthesitis-related arthritis, who usually test positive for HLA-B27, present with acute anterior uveitis with a moderate to severe anterior chamber fibrinous reaction*

Joint pain is a key systemic feature of JIA. One significant characteristic of this joint pain is its association with morning stiffness, possibly due to circadian variations in cytokines (especially IL-6) and other chemokines that mediate the pathological process of the disease. The pattern and extent of joint involvement in JIA vary widely, and affected children may exhibit various other systemic features. It is important to recognize that JIA is an umbrella term encompassing seven distinct categories, classified based on clinical features present within the first six months of illness. The current definition and classification of JIA have been established by the International League of Associations for Rheumatology (ILAR). Ophthalmologists must be aware of the various systemic features of JIA.

Table 2: Overview of the epidemiological and systemic features of the seven categories of Juvenile Idiopathic Arthritis, established by the International League of Associations for Rheumatology (ILAR)

Categories of JIA	F: M	Systemic Involvement	Uveitis	Laboratory
Systemic Arthritis	1:1	Arthritis in one or more joints Fever of at least 2 weeks and daily quotidian at least 3 days One or more of: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly, and/or splenomegaly, serositis	—	—
Oligoarthritis	3:1	1–4 joints during the first 6 months of disease	Chronic asymptomatic	High positive ANA
Rheumatoid Factor- Positive Polyarthritis	4:1	5 or more joints during first 6 months of disease	—	Two or more positive RF at least 3 months apart
Rheumatoid Factor- Negative Polyarthritis	3:1	5 or more joints during first 6 months of disease	Chronic asymptomatic	RF Negative
Enthesitis-Related Arthritis	1: 4	Arthritis and enthesitis or or Arthritis or enthesitis and at least two of: sacroiliac joint tenderness and/ or inflammatory lumbosacral pain; presence of HLA-B27antigen; onset of arthritis in a boy older than 6 years; acute symptomatic anterior uveitis; History of ankylosing spondylitis or enthesis related arthritis or sacroiliitis with inflammatory bowel disease or Reiter syndrome or anterior uveitis in a first degree relative	Acute Symptomatic	HLA B27 positivity
Juvenile Psoriatic Arthritis	2:1	Psoriasis and arthritis or Arthritis and at least two of: dactylitis, nail pitting or onycholysis, psoriasis in a first degree relative	Chronic Asymptomatic or Acute Symptomatic	—
Undifferentiated Arthritis	—	Arthritis that does not fulfil criteria in no other category or more than one of above categories	—	—

Table 3: German (The German version of the Juvenile Arthritis Multidimensional Assessment Report) and United State (2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis) guidelines on Screening of Children with Juvenile Idiopathic Arthritis

Types of JIA	ANA	JIA onset	Duration	Screening interval as per German guidelines	Screening interval as per US Guidelines
OA, RF- PA, PsA, UA	Positive	≤6 years	≤4 years	3 months	3 months
OA, RF- PA, PsA, UA	Positive	≤6 years	>4 years	6 months	6-12 months
OA, RF- PA, PsA, UA	Positive	≤6 years	≥7 years	12 months	6-12 months

OA, RF- PA, PsA, UA	Positive	>6 years	≤2 years	6 months	6-12 months
OA, RF- PA, PsA, UA	Positive	>6 years	>2 years	12 months	6-12 months
OA, RF- PA, PsA, UA	__	≤ 6 years	≤4 years	6 months	6-12 months
OA, RF- PA, PsA, UA	__	≤ 6 years	>4 years	12 months	6-12 months
OA, RF- PA, PsA, UA	__	>6 years	Not Available	12 months	6-12 months
ERA, RF+ PA, SA	Not Available	Not Available	Not Available	12 months	6-12 months

[OA= oligoarthritis, RF-PA = Rheumatoid factor positive Arthritis, PsA = Psoriatic Arthritis, UA = Undifferentiated arthritis, ERA = Enthesitis-related arthritis, SA = Systemic Arthritis]

provides an overview of the epidemiological and systemic features of the seven JIA categories. The Paediatric Rheumatology International Trials Organization (PRINTO) is working to revise the ILAR classification system for JIA to create more homogenous subgroups of the disease and align with classification methods for adult rheumatic diseases.[11]

Systemic features of ILAR subtypes of JIA associated with higher risk of uveitis

Among various categories of JIA, the risk of uveitis is higher in children with oligoarthritis, rheumatoid factor (RF)-negative polyarthritis, Psoriatic JIA, and ERA. Various guidelines are aimed at screening these categories of JIA. While German and US guidelines put emphasis on ILAR categorization of JIA, antinuclear positivity, the age of the onset of the disease and duration of JIA, the UK guidelines are slightly different.[12,13] According to UK guidelines, screening should be conducted every two months for the first six months after arthritis onset, followed by screenings every 3–4 months for the recommended duration. If immunosuppressive therapy is discontinued, screening should resume at two-month intervals for six months before returning to the previous schedule. While the risk of uveitis is minimal in systemic JIA and RF-positive polyarticular JIA, an initial screening may still be necessary. It is important to note that even with adherence to scheduled screening in these countries, more than 50% of children with JIA-associated uveitis still develop complications such as cataract, glaucoma, and posterior synechiae. Therefore, more frequent screening—at intervals shorter than three months—may be required for children at higher risk of vision impairment. Furthermore, if active uveitis or signs of previous ocular inflammation are detected, examination intervals should be further reduced to ensure close monitoring.[14,15]

Oligoarthritis: This JIA subtype is defined by the involvement of one to four joints within the first six months of disease onset, primarily affecting the large joints of the lower limbs. Oligoarticular JIA typically begins between the ages of 2 and 4 years, with a female-to-male ratio of 3:1. In nearly half of the cases, it presents as monoarticular arthritis, often asymmetrical. Usually one or two large joints of lower extremities are involved, with the knee the most commonly affected; followed by the ankle, wrist, and elbow (Figure 2).

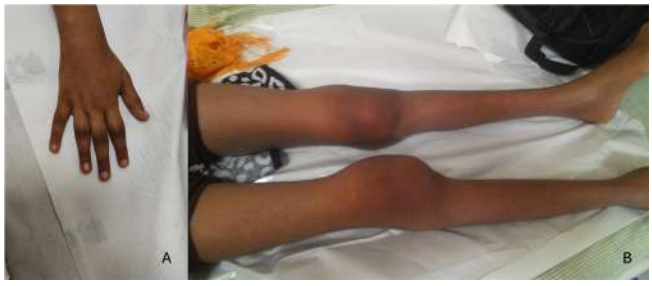

Figure 2: *Joint involvement in children with Juvenile Idiopathic Arthritis*

The small joints of the hands and feet are affected in a smaller proportion of cases. Constitutional and systemic symptoms are rare in this subtype, and if present, they should warrant reconsideration of the initial diagnosis of oligoarthritis. Risk factors for uveitis in oligoarthritis and RF-negative polyarthritis include early disease onset, positive ANA, and a shorter duration of illness. ANA positivity is detected in up to 95% of children with oligoarticular JIA and

this prevalence of ANA positivity is notably higher in girls with early-onset disease.

Rheumatoid Factor (RF)-negative Polyarthritis: This subtype of JIA is defined by the involvement of five or more joints within the first six months of disease onset, while excluding cases with systemic arthritis, psoriasis, males who are HLA-B27 positive with arthritis onset after age six, and those with rheumatoid factor (IgM) detected in two separate tests taken three months apart. It predominantly affects girls more than boys, with a female-to-male ratio ranging from 2:1 to 4:1. The arthritis can be asymmetrical and often involves the small joints of the hands and feet, as well as the cervical spine and temporomandibular joints. Larger joints, including the hips, shoulders, knees, wrists, and ankles, may also be affected. RF-negative polyarticular JIA is sometimes associated with systemic symptoms such as low-grade fever, fatigue, poor growth, weight loss, elevated acute-phase reactants, mild anaemia, and ANA positivity, which is observed in up to 50% of cases.

Psoriatic JIA: Psoriatic JIA is defined as juvenile-onset arthritis occurring in the presence of psoriasis or at least two of the following minor criteria: nail pits/ onycholysis, dactylitis, or a first-degree family history of psoriasis. It accounts for 2% to 5% of all JIA cases, with a slight female predominance and a bimodal age of onset, typically between 2 to 4 years and 10 to 12 years. In most cases, skin symptoms appear after arthritis, with psoriasis usually developing within two years of arthritis onset. Skin lesions are characterized by well-demarcated, erythematous, scaly patches found on extensor surfaces such as the elbows, knees, scalp, and trunk. In children under two years old, psoriatic diaper rash is a common presentation. Psoriatic JIA does not follow a specific pattern of joint involvement and can resemble either oligoarthritis or polyarthritis, though the majority of affected children present with an oligoarticular onset (involving fewer than five joints). The most common nail sign in psoriasis and psoriatic arthritis is nail pitting, which appears as superficial depressions in the nail plate due to inflammation of the proximal nail matrix. Onycholysis, or separation of the nail plate from the nail bed, typically begins at the tip and progresses proximally. Dactylitis, also known as “sausage finger,” is characterized by severe inflammation of the fingers, causing them to swell and take on a sausage-like appearance.

Enthesitis-related arthritis: ERA is characterized by inflammation at the entheses, which are the sites where tendons and ligaments attach to bones. It is considered the paediatric counterpart of adult spondyloarthropathy. However, unlike adult spondyloarthropathy, ERA typically presents with peripheral joint involvement and enthesitis, while axial involvement tends to appear as a later feature. Pain and swelling at the entheses, commonly affecting areas such as the heel (Achilles tendon), knees, hips, and lower back is noted in ERA.

Differential Diagnoses

Several conditions can mimic JIA associated uveitis. The Standardization of Uveitis Nomenclature (SUN) Working Group recommends ruling out certain conditions before reaching a diagnosis JIA-associated chronic uveitis.[16] A positive serologic test for syphilis using a treponemal test should be excluded. Additionally, evidence of sarcoidosis, such as bilateral hilar adenopathy on chest imaging or a tissue biopsy demonstrating noncaseating granulomas, need to be excluded. Other granulomatous diseases, including familial juvenile systemic granulomatosis, should also be ruled out. Furthermore, an aqueous specimen PCR positive for cytomegalovirus (CMV), herpes simplex virus (HSV), or varicella-zoster virus (VZV) indicates an alternative diagnosis and should be investigated accordingly. Two conditions that may impose serious challenge in the diagnosis of JIA are discussed here:

Blau Syndrome/Early Onset Sarcoidosis: Blau syndrome and early-onset sarcoidosis (EOS) can sometimes be mistaken for JIA due to overlapping symptoms; however, they are distinct conditions. Familial cases are referred to as Blau syndrome, while sporadic cases are classified as EOS. A mutation in the NOD2 gene is responsible for both conditions and serves as a confirmatory test to differentiate them from

JIA. They typically present before the age of five and are characterized by a classic triad of skin rash, arthritis, and uveitis. A history of intermittent fever may also be observed. A key pathological feature is the presence of noncaseating granulomas in affected tissues. Lymphocytic emperipolesis within multinucleated giant cells is a distinctive characteristic of Blau syndrome granulomas, which are typically surrounded by a dense lymphocytic corona. Unlike sarcoidosis, lung involvement is rare in Blau syndrome.

Sarcoidosis: Sarcoidosis is rare in children, but can occur. Presentation is typically granulomatous anterior uveitis, though nongranulomatous anterior uveitis can occur. Posterior segment involvement is common in ocular sarcoidosis and periphlebitis with exudation, optic swelling, choroidal granuloma can be seen. Children with sarcoidosis can often present with constitutional symptoms (e.g. fatigue) and pulmonary involvement. Extrapulmonary manifestations can include musculoskeletal, and dermatologic involvement.

Laboratory Investigations:

JIA is diagnosed primarily through clinical evaluation, necessitating thorough ocular and systemic examinations by an ophthalmologist and rheumatologist. While the diagnosis is clinical, certain inflammatory markers can provide supportive evidence, including elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, as well as leukocyte and platelet counts. ANA are often associated with oligoarthritis and a heightened risk of anterior uveitis. Although rheumatoid factor (RF) is not diagnostically definitive, it can be valuable in classifying children with polyarthritis. In patients presenting with granulomatous anterior uveitis, tuberculin sensitivity testing, interferon-gamma release assays, and serum angiotensin-converting enzyme (ACE) levels can aid in excluding tuberculosis and sarcoidosis. While sarcoidosis may involve the joints, the presence of ANA and the characteristic pattern of joint involvement typically suggest a diagnosis of JIA. However, it's important to note that a significant proportion (29%) of patients with biopsy-confirmed sarcoidosis have been reported to exhibit positive ANA titres.[17] Detection of NOD2 gene mutation can be a valuable test in differentiating children with suspected Blau Syndrome/ Early Onset Sarcoidosis.

Certain biomarkers in JIA have been associated with the risk of developing uveitis. In patients with oligoarticular and polyarticular JIA, a high ESR is considered a predictor of uveitis risk.[18] Elevated levels of the proinflammatory protein S100A12 (calgranulin C), a calcium-binding protein primarily produced by granulocytes, have been associated with a higher likelihood of uveitis when levels reach ≥250 ng/ml at disease onset.[19] Additionally, RF positivity has been linked with low risk of uveitis or reported to have "protective" effect by few authors. However, uveitis occurring in patients with RF positivity shows severe clinical course.[20]

Treatment

The treatment of JIA is challenging and requires a multidisciplinary approach involving both a rheumatologist and an ophthalmologist. In children with JIA-associated uveitis, close coordination between these specialists is essential to assess the disease burden comprehensively. When both joint and ocular inflammation are active, achieving remission should be the primary goal of therapy, with both specialists working in tandem. For the rheumatologist, attaining inactive disease as early as possible is crucial to improving overall outcomes, including better quality of life, shorter periods of active disease, and reduced long-term joint damage. Simultaneously, the ophthalmologist's priority is to ensure a quiet eye, preventing structural and functional damage to ocular tissues and thereby preserving the child's visual acuity.

Topical corticosteroids and cycloplegics remain the mainstay of treatment for anterior chamber inflammation. However, it is important to understand that in JIA-associated uveitis, topical therapy plays only a supportive role. The dosage of topical corticosteroids should be carefully titrated according to the degree of inflammation and tapered gradually as the inflammation subsides. Regular monitoring by the ophthalmologist is essential to optimize the use of topical corticosteroids

and minimize side effects such as cataract formation and ocular hypertension. In a retrospective study of 75 children with JIA-associated uveitis, Thorne et al. found that no cataract developed in those receiving ≤2 drops per day. Eyes treated with ≤3 drops daily had an 87% lower risk of developing a new cataract during follow-up compared to those receiving higher doses of topical corticosteroid.[21]

Regional use of corticosteroid such as subtenon injection should be avoided in children with JIA-associated uveitis. Long-term use of systemic corticosteroid is usually avoided in children, and the successful management of JIA depends on the use of appropriate corticosteroid-sparing agents. Various immunosuppressive agents or conventional disease-modifying antirheumatic drugs (cDMARDs) have been used in the management of JIA and also JIA-associated uveitis. Methotrexate has demonstrated a high level of efficacy along with an acceptable safety profile and remains an anchor drug in the management of JIA. The drug can be administered either orally or via subcutaneous injection. Details of immunosuppressives used in the management of JIA-associated uveitis is discussed in

Table 4: Overview of commonly used immunosuppressive agents in the treatment of Juvenile Idiopathic arthritis

Drug	Mechanism of Action	Dose	Adverse Effect	Monitoring
Methotrexate	Antimetabolite; inhibitor of dihydrofolate reductase	0.5–1.0 mg/kg per week or 10–20 mg/m2 with a maximum dose of 25 mg/wk	Hepatotoxicity, Bone marrow suppression, Interstitial pneumonia	CBC, Liver Enzymes, Albumin, Creatinine Every 2 months
Mycophenolate mofetil	IMP dehydrogenase inhibitor (purine metabolism)	600 mg/m^2 twice daily	Gastrointestinal symptoms, Leukopenia, lymphocytopenia, and elevation of liver enzymes	CBC
Azathioprine	Alters Purine Metabolism	2-3 mg/kg/day	Rash, hepatotoxicity, bone marrow suppression	CBC, Liver Enzymes Every 2 months (CBC every 2-3 weeks with change of Dose)
Cyclosporine	T-cell inhibitor	2.5-5 mg/kg/day	Nephrotoxicity, Hepatotoxicity, Gingival Hyperplasia, Myalgia, Tremors, Paraesthesia, Hypomagnesemia, and Hirsutism.	Blood Pressure, Creatinine Every Month . Periodic CBC, Potassium, Liver Enzymes

Table 5: Over view of Biological Agents and Janus Kinase (JAK) Inhibitors used in the management of Juvenile Idiopathic Arthritis (JIA)

Drug	Mechanism of Action	Dose	FDA Approval
Etanercept	TNF suppression, fusion protein	0.8 mg/kg/week or 0.4 mg/kg two times a week	Polyarticular JIA ages ≥2 years
Infliximab	TNF suppression, anti TNF monoclonal chimeric antibody	5–10 mg/kg/month(maximum 200 mg/month)	JIA-related uveitis
Adalimumab	TNF suppression, anti TNF human monoclonal antibody	<30 kg:20 mg/every 2 weeks >30 kg:40 mg/every 2 weeks	Polyarticular JIA Ages ≥2 years
Tocilizumab	Il-6 receptor antagonist	≤30 kg, 12 mg/kg/2–4 weeks ≥30 kg, 8 mg/kg/2–4 weeks(maximum dose 400 mg)	Systemic JIA and Polyarticular JIA ages ≥2 years

Rituximab	CD20 antigen suppression	375 mg/m2/weeks, for 4 weeks, (maximum dose 500 mg)	
Abatacept	T cell costimulator ; soluble fusion protein	10 mg/kg/4 weeks (maximum dose 500 mg)	
Tofacitinib *	Inhibits JAK1, JAK2 and JAK3	3.2 mg twice daily if body weight 10-20 kg, 4 mg twice daily if body weight 20-40 kg 5 mg twice daily if body weight > 40 kg	Polyarticular JIA Ages ≥ 2 years
Baricitinib *	Inhibits JAK1 & JAK2	2mg daily if body weight < 30 kg, 4 mg daily if body weight > 30 kg	
Upadacitinib*	Inhibits JAK1	15 mg/daily	

[* = JAK Inhibitors, FDA= The United States Food and Drug Administration]

In cases where immunosuppressive agents fail to control the disease or uveitis recurs, a "step-up approach" is adopted, introducing a biological agent. Various biological agents have been used in JIA management, as outlined in with adalimumab being the most commonly used. Adalimumab, a TNF-alpha blocker, is considered the first-choice biological agent for moderate-to-severe JIA-associated uveitis, supported by favourable outcomes and a better safety profile from two international trials, SYCAMORE and ADJUVITE.[22,23] Adalimumab was the first FDA-approved biologic for JIA-associated uveitis, and more recently, Abatacept, Canakinumab, Golimumab, Etanercept, and Tocilizumab have also received FDA approval for the treatment of JIA. Adalimumab has been found to be very effective in the management of JIA and JIA-associated uveitis; however, there are some reports of children with JIA in whom the drug was ineffective.[24] In cases of diminishing efficacy over time with the drug, assessing antibodies against adalimumab and drug trough levels can be helpful; however, these tests are not readily available in India.[25] Methotrexate is often used in combination with an anti-TNF-alpha agent, which may help reduce the development of antibodies. Humanized monoclonal antibodies targeting the IL-6 receptor, such as tocilizumab, have demonstrated effectiveness in JIA-associated uveitis cases where anti-TNF-alpha therapy failed due to the presence of anti-drug antibodies. Additionally, the risk of granulomatous diseases, particularly tuberculosis, is a significant concern in a tuberculosis-endemic country like India. In India, several biosimilars of adalimumab have been launched, reflecting a growing market for these alternatives to the original biologic.

Table 6: Biosimilars for Adalimumab Available In India

List of Biosimilars for Adalimumab Available In India
Exemptia® *
Adalirel® *
Adfrar *
Adalipca®
Humimab™
Mabura™
Cadalimab™
Amab®
Adaly™
Adlumab™
Plamumab

(* available as both 20 mg and 40 mg)

The introduction of these biosimilars is significant, as they provide more treatment options for patients while aiming to reduce healthcare costs. However, the cost of treatment in India remains a crucial factor for long-term therapy with biological agents, even with the biosimilars.

Janus kinase (JAK) inhibitors are emerging as a promising treatment option for JIA, and JIA-associated uveitis. JAK inhibitors work by blocking the intracellular signalling pathways of various pro-inflammatory cytokines, which play a critical role in the pathogenesis of JIA.[26] Tofacitinib, a predominately JAK1/JAK3 enzyme inhibitor, is proven to be efficacious in the management of JIA-associated Uveitis.[27] Tofacitinib is the

first Janus kinase inhibitor that has been extensively studied in several forms of JIA recently. Recently, FDA approved tofacitinib for patients with polyarticular course JIA. Baricitinib, a JAK1/JAK2 inhibitor taken once daily, was shown to be effective and safe for patients with polyarticular-course JIA—including polyarticular, oligoarticular, psoriatic, and enthesitis-related JIA—who had an inadequate response or intolerance to previous cDMARDs or biological agents.[28] While JAK inhibitors have shown promise, they are not without risks. Adverse events such as infections, thrombotic episodes have been reported in patients.

Management of Complications:
As discussed earlier, children with JIA-associated Uveitis often presents with complications, primarily due to its asymptomatic nature. Cataract is one of the most common complications of JIA-associated uveitis, with its development significantly associated with the presence of posterior synechiae, active uveitis, and the use of topical corticosteroids at presentation. While successful cataract surgery with intraocular lens (IOL) implantation can restore vision and reduce the risk of amblyopia in these children, achieving this outcome is challenging.

Performing cataract surgery in children with JIA presents significant challenges, and the decision to implant an IOL remains controversial due to the potential postoperative complications. These complications include the development of anterior and posterior synechiae, pupillary membrane formation, and secondary posterior capsule opacification (Figure 3).

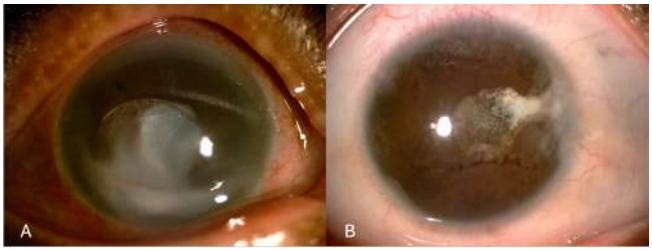

Figure 3: *Complications of cataract surgery in children with Juvenile Idiopathic Arthritis denoting poor control of inflammation*

The increased risk of these issues is largely attributed to insufficient control of preexisting inflammation, as well as inflammatory responses induced by the surgery itself. Additionally, the presence of an IOL may further exacerbate ocular inflammation by providing a surface for inflammatory cells and debris to accumulate, potentially leading to cyclitic membrane formation, which can result in hypotony and, in severe cases, phthisis bulbi. Other postoperative risks include secondary glaucoma, macular edema, and retinal detachment.

Implanting an IOL in children with JIA requires careful patient selection, as certain conditions serve as absolute contraindications. Active intraocular inflammation poses a significant risk, as persistent inflammation can lead to severe postoperative complications. Hypotony and ciliary body atrophy further compromise the eye's ability to maintain intraocular pressure, increasing the likelihood of poor surgical outcomes. Severe posterior synechiae and a shallow anterior chamber make IOL placement technically challenging. Additionally, IOL implantation is generally avoided in children under four years of age. If the fellow eye has experienced complications following IOL implantation, this may also deter surgeons from proceeding with implantation in the affected eye. Given these challenges, careful preoperative assessment and individualized decision-making are essential to optimizing visual outcomes while minimizing complications. Ganesh et al. found the factors associated with favourable outcome following cataract surgery with IOL implantation were strict preoperative, and postoperative control of inflammation, absence of amblyopia, and older age of the child. Thus, the first crucial step is to achieve optimal control of inflammation before proceeding with cataract surgery. It is essential to maintain an inflammation-free state for at least three months before considering surgical intervention. The next step involves sustaining this control in the postoperative period to ensure a successful surgical outcome.

Glaucoma is a common cause of irreversible visual loss and affects between 14% and 48% of the children with JIA-associated uveitis.[29] Elevated intraocular pressure (IOP) in JIA-associated uveitis is primarily managed with topical glaucoma medications, utilizing various groups of drugs that work through different mechanisms. However, when medical therapy proves insufficient, surgical intervention may be necessary to achieve

adequate IOP control. Unfortunately, surgical procedures often come with significant risks, including poor outcomes, the need for repeat surgeries, and potential complications. A study by Merayo-Lloves et al. [30] reported that 16% of patients with JIA-associated uveitis developed chronic secondary glaucoma over a 10-year follow-up period. For cases of refractory glaucoma, the preferred treatment options were Mitomycin-C trabeculectomy or the implantation of a glaucoma drainage device. Despite aggressive management of both uveitis and secondary glaucoma, 9% of their JIA patients still exhibited inadequate glaucoma control. [30] A recently published retrospective analysis of 45 eyes with JIA-associated uveitis and glaucoma found that glaucoma drainage devices demonstrated higher success rates than trabeculectomy.[31] However, hypotony was a frequent postoperative complication in both treatment groups, particularly within the first six months, and was observed more often following trabeculectomy. Other reported complications included hyphema, choroidal detachment, optic disc edema, and transient IOP elevation, affecting both surgical groups.[31] Notably, patients who underwent valve implantation required fewer secondary surgical interventions compared to those who had trabeculectomy.[31] Additionally, a study by Välimäki et al. highlighted that implantation of a glaucoma drainage device (Molteno implantation) was the most effective approach for managing uncontrolled secondary glaucoma in JIA-associated uveitis.[32] The failure rate of trabeculectomy in children with JIA was found to be high, and the use of mitomycin in paediatric patients was deemed impractical. [32]

JIA remains a challenging condition in India due to a lack of awareness among both the general population and healthcare providers. The disease is often suspected but not adequately screened, leading to delayed diagnosis and making treatment more complex. There is a pressing need for epidemiological studies in community settings to determine the true burden of JIA in India. Additionally, larger clinical trials are essential to identify the most effective immunosuppressive such as JAK inhibitor therapies for these children in India. In the current era of long-term biologic treatments with monoclonal antibodies and fusion proteins, accessibility remains a major concern, as many Indian patients struggle to afford these therapies due to socioeconomic constraints.

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Sarcoidosis associated uveitis in children

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History

First described by Sir Jonathan Hutchinson in 1869, sarcoidosis is a multisystem granulomatous illness with an uncertain aetiology.[1] Caesar Boeck gave it its name in 1899 and in 1909, the first ocular involvement was described by Schumacher in a case of nodular iritis.[1] Sarcoidosis is a multisystemic granulomatous disease that causes non-caseating granulomas to grow in affected organs as a result of T lymphocyte and mononuclear phagocyte buildup.[2] It can involve any, and more commonly multiple body organs, and often manifests with various symptoms.[3] The lungs, skin, lymph nodes, and eyes are among the organs that are impacted by the illness. The reported incidences of sarcoidosis vary between 1 to 50 per 100,000 per year.[4] In 3% to 15%, sarcoidosis begins in childhood, 70% with an onset in infancy and 30% at school age or in adolescence.[5] About 60% are girls.[4] The African-Americans are younger at ophthalmic presentation than Caucasian patients.[6]

Like other autoimmune disorders, sarcoid uveitis has a complex aetiology that may involve immune system activation, environmental factors, and genetic predisposition.[7] It is thought to be caused due to the exaggerated T cell immune response to multiple self and non-self antigens capable of generating a Th1-mediated response in genetically susceptible individuals. Among the genetic variables found, sarcoidosis has been associated with the tumour necrosis factor-alpha (TNF-α) G-308A (rs1800629) single nucleotide polymorphism (SNP).[8-10] TNF-α is a major pro-inflammatory cytokine that is essential for granuloma formation, neutrophil activation, cytokine production, and inflammatory responses. Sarcoidosis has also been linked to other genes or SNPs, including the butyrophilin-like 2 (BTNL2) G16071A (rs2076530) SNP and several human leucocyte antigens (HLA).[9,11,12]

Sarcoid uveitis in children presents unique diagnostic and therapeutic challenges, necessitating a thorough understanding of its clinical features, diagnostic criteria, and management strategies. This article aims to provide ophthalmologists with an updated review of sarcoid uveitis in children, incorporating insights from recent studies.

Clinical Features

Any area of the eye and surrounding tissues may be affected by ocular sarcoidosis in children. Various forms of uveitis, scleritis, episcleritis, abnormalities of the eyelids, conjunctival granuloma, optic neuropathy, enlargement of the lacrimal gland, and orbital inflammation are among the conditions that may be induced in paediatric sarcoidosis.[13] One important and frequently early symptom of ocular paediatric sarcoidosis is sarcoid uveitis, which differs from adult uveitis in that it is typically asymptomatic but can also develop into a chronic condition that damages the ocular components.[13] Ocular involvement occurs either as an isolated finding or as part of systemic disease. It is usually bilateral with comparable symptoms and a similar clinical progression in both eyes.[14] The clinical features widely vary depending on the age of onset and the extent of systemic involvement. The most common ocular manifestations include:

Anterior Uveitis: This is the most frequent form of uveitis in paediatric sarcoidosis, characterized by inflammation of the iris and ciliary body. Symptoms may include redness, pain, photophobia, and blurred vision. On examination, patients may exhibit non-granulomatous anterior uveitis with fine keratic precipitates or granulomatous anterior uveitis, which is typified by iris nodules and mutton-fat keratic precipitates (Figure 1).

While anterior uveitis is present in 77% of cases during infancy (0–5 years), it is only recorded in 30% of cases throughout the 8–15 year age group, which is comparable to adults.[4]

Intermediate Uveitis: This form involves inflammation of the vitreous and peripheral retina. Children may present with floaters and decreased vision. Snowbanking and snowball opacities in the vitreous are hallmark findings.

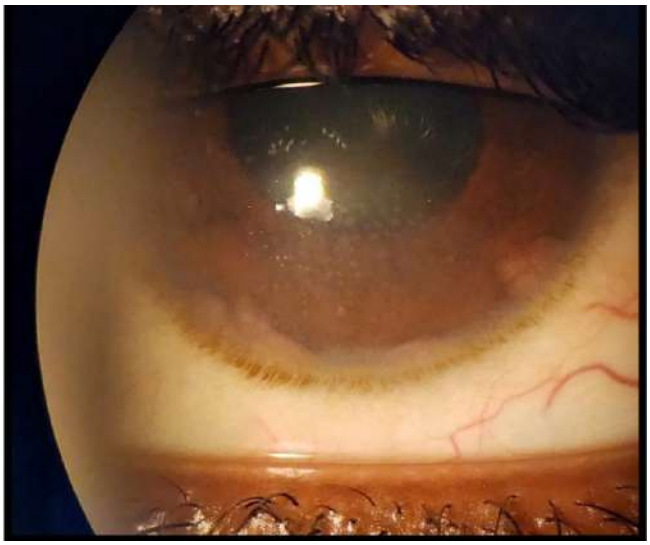

Figure 1: *Slit lamp examination of an 8-year boy showing mutton fat keratic precipitates with tented peripheral anterior synechiae in a case of granulomatous acute anterior uveitis*

Posterior Uveitis: Less common in children, posterior uveitis presents with vitritis, choroiditis, choroidal granuloma, retinal vasculitis, perivascular sheathing and optic nerve involvement. Symptoms may include visual field defects and decreased vision. But retinal periphlebitis is relatively an uncommon finding in paediatric sarcoidosis.[4]

Panuveitis: This form involves inflammation of all layers of the uveal tract and can present with a combination of the above symptoms.

Children with ocular sarcoidosis may experience fever, hepatosplenomegaly, exhaustion, weight loss, lymphadenopathy, and respiratory problems as systemic signs. Musculoskeletal involvement and cutaneous symptoms like erythema nodosum are also frequent.

Types of Childhood Sarcoidosis

There are two main types of paediatric sarcoidosis based on the age of onset of symptoms:

Infantile sarcoidosis: It generally refers to the rare form of sarcoidosis diagnosed often within the first year of life. It can cause both acute iridocyclitis with tiny keratic precipitates and chronic granulomatous iridocyclitis with mutton fat keratic precipitates and iris nodules. When a child with Still disease gets uveitis, we should rule out infantile sarcoidosis.

Early-onset sarcoidosis: Early-onset sarcoidosis (EOS) where the features begin before 5 years of age. It is often characterized by a triad of arthritis (primarily knee and wrist sarcoidal arthritis), uveitis (mainly anterior), and skin rash (mainly erythema nodosum) with less common pulmonary involvement.[15-18] Blau et al. described in 1985 is a rare autosomal dominant inflammatory hereditary disease characterised by the clinical triad of granulomatous dermatitis, recurrent granulomatous uveitis, rash and camptodactyly, is another illness that shares clinical similarities with infantile sarcoidosis (Figure 2).[4,19] It falls within the category of inherited auto-inflammatory diseases. Recently, NOD2 (CARD15) was shown to be the Blau syndrome susceptibility gene on chromosome 16q12; this gene has also been linked to the onset of Crohn's disease.[4,20]

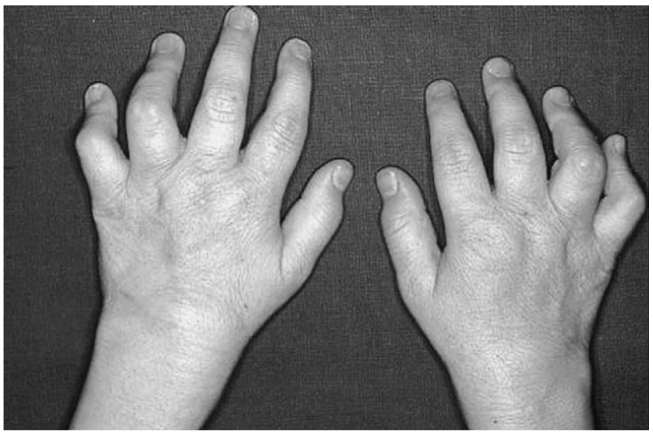

Figure 2: *A camptodactyly as a part of the Blau syndrome in a 5-year girl. (Source: Manfred Zierhut, Uveitis in Children 2005, International Ophthalmology Clinic4)*

Late-onset sarcoidosis: The clinical features beginning after 5 years of age and resembling adult sarcoidosis is known as Late-onset sarcoidosis.[18,21,22] While lung illness and lymphadenopathy are more common in these school-age and adolescents, uveitis and arthritis are far less common.[4] Similar to adults, older children typically have hilar lymphadenopathy, and up to 50% of them have interstitial lung disease and multiorgan involvement. Twelve per cent of these children go on to develop chronic conditions.[23]

Diagnosis

In children with sarcoid uveitis, early diagnosis is challenging and is crucial, due to more severe complications. Imaging, laboratory testing, and clinical findings are all necessary to diagnose sarcoidosis-associated uveitis in children. The diagnostic procedure consists of:

Laboratory Tests: Elevated serum calcium, C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) with anaemia, leukopenia, and eosinophilia and other acute phase reactants may be found raised during laboratory testing but these are nonspecific inflammatory markers.[24,25]

Systemic Imaging: Bilateral hilar lymphadenopathy or pulmonary infiltrates, which are indicative of sarcoidosis, may be shown on a chest X-ray or high-resolution computed tomography (HRCT). The Scadding staging system[26] is used to classify participants with sarcoidosis into four stages:

1) Bilateral hilar lymphadenopathy (BHL),

2) Pulmonary infiltration with BHL,

3) Pulmonary infiltration without BHL, and

4) Pulmonary fibrosis.

Even in systemically asymptomatic individuals with uveitis, CT chest imaging established a diagnosis of sarcoidosis in 42.86% of cases based solely on clinical-radiological criteria. In contrast, a confirmed diagnosis of sarcoidosis was achieved in only 28.57% through EBUS/TBNA-guided cytological examination.[27]

Ocular Imaging: The degree of ocular involvement can be determined with the use of ocular imaging techniques including optical coherence tomography, fundus fluorescein angiography, and indocyanine green angiography. Multimodal imaging with widefield fundus photography, optical coherence tomography and angiography can help in the diagnosis of sarcoid uveitis and in the monitoring of treatment response.[28]

Biopsy: The gold standard for diagnosis is histopathological confirmation of non-caseating granulomas in afflicted tissues, such as lymph nodes, lacrimal glands, or conjunctival biopsies.[15] But in children, a biopsy could be difficult to obtain. Recent research has demonstrated that positron emission tomography (PET) scans, may be used to guide biopsy locations and detect hidden systemic involvement in paediatric

sarcoidosis for a conclusive diagnosis.[15]

Ocular Fluid Analysis: Aqueous or vitreous humour analysis may be done to assess the inflammatory cells and angiotensin level when the diagnosis is unclear. There are reports on significantly higher CD4/CD8 ratio in the vitreous and aqueous humour (OR 38, 95% CI 7.0–205.2) of sarcoid uveitis vs other forms of uveitis.[29 30]

Serum biomarkers: Elevated Lysozyme and angiotensin-converting enzyme (ACE) levels can aid in diagnosis, but younger individuals exhibit higher levels of angiotensin-converting enzyme (ACE), a finding that warrants careful interpretation.[31] Hence, in paediatric sarcoid, the sensitivity and specificity have been reported to be 22.2% and 87.5% respectively with a positive predictive value of 14.3% and negative predictive value of 92.3% resulting in the diagnostic values of a positive likelihood ratio of 1.8, and negative likelihood ratio of 0.9.[31]

Bronchoalveolar Lavage and Biopsy: A transbronchial biopsy revealing non-caseating granulomas validates pulmonary involvement in a late-onset variant of paediatric sarcoidosis.

Genetic testing: Mutations in the NOD2 gene can definitively diagnose early-onset sarcoidosis (Blau syndrome).[19]

Miscellenaous tests: A negative Mantoux test and decreased value in schiermer test can also aid to diagnose sarcoid uveitis.[32]

There could be several reasons why the diagnosis is delayed, including the problems in evaluating young toddlers and preverbal age.[25]

Diagnostic Criteria

The first International Workshop on Ocular Sarcoidosis (IWOS) proposed international criteria in 2009.[33] In 2017, with the revised IWOS criteria, the classification of ocular sarcoid (OS) has become simpler, with only three categories (definite OS, presumed OS and probable OS).[34]

Table 1: Revised International Workshop on Ocular Sarcoidosis (IWOS) criteria for the diagnosis of ocular sarcoidosis (OS) (2017)[34]

S No	Criteria	Features
I	Other causes of granulomatous uveitis must be ruled out.	
II	Intraocular clinical signs suggestive of Ocular Sarcoidosis	1. Mutton-fat keratic precipitates (large and small) and/ or iris nodules at pupillary margin (Koeppe) or in stroma (Busacca). 2. Trabecular meshwork nodules and/or tent-shaped peripheral anterior synechia. 3. Snowballs/string of pearls vitreous opacities. 4. Multiple chorioretinal peripheral lesions (active and atrophic). 5. Nodular and/or segmental periphlebitis (±candle wax drippings) and/or macroaneurysm in an inflamed eye. 6. Optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule. 7. Bilaterality (assessed by ophthalmological examination including ocular imaging showing subclinical inflammation).
III	Systemic investigation results in suspected Ocular Sarcoidosis	1. Bilateral hilar lymphadenopathy (BHL) by chest X-ray and/or chest computed CT scan. 2. Negative tuberculin test or interferon-gamma releasing assays. 3. Elevated serum ACE. 4. Elevated serum lysozyme. 5. Elevated CD4/CD8 ratio (>3.5) in bronchoalveolar lavage fluid. 6. Abnormal accumulation of gallium-67 scintigraphy or 18F-fluorodeoxyglucose positron emission tomography imaging. 7. Lymphopenia. 8. Parenchymal lung changes consistent with sarcoidosis, as determined by pulmonologists or radiologists.

IV	Diagnostic criteria	
	Definite Ocular Sarcoidosis	Diagnosis supported by biopsy with compatible uveitis.
	Presumed Ocular Sarcoidosis	Diagnosis is not supported by biopsy, but BHL presents with two intraocular signs.
	Probable Ocular Sarcoidosis	Diagnosis not supported by biopsy and BHL absent, but three intraocular signs and two systemic investigations selected from two to eight are present.

Figure 3 presents an approach to diagnose paediatric sarcoid and rule out other differential diagnoses.

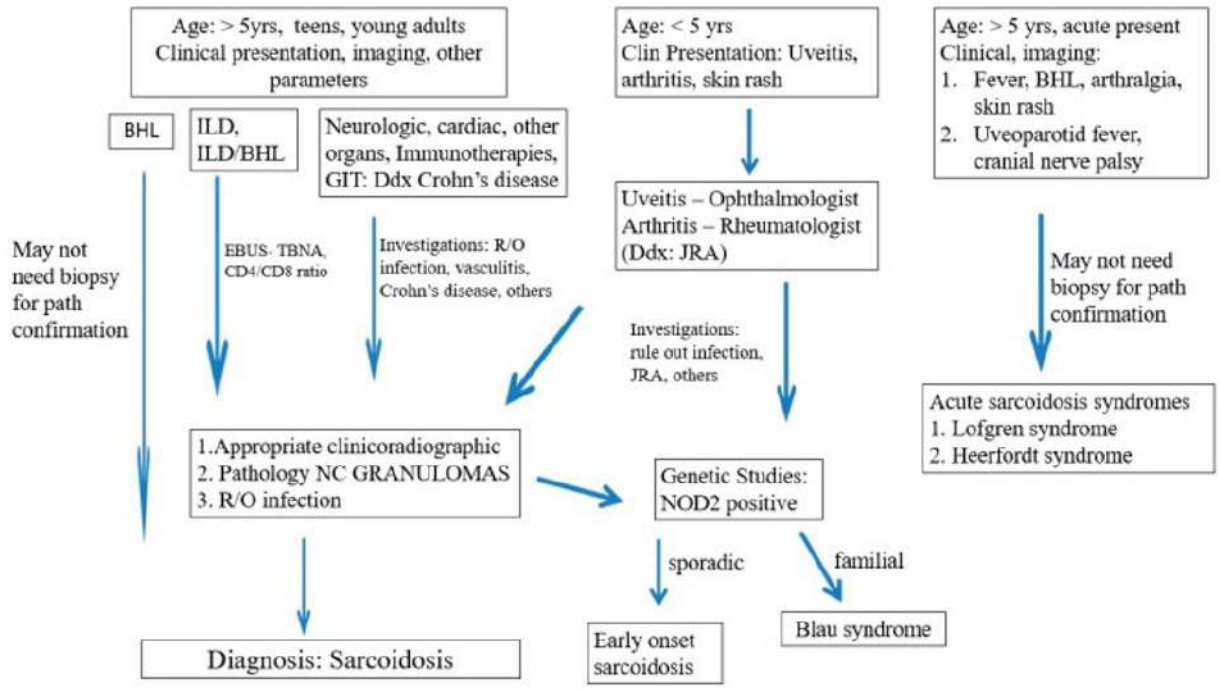

Figure 3: *Flowchart of Diagnostic Considerations of Paediatric Sarcoidosis (Source: Pediatric sarcoidosis: a review with emphasis on early onset and high-risk sarcoidosis and diagnostic challenges. Diagnostics. 2019 Oct 25;9(4):160.)23*

Legends: *BHL Bilateral hilar lymphadenopathy, ILD Interstitial lung disease, GIT gastrointestinal tract, EBUS-TBNA endoscopic bronchial ultrasound-transbronchial needle aspiration, NG non-necrotizing granulomas, JRA Juvenile rheumatoid arthritis, NOD2 Nucleotide-binding oligomerisation domain 2*

Management

For treatment to achieve optimal success, it is imperative to adopt a comprehensive multidisciplinary approach that actively engages paediatricians, immunologists and a diverse team of specialists. Treatment goals include controlling inflammation, preserving vision, avoiding complications and managing systemic involvement.

The therapy strategy consists of:

Corticosteroids: For anterior uveitis, topical corticosteroids (1% prednisolone acetate) is applied. Injections of periocular or intraocular steroids for posterior or refractory intermediate uveitis. Oral prednisone, a systemic corticosteroid (0.5-1mg/kg body weight) with a slow taper, for severe or systemic disease involvement.

Immunosuppressive agents: The primary long-term treatment goal is to achieve corticosteroid-free remission through the use of corticosteroid-sparing immunomodulatory therapy. The first-line steroid-sparing medication is methotrexate. In cases of intolerance or insufficient response, leflunomide, azathioprine, or mycophenolate mofetil may be utilized but safety profiles should be monitored, before escalating to more robust drugs that may carry a higher risk of adverse effects.[25]

Biologic therapies: For refractory patients, biologic medicines (TNF-α inhibitors

such as Adalimumab and Infliximab) are used. However, one should be aware of the biologics-induced sarcoid uveitis presenting with bilateral granulomatous keratic precipitates and panuveitis with chorioretinal infiltration with the biologics. Biologics are a double-edged sword where it can aid in refractory cases but can also lead to cytokine imbalances with granuloma formation leading to sarcoid uveitis.[35] The use of etanercept was associated with higher induction of uveitis (56% of cases experiencing first episodes of uveitis) compared to other biologic agents.[35]

Recent therapy: Newer options for paediatric sarcoid uveitis could be targeted medicines such as interleukin (IL) inhibitors and Janus kinase (JAK) inhibitors, which have been investigated as a result of recent developments in our understanding of the immunopathogenesis of sarcoidosis. Paediatric sarcoidosis-associated uveitis may benefit from developments in targeted therapy, genetic testing, and imaging. Future studies should concentrate on improving therapeutic approaches and comprehending the immunopathogenesis of the illness in children.

Complications: Chronic uveitis and delayed therapy can lead to complications such as glaucoma, cataracts, band keratopathy and permanent vision loss. Around 10–40% of sarcoid uveitis under eight years of age develop band keratopathy.[36]

Monitoring: High-risk blood monitoring tests should be carried out on a frequent basis during therapy. These blood tests include creatinine, BUN, liver function tests, and full blood counts. Live virus vaccination should be avoided by patients receiving immunomodulatory therapy with traditional drugs and biologic response modifying therapies.

Until remission is achieved, paediatric sarcoid uveitis patients should undergo regular checkups. Once remission is reached, the interval between follow-up appointments may be extended; however, based on the child's uveitis history and the medications being used, it is generally recommended that the child be seen every 8 to 12 weeks during the early post-remission phase. Close monitoring is done for visual acuity, intraocular pressure and structural complications.[25] For long-term management strategies to assess the effects of quality of life using Patient Reported Outcome metrics (PROM) have to be used.[25] A few paediatric QoL tools are specific to eyesight like the Effects of Youngsters' Eyesight on QoL (EYE-Q),[37,38] the first tool for uveitic patients, validated in patients with uveitis, JIA, and normal vision can be adopted in paediatric sarcoid uveitis cases.

Conclusion

Because of its rarity and varied presentation, sarcoidosis-associated uveitis in children can be difficult to diagnose. From anterior uveitis to vision-threatening posterior segment involvement, ocular symptoms can vary widely. Accurate diagnosis requires a multifaceted strategy that includes imaging, clinical assessment, and histological confirmation. Preventing long-term visual impairment requires early intervention, multidisciplinary cooperation, and a high index of suspicion. Further research is needed to understand the disease's pathogenesis and to develop targeted therapies for paediatric populations.

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Blau Syndrome Associated Uveitis

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Introduction

Classically inherited as an autosomal dominant[1] disorder, Blau syndrome consists of the clinical triad of granulomatous dermatitis, arthritis and uveitis[2]. Usual age of onset is 2 years, however ocular complaints present at around 4 years of age[3]. Patients can present with a maculopapular skin rash[4] to a dermatologist, or boggy swelling of joints[3] to a rheumatologist or blurred vision[5] to an ophthalmologist. Due to its close resemblance with other systemic disorders such as Juvenile idiopathic arthritis (JIA)[6] and Sarcoidosis,[7] it becomes essential to differentiate these subtypes for efficient and timely management.

Pathophysiology

NOD2 receptor in the cytosol of macrophages senses muramyl dipeptide (MDP) within bacterial cell wall causing activation of nuclear factor kappa B (NF-κB)[8] and its downstream pathways causing immune mediated destruction of the bacteria, thereby protecting the body against the invaders. A mutation in the nuclear binding domain (NBD)[9] of the NOD2 gene on chromosome 16[10] leads to constitutive activation of the NFkB pathway independent of MDP stimulus, thus leading to self tissue destruction.

This is accompanied with the formation of non caseating granulomas mediated via Interferon gamma and TNF alpha.[11]

Although most cases are inherited in an autosomal dominant manner[1] running in families, some sporadic cases have also been reported, sharing the pathology with early onset sarcoidosis.[7]

Clinical Findings

The typical triad of polyarticular arthritis, dermatitis and uveitis is very rare to be seen simultaneously. It's usually sequential rather than simultaneous presentation.

A **skin rash**[1,2,7] is usually the first symptom to develop, usually noted in infancy, maculopapular to begin with which later appears scaly and pigmented.

The most common clinical presentation is **polyarticular boggy arthritis**[3,12] seen in more than 90% patients. It mainly involves the peripheral joints such as- Proximal interphalangeal (PIP) joints in fingers, wrist, ankle, knees with underlying tenosynovitis usually presenting at 2-4 years of age. There is no movement restriction (non erosive) but over many years joint contractures may develop causing permanent deformities.

Isolated ocular involvement is very rare, it usually is accompanied with either dermatological findings or joint involvement at around 4-5 years. Though less common, ocular involvement causes great morbidity[13] in the form of visual impairment.

The baseline VA at presentation could range from 20/20 to 20/400, which may worsen over the years.[14]

Upto 94%[14] cases present with **bilateral granulomatous panuveitis** with characteristic **multifocal choroiditis,**[15] more in chronic cases.

A fraction of patients may present with anterior uveitis[16] with characteristic nummular corneal opacities and large keratic precipitates, corneal edema, inflammatory reaction in the anterior chamber in the form of cells/ flare and even secondary angle closure glaucoma has been reported in some cases.[17]

Optic nerve involvement can present with disc edema or pallor with characteristic juxtapapillary nodules or excrescences.[18]

In late stages, inflammatory sequelae can develop such as band shaped keratopathy, cataracts, glaucoma, macular edema, retinal detachment and optic atrophy.[5]

Differential Diagnoses

Table 1- showing the differential diagnoses of Blau syndrome[7,12,19]

Differentiating features	Blau Syndrome	Sarcoidosis	Juvenile Idiopathic Arthritis
Age of onset	2-4 years	Late teens, 20s,	Most common rheumatic disease in children, 8-15 years
Pathogenesis	NOD2 gain of function, inherited	NOD2 gain of function, sporadic	Autoimmune mechanism
Arthritis	90% cases, boggy, Polyarticular- PIP joints, wrist, ankle, knees	5-15%, oligoarticular	Oligoarticular> polyarticular. Limp, joint stiffness more in morning.
Dermatitis	Papulosquamous skin rash	Large papules, plaques, nodules, erythema nodosum	Migratory reddish scaly rash

Uveitis	Bilateral granulomatous panuveitis, anterior uveitis	Bilateral granulomatous anterior / panuveitis, scleritis, episcleritis	Asymptomatic chronic anterior uveitis> acute
Other organ involvement	Less common pulmonary involvement, Fever, lymphadenopathy, cranial neuropathy	Pulmonary (90%)- hilar LN enlargement, interstitial lung disease, seizures, hypercalcemia	Constitutional symptoms- fatigue/ reduced appetite/ fever

Diagnosis

Based on strong clinical suspicion, targeted NOD2 sequencing[6] coupled with skin biopsy[20] to look for the non caseating granulomas helps in confirmation of Blau syndrome.

Treatment

These patients do not respond very well to steroids especially topical, thus necessitating the use of high dose systemic steroids, immunosuppressive agents and biological Disease Modifiers.[21]

Firstline- high dose oral steroids/intravenous pulse 1-1.5mg/kg/day. Combined with Methotrexate low dose 10-15mg/m^2/week for its steroid sparing effect

Adding TNF alpha inhibitors such as Adalimumab or Infliximab helps to prevent disease relapse. They are increasingly being used as first line in the treatment of Blau Syndrome

If the disease activity is still not controlled, consider switching over to another TNF alpha inhibitor or other biologicals such as Anakinra, Canakinumab (IL-1 inhibitors), or IL-6 inhibitors- Tocilizumab in refractory cases.

Still more research is needed in this field to establish holistic treatment for better disease control.

Long-term Outcomes

Over time the VA of these patients declines progressively due to chorioretinal atrophy secondary to chronic panuveitis, complicated cataract, glaucoma, optic atrophy amongst many others.[13]

It requires collective efforts on the part of pediatricians and ophthalmologists to diagnose this rare disorder and intervene early.

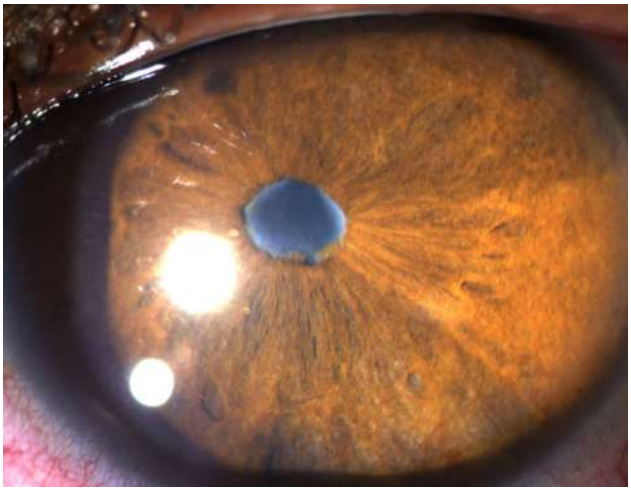

Figure 1. *A 17-year-old Asian Indian male with Blau syndrome with anterior uveitis with 360-degree posterior synechiae and complicated cataract.*

Image courtesy: *Dr. Atul Arora, Prof. Vishali Gupta, Postgraduate Institute of Medical Education and Research, Chandigarh*

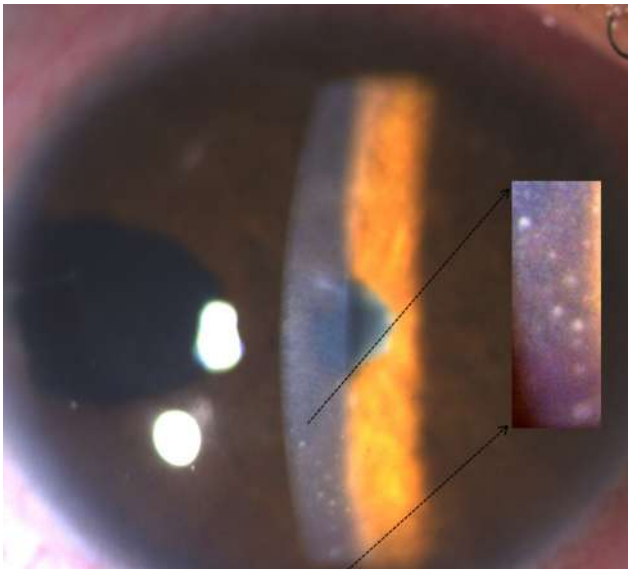

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Figure 2. *Anterior segment photograph of a 20-year-old male patient with recurrent anterior uveitis showing keratic precipitates (magnified image in inset). He had also undergone surgical peripheral iridotomy due to secondary angle closure glaucoma.*

Image courtesy: *Dr. Atul Arora, Prof. Vishali Gupta, Postgraduate Institute of Medical Education and Research, Chandigarh*

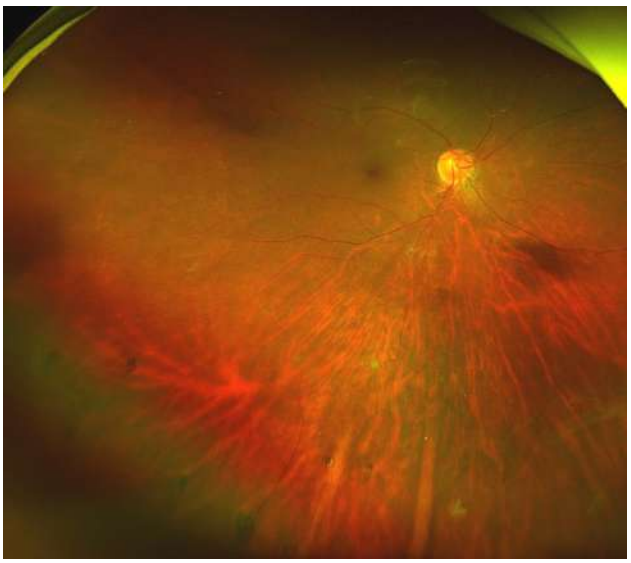

Figure 3. *Ultra-wide field fundus photograph of a patient with Blau syndrome shows chorioretinal scars.*

Image courtesy: *Dr. Atul Arora, Prof. Vishali Gupta, Postgraduate Institute of Medical Education and Research, Chandigarh*

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Sunset Glow in Young Eyes: Insights into Paediatric Vogt-Koyanagi-Harada (VKH) Syndrome

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Introduction

Paediatric uveitis is a rare but potentially sight-threatening inflammatory condition affecting the uveal tract and other parts of the eye, in children.[1] It may account for upto 5-16% of all uveitis cases, as per various reports from tertiary centres.[2,3] Unlike adult uveitis, paediatric uveitis presents with challenges due to difficulty in examination, children's inability to express discomfort and some phenotypes lacking symptoms, irrespective of severity of disease. Chronicity and frequent recurrences of inflammation are also well known, which may all lead to delayed diagnosis and an increased risk of complications, right at the first presentation, and the added long term risk of developing amblyopia.[4] The management of paediatric uveitis requires a multidisciplinary approach, involving ophthalmologists, rheumatologists, and other specialists to optimize outcomes while simultaneously minimizing treatment-related adverse effects.

Vogt-Koyanagi-Harada syndrome (VKH) is a bilateral granulomatous panuveitis with multisystem affection including eyes, ears, skin and the central nervous system. Ophthalmologically, it may present with varied severity of non-granulomatous or granulomatous anterior uveitis, vitritis, optic disc swelling and multiple serous retinal detachments.[5] It is a disease of young adults and the middle age, but may also occur in children and elderly. It is believed to involve an autoimmune response against melanocytes, triggered by environmental or genetic factors.[6] The diagnosis of paediatric VKH syndrome is based on clinical findings, supported by imaging and laboratory tests that help differentiate it from other inflammatory conditions. Early diagnosis and treatment are essential in managing the disease, with corticosteroids and immunosuppressive agents commonly used in the treatment protocol, with biologics also being increasingly used. However, the optimal management approach for children remains an ongoing debate, as treatment regimens need to be tailored to minimize side effects while achieving long-term disease control. This paper will explore the current understanding of paediatric VKH syndrome, including its epidemiology, pathophysiology, clinical presentation, diagnostic challenges, and treatment strategies, with the goal of improving outcomes for affected children.

Epidemiology

VKH is one of the most common causes of panuveitis in India. In a large population based study from a tertiary centre, panuveitis in children accounted for about 9% of all childhood uveitis.[7] In another study from a tertiary centre in South India, paediatric VKH accounted for about 9% of all VKH cases.[8] The prevalence of VKH in children ranged from 3-13%, as per various published reports.[8–10] However, this estimated prevalence varies by region, with higher rates in Asia, India, the Middle East, and Latin America.[11]

The disease typically presents in older children and young adolescents, but the earliest reported case was in a three year old.[12] The mean age at presentation is between 10-13 years of age, with most groups reporting a female preponderance.[8,13],[11] The prevalence in pre-school or children of amblyogenic age has been reported to be low, with just ten cases between the age of three and five.[13,9,14]

Pathophysiology

Various adult studies have suggested VKH to be an autoimmune CD4+ T cell mediated reaction against melanocytes, with tyrosinase peptide antigen particularly targeted.[15,16] The exact triggers for this to happen are not entirely known, however, expression of HLA DRB1*0405 and viral infections, are thought be responsible.[17] To support this, there have been histopathology studies of chronic VKH revealing choroidal melanocyte loss and infiltration of both T and B lymphocytes, with CD4+ lymphocytes predominating.[18,5] Similarly, immunohistochemical analysis of skin vitiligo patches shows melanocyte loss, melanin-laden macrophages, and mononuclear cell infiltration, primarily T lymphocytes expressing HLA-DR.[19]

The alleles HLA DRB1 and DQB1 have been associated with increased susceptibility to VKH syndrome.[20] There have been many other alleles described in various populations in specific regions/countries. A study which included adults and children with VKH syndrome from South India, found a higher frequency of occurrence of HLA-DRB1*0405/0410 alleles in cases with VKH syndrome, when compared with healthy controls. They also proposed the epitope S57-LLEQRRAA [67–74] in the third hypervariable region of the DR β-1-chain could be relevant to the susceptibility

to VKH syndrome.[21] Moreover, they did not find an association of HLA-DRB1 with sympathetic ophthalmia patients. There has also been a recent shift to identify Killer Immunoglobulin like Receptors (KIRs) genes, and these may not only increase the susceptibility to develop VKH, but may also protect against the disease.[22,23] A detailed description of genetic associations is beyond the scope of this paper, as none have been specifically identified in children. The exact reasons for paediatric susceptibility to VKH syndrome remain unclear and require further research.

Clinical features described in phases

Four phases have been described in VKH

with each manifesting with different ocular and extraocular clinical features - prodromal, acute uveitic, convalescent, and chronic recurrent phases.

Prodromal phase

This may present with one or more of the following symptoms of headache, meningismus, fever, nausea, vertigo, orbital pain and auditory disturbances (including sensorineural hearing loss and tinnitus), i.e. extraocular symptoms. This usually lasts a few days to a few weeks and often the history may be obtained in retrospect. Pleocytosis of the cerebrospinal fluid has also been noted in this phase.[24] The occurrence of these symptoms in children have varied in literature. The frequency of headaches in children presenting with VKH has been reported to range from 36-60%, the most common extraocular symptom.[25,9] Auditory disturbances have also been noted to a varying degree in paediatric population, in some series as high as 69%.[9] Fever and meningismus have been reported to be common in pre-school children.[14] A pharyngitis like illness has also been reported as a prodrome in young children.[26] The rest of the extraocular manifestations have only been rarely reported in the paediatric population. It has also been noted by some authors, that ocular manifestations may occur before children develop extraocular manifestations.

Acute uveitic phase

This phase presents after the prodromal phase and commonly brings patients to clinics due to vision loss which may be bilateral or rarely sequentially involving both eyes. The duration of symptoms at presentation, usually associated with vision loss, has been noted to vary between 6-9 weeks by various authors, thus, implying a delay in presentation.[11,25] Acute vision loss has been noted to be the most common symptoms in this phase with nearly 90% or more children presenting with this complaint.[8,25] Vision has specifically been noted to be much worse in children compared to adults by various groups, with mean presenting visual acuity as low as 20/200 – 20/400 or worse in more than half of the eyes.[13,8] Other common symptoms at presentation include redness, pain, photophobia and floaters, in the order of frequency.

A bilateral panuveitis, choroidal thickening, multiple serous detachments and vitritis have been classically described in this phase.[27] Clinical signs include conjunctival injection, anterior segment inflammation in the form of non-granulomatous or granulomatous inflammation. Studies have also reported the absence of anterior segment inflammation in some children. Granulomatous inflammation in children has been reported less commonly than in adults, ranging from nearly 20%-36%.[8,25] Martin et al, in their series of paediatric cases from Southern India, noted 95% of eyes in their series to show the presence of keratic precipitates (Figure 1b). The presence of iris nodules in children have noted to range from 8%-60% in various studies.[9,11] Posterior synechiae have also been noted in these children, which may occur at presentation, as well as along the course of follow up, a marker for delayed onset of treatment and poor prognosis.[11] The most common posterior segment findings include serous retinal detachments, disc hyperemia and optic disc swelling, with studies reporting them in 60-100% of children (Figure 1c).[8,9,11] Tabbara et al, have described posterior multifocal nummular choroiditis without exudative retinal detachment, who later developed Dalen Fuchs' nodules in the mid peripheral fundus. Serous retinal detachments have been noted to have a 100% positive predictive value and a high negative predictive value for diagnosing VKH in this phase.[28]

Adults in this phase, may also present with acute uveitis, raised pressures and a shallow anterior chamber, which is reported to respond better to steroids than antiglaucoma medication.[29] This has been hypothesized to be due to a transient swelling of the ciliary body and a forward displacement of iris lens diaphragm.[30] This presentation has fortunately not been encountered till date in children. The inflammation has been described to start with multifocal areas of choroidal thickening, followed by a breakdown of retinal pigment epithelium (RPE) causing multiple serous retinal detachments, This inflammation may spread to the vitreous and eventually to the anterior segment, which may not always be sequential.[27,5]

Convalescent phase

Occurring a few months to years after the acute uveitic phase, the convalescent phase is characterized by multisystem depigmentation and may last a few months. There occurs depigmentation of uveal tissue of the eye, skin and hair – leading to

a sunset glow fundus, vitiligo and poliosis respectively. Perilimbal depigmentation, first described in Japanese patients, is an early sign of this phase, appearing within a month of uveitis onset.[31] Choroidal depigmentation gives the ocular fundus a bright orange red 'sunset-glow' appearance, typically seen at least 2–3 months after the uveitic phase. The sunset glow fundus has been noted to be a common outcome in most paediatric VKH series. Additionally, Dalen-Fuchs nodules can appear in the midperipheral fundus, seen as multiple small yellow, well circumscribed areas of hypopigmentation.[27] The occurrence of these have been noted to be as high as 77% in some series with a few groups reporting them to be present in some children at presentation itself.[9,25] Some children may also develop peripheral iris depigmentation and poliosis which has known to reverse with immunosuppression.[32,33]

Vitiligo and alopecia are also other reversible signs which may be noted in this phase. Some patients may also present with cutaneous signs before uveitis develops. Vitiligo in preschool children has been noted to commonly involve the back and buttocks.[14] Vitiligo has also been known to worsen on treatment de-escalation, which may be tolerated in the absence of uveitis.[34,35]

Chronic recurrent phase

This phase develops 6 to 9 months after the initial presentation and is characterized by recurrent granulomatous anterior uveitis with ocular complications like posterior synechiae, raised pressures, cataracts, band shaped keratopathy, retinal pigment epithelial(RPE) hyperplasia, choroidal neovascular membranes, sub retinal fibrosis and hypotony to name some.[8,9,14,25] Posterior segment inflammation is uncommon.

Diagnosis and Investigations

Diagnosis of VKH syndrome is based on the revised diagnostic criteria for Vogt-Koyanagi-Harada syndrome.[36] The diagnosis of paediatric Vogt-Koyanagi-Harada (VKH) syndrome relies on a combination of clinical findings, supportive investigations and excluding alternative diagnoses.

Ophthalmic Investigations

Investigations include fundus photographs and wide field clinical photos to document the disease at presentation. Autofluorescence may be an additional tool in paediatric VKH syndrome as it is non-invasive, where diffuse hyper and hypoautofluorescence may be noted in the acute phase of serous retinal detachment due to blocked signal.[37] In chronic phase, granular hypoautofluorescence may detect areas of RPE loss or damage, but hyperautofluorescence pattern may be noted due to complications like cystoid macular oedema, RPE proliferation and subretinal fibrosis.[38,39] Since it helps evaluate the health of RPE, it may have prognostic implications along the course of follow up.

Fundus fluorescein angiography (FFA) has several characteristic features in various phases that may help in establishing a diagnosis of VKH syndrome. Early phase of the angiogram in acute VKH may reveal characteristic early phase choroidal hypofluorescence, early pin point peripapillary hyperfluorescent dots, disseminated spotted choroidal hyperfluorescence (Figure 1d). The mid to late phases may reveal pooling of the dye underneath the serous retinal detachment pockets and optic disc hyperfluorescence (Figure 1e).[40,41] In the chronic stage of the disease, there may occur spotted hyper and hypofluorescence, retinal vascular hyperfluorescence and optic disc hyperfluorescence. Convalescent stage and chronic recurrent stage may additionally show retinal pigment epithelial migration leading blocked fluorescence and hyperfluorescent dots along the equator.

Indocyanine green angiography (ICGA) provides a detailed evaluation of **choroidal involvement,** which is a hallmark of the disease. Unlike fluorescein angiography (FA), which primarily assesses the retinal circulation, ICGA allows visualization of **choroidal vasculature**, detecting inflammation even in the absence of significant retinal findings. Hence it may be useful in early presentations where the inflammation may not be as marked and in atypical cases with asymmetric presentations where the other eye may show subclinical inflammation. In acute VKH syndrome, ICGA may show delayed choroidal perfusion and the presence of

multiple hyperfluorescent dark dots which correspond to choroidal inflammation and granuloma, noted in the early and mid phases.[42] Late phases of ICGA may reveal choroidal vascular staining or leak due to ongoing inflammation, segmental hyper and hypofluorescence. In chronic VKH syndrome, ICGA may reveal choroidal atrophy with choroidal vascular thinning. Persistent hypofluorescent dots on ICGA in the absence of inflammation clinically, while on treatment has been suggested to be a marker for subclinical disease activity.[42,43] Performing ICGA and FFA may be challenging in children due to the invasive nature of the investigations.

Optical coherence tomography (OCT) is a non-invasive imaging tool in diagnosing and monitoring **paediatric VKH syndrome.** It helps assess structural changes in the retina and choroid, aiding in both early detection and disease progression monitoring. In the **acute phase**, OCT typically reveals **serous retinal detachments** often appearing as **multifocal or septate cystic spaces along with undulations of the retinal pigment epithelium**.[44] Additionally, **choroidal thickening**, a hallmark of VKH, can be detected using **enhanced depth imaging OCT (EDI-OCT)**, reflecting inflammation of the choroidal stroma.[45] As the disease progresses into the **chronic phase**, persistent inflammation may lead to **retinal pigment epithelium (RPE) alterations, outer retinal atrophy, and choroidal thinning,** which can contribute to long-term visual impairment.[46] Hyperreflective dots within the retina and subretinal space, likely representing inflammatory cell infiltrates, are also commonly observed. OCT is also useful for monitoring **treatment response**, as resolution of serous retinal detachments and retinal pigment epithelium undulations, along with reduction in choroidal thickness correlate with disease control, while persistent outer retinal disruption may indicate a higher risk of recurrence or poor visual prognosis. It is also invaluable to diagnose complications such as sub retinal neovascular membranes and fibrosis in late stages.[47,48] Given its **non-invasive nature and ability to detect subclinical disease**, it is a very reliable investigation in children where it may be difficult to obtain FFA or ICGA.[14]

Ultrasound B-scan may demonstrate diffuse choroidal thickening and also delineate exudative retinal detachments involving the posterior pole and inferior retina, vitreous inflammation and scleral thickening posteriorly.[49] It may also be useful when fundus examination is challenging due to media opacities.

Laboratory investigations may include complete blood counts, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) – acute markers of systemic inflammation, serology to exclude infectious causes (TB, syphilis), and other tests performed prior to starting immunosuppression such as liver and renal function tests. Lumbar puncture for cerebrospinal fluid analysis may reveal pleocytosis; however, it is not routinely performed in children due to the inherent challenges and invasiveness. It may be considered in cases with atypical presentations. Where available HLA typing may also be done to support the diagnosis, however, the diagnosis of VKH remains clinical and is independent of this.

Differential Diagnosis

Paediatric VKH syndrome shares clinical features with several other inflammatory and immune mediated disorders. The following conditions should be considered when evaluating a child with suspected VKH:

Sympathetic Ophthalmia (SO) – Like VKH, SO is a bilateral granulomatous uveitis, but it occurs following ocular trauma or surgery, usually with a history of penetrating eye injury.

Infectious Uveitis – Tuberculosis (TB)-associated uveitis can mimic VKH with choroidal inflammation and granulomatous anterior uveitis. However, a history of TB exposure, positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA), and the presence of systemic TB symptoms help differentiate it from VKH.

Sarcoidosis – Paediatric sarcoidosis can present with granulomatous uveitis similar to VKH. However, systemic findings such as hilar lymphadenopathy, lung involvement, and skin or joint manifestations may

suggest sarcoidosis rather than VKH. Serum angiotensin-converting enzyme (ACE), lysozyme levels and imaging studies may aid in differentiation.

Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) – This condition is characterized by multiple placoid lesions at the level of the retinal pigment epithelium, resembling early VKH choroiditis. However, APMPPE is often associated with viral prodromal symptoms and typically resolves spontaneously without leading to chronic inflammation.

Paediatric lupus choroidopathy – This has rarely been known to present with serous retinal detachments, although typically associated with other signs of retinal vasculitis and ischemic optic neuropathy.[50,51]

Posterior Scleritis – Posterior scleritis is usually unilateral but may rarely be bilateral when associated with a systemic disease. This condition can present with choroidal thickening and serous retinal detachments, mimicking VKH. However, pain is an important marker and B-scan ultrasonography often reveals flattening of posterior globe and a characteristic sub tenons fluid collection around the optic nerve head - "T-sign," which is not seen in VKH.[52]

Childhood Leukemias – Paediatric leukemias – specifically acute lymphoblastic leukemia and acute myeloid leukemia have been reported in literature to present with exudative retinal detachments among other signs which may be more specific to a blood dyscrasia.[53,54]

Diagnosis may not always be straightforward due to difficulties encountered with view to the fundus, difficulty in performing ancillary tests, cooperation to examination and late presentation. Evolution of disease may offer some clues to make a diagnosis of VKH along the course of follow up.[32]

Treatment

The treatment of **paediatric Vogt-Koyanagi-Harada (VKH) syndrome** aims to control intraocular inflammation rapidly, prevent disease progression, and minimize long-term complications**. High-dose systemic corticosteroids** are the first-line therapy, typically initiated with intravenous methylprednisolone or high-dose oral prednisone in conjunction with antacids. Early and aggressive steroid therapy can significantly reduce the risk of chronic inflammation and associated complications such as choroidal depigmentation and retinal pigment epithelium (RPE) damage. There is a strong association between **rapid corticosteroid tapering** and **recurrent inflammation** in children with VKH.[11] Corticosteroid use **in children** poses risks such as **growth retardation, cataracts, ocular hypertension, myopathy, and adrenal suppression. Additionally, immunosuppression may be warranted due to inadequate control with corticosteroids alone.** It is well established that **immunosuppressive agents** such as azathioprine, methotrexate, or mycophenolate mofetil are often required to achieve better inflammation control and reduce steroid dependency.[55] Most retrospective studies on paediatric VKH syndrome have reported nearly 70-75% of children may require additional immunosuppression.[13,25] Starting both corticosteroids and immunosuppressants sequentially or together may now be the norm in most tertiary centres worldwide.

For refractory or severe cases, several case reports have shown **biologic therapies** targeting inflammatory pathways to be useful. **Anti-TNF agents** like infliximab and adalimumab have been used successfully in steroid-resistant paediatric VKH cases.[56,57] Several case reports have additionally shown the efficacy of adjuvant anti-CD20 antibody – Rituximab, in controlling the ocular inflammation in cases of VKH syndrome in children.[33,58] These may be given with a multidisciplinary team consisting of paediatricians and rheumatologists as well, to help ensure **supportive measures,** including topical corticosteroids and cycloplegic agents, to help manage anterior segment inflammation and prevent synechiae formation. Regular monitoring with **optical coherence tomography (OCT) and indocyanine green angiography (ICGA)** allows for early detection of subclinical disease activity, ensuring timely treatment adjustments. Early and sustained immunosuppressive therapy improves

long-term visual prognosis and helps prevent irreversible structural damage. AlBloushi et al. emphasized that **timely and appropriate immunosuppressive therapy** in the early stages of acute VKH disease, especially before the onset of anterior segment inflammation, is essential for preventing **chronic recurrence** and related complications.[59] The response to treatment has been variable in literature ranging from benign course with good response to aggressive disease. Long-term follow-up is essential, as **relapses are common**, especially in paediatric patients. A recent study also noted the absence of long term complications in the group which present early before the onset of anterior segment signs, as compared with acute VKH cases associated with anterior segment inflammation or those with delayed presentation.[59]

Complications

Cataract and glaucoma are the most common complications in the paediatric age group. Cataract may be seen in as many as 35% of cases with posterior subcapsular cataract being the commonest, and glaucoma may be noted in at least half cases of paediatric VKH syndrome.[25,60] It has been well established in literature that cataract surgery may only be considered once adequate control of inflammation has been achieved and this control must maintained in the postoperative period as well, possibly with augmentation of immunosuppression. A minimum of 3 month inflammation free period has been recommended but this may have to be adjusted considering the case in question. The question of implantation of intraocular lens (IOL) with the cataract surgery has been debatable in children with uveitis. With the advances in cataract surgery techniques and treatment options for inflammation, the outcomes in various uveitic entities have been good in the recent literature. The cases where IOL implantation may be avoided may be the ones where there is active inflammation despite maximum medication, eyes with hypotony, rubeosis or when IOL related complications have occurred in the other eye.[61] These may not be specific for children with VKH syndrome which makes any recommendations difficult. There have been cases reported in literature where the outcomes were good post cataract surgery as well as those that need an IOL explantation to control inflammation.[25,62]

The presence of chronic posterior synechiae and in some cases anterior synechiae may cause raised pressures or secondary glaucoma, as well as the long term use of corticosteroids, either topical or systemic. The management of glaucoma may be with topical medication, with some cases needing a surgical intervention in various possible forms including filtering surgery or a tube implantation.[63] Hypotony may also be a possible complication in children with chronic disease. Epilens membranes have also been noted to occur in literature. The occurrence of band shaped keratopathy has varied in children with VKH syndrome, with some studies reporting it to be as high as 66%.[10,64] Poorly controlled VKH with prolonged inflammation can cause widespread depigmentation (sunset glow fundus, Figure 2a), leading to RPE hyperplasia and fibrosis (Figure 2b). Extensive RPE changes may further result in subretinal neovascular membranes (Figure 2c) and a further drop in vision, and these have been reported to be as high as 70% in children with VKH syndrome.

Although amblyopia is a concern in children, most case series have noted their cohorts of children to be beyond the amblyogenic age groups. However, this may be of significant concern in the very young or pre-school age, despite this being extremely uncommon in this age bracket. Amblyopia co-management with paediatric ophthalmology team, if available at tertiary centres is essential. Recurrence of intraocular inflammation have been noted to occur in most cohorts between 35-45%, anterior recurrence being the commonest reported. Anterior with posterior segment recurrence was noted to be as high as 50% in children with VKH in a series from Southern India.[25]

Paediatric vs adult VKH syndrome – as has been documented in literature (Table 1)

Parameter	Adults	Children
Presentation	Usually at onset of symptoms, early	Delayed presentation a possibility
Phase of VKH at presentation	Usually present with acute symptoms, acute uveitis	May present in any stage, including chronic recurrent
Clinical features - ocular	Neurosensory detachments in most	Depigmentation may be noted at presentation due to delay
Systemic features	Systemic manifestations in 60-85%[5,65]	-May develop systemic manifestations later, variable frequency 36-69%. -May be under reported.
Complications	All complications and recurrences reported	-Recurrences and complications may be higher than in adults -Amblyopia management may be necessary

Conclusion

Paediatric Vogt-Koyanagi-Harada (VKH) syndrome is a rare but serious condition that requires early diagnosis and intervention with corticosteroids and immunosuppressive agents, to control inflammation, reduce the risk of recurrence, and preserve vision. Although the condition is often associated with significant ocular complications, timely and effective management can significantly improve outcomes. Further research into the long-term effects of treatment, the role of biologics, and the potential for vision recovery in children with VKH is needed. Multidisciplinary care, including ophthalmologists, rheumatologists, and paediatric specialists, may be crucial to ensure optimal care for children with VKH syndrome.

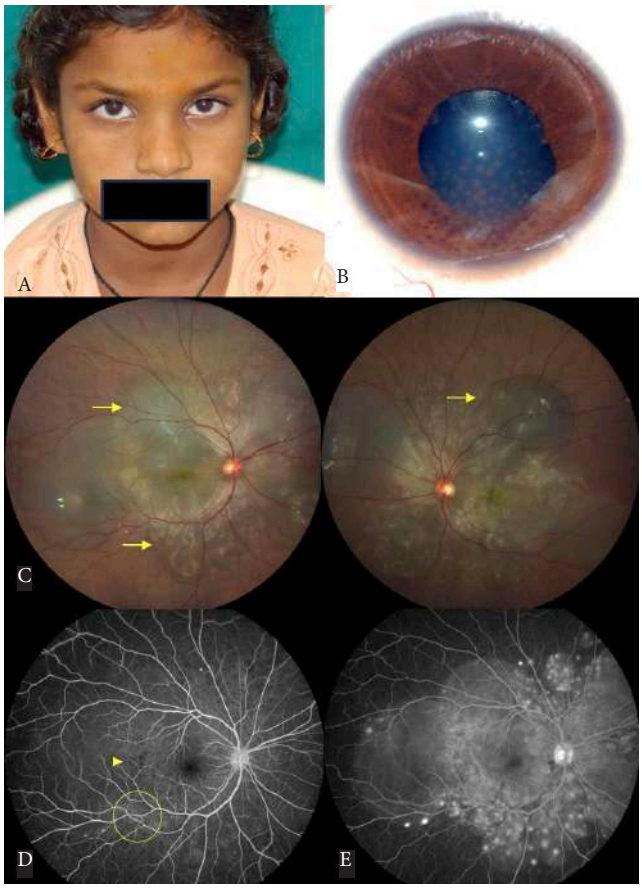

***Figure 1A**: Vitiligo on the cheeks of a child with VKH syndrome; Figure 1B. Granulomatous KPs; Figure 1C. Child with acute VKH syndrome presenting with bilateral multiple neurosensory detachments (yellow arrows); Figure 1D,E. FFA pictures of the same child showing multiple pin point hyperfluorescence (yellow circle) and patchy choroidal hypofluorescence (yellow arrow head) in the early phases, late pooling and leak*

***Image courtesy:** Prof. S.R. Rathinam, Aravind Eye Hospital and PG Institute, Madurai*

Figure 2: *Complications of VKH syndrome. Figure 2A. Child with VKH syndrome with bilateral sunset glow fundus and retinal pigment epithelial hyperplasia; Figure 2B. Sub retinal fibrosis and peripheral hypopigmented patches or Dalen Fuchs nodules; Figure 2C. Small peripapillary haemorrhage (yellow arrow) in an inflamed eye with VKH syndrome, showing the presence of a neovascular net flow signal on OCT angiography*

Image courtesy: *Dr. Mudit Tyagi, L.V. Prasad Eye Institute, Hyderabad*

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TINU (Tubulointerstitial nephritis and uveitis)

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Introduction

Tubulointerstitial nephritis and uveitis (TINU) is a rare and an underdiagnosed disease. It requires the collaboration of ophthalmologists, nephrologists, rheumatologists and sometimes pediatricians to confirm the diagnosis.

There have been many reports of its occurrence in children, in recent years.

Uveitis is usually mild and bilateral.

It was first described by Dobrin and his associates in 1975 and named Dobrin's syndrome. He described two young patients with bilateral non granulomatous uveitis, associated with renal failure. Other features included lymph node and bone marrow granulomas and hypergammaglobulinemia. Although most etiologies were ruled out, eosinophilic interstitial nephritis was noted.[1]

A meta-analysis conducted by Mandeville, nearly 25 years later, revealed a total of 133 patients. Uveitis preceded systemic involvement by up to 2 months in 21% cases or occurred after systemic involvement in 65% patients. Only 2 cases had granulomatous uveitis. [Table 1].[2]

Table 1

Mandeville criteria for Diagnosis of TINU[2]	
A. Diagnostic criteria for acute interstitial nephritis (AIN): • Histopathologic diagnosis • Clinical diagnosis: 1. Abnormal renal function (elevated serum creatinine or creatinine clearance) 2. Abnormal urine analysis 3. A systemic illness lasting 2 weeks, characterized by the combination of following symptoms and laboratory findings: a) Fever, weight loss, anorexia, malaise, fatigue, rash, abdominal/flank pain, arthralgia, myalgias b) Evidence of anemia, abnormal liver function, eosinophilia, or ESR 40mm/hr.	**B. Characteristics of Uveitis:** • Typical: 1. Bilateral anterior uveitis with or without intermediate uveitis or posterior uveitis 2. Onset of uveitis 2 months before or 12 months after AIN • Atypical: 1. Unilateral anterior uveitis or intermediate uveitis or posterior uveitis or a combination of these categories Onset of uveitis 2 months before or 12 months after AIN [2]

Definite TINU[2,6]	**Probable TINU[2,6]**	**Possible TINU[2,6]**
Bilateral anterior uveitis (Onset of uveitis 2 months before or 12 months after AIN) **AND** Interstitial nephritis on renal biopsy or complete clinical criteria	Atypical uveitis and positive renal biopsy **OR** Typical uveitis and incomplete interstitial nephritis clinical criteria	Atypical uveitis and incomplete interstitial nephritis clinical criteria

Epidemiology[2]
TINU mainly affects females, with a median onset age of 15 years.
Racial association-nil
Ethnic association- nil

Etiology and Risk Factors:
Certain **HLA genotypes** like HLA-DQA1*01, HLA-DQB1*05, and HLA-DRB1*01) increase the risk of developing TINU.[2]

Infection in a patient with AIN[2,4]
↓
Stimulates of T- Lymphocytes
↓
Activates B Lymphocytes
↓
Production of Anti mCRP antibodies (Modified C REACTIVE PROTEIN)[2,3]
↓
These anti mCRP antibodies act both on the kidneys and eye[2,3]

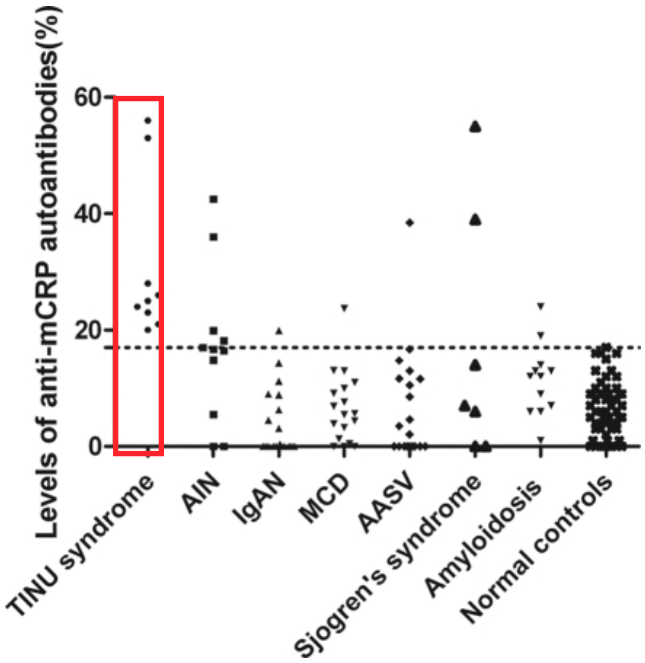

Chart from Tan Y and colleagues[3]

Drug Induced TINU: Hypersensitivity or hapten induced cytokine production with immune reaction, to certain medications may trigger the onset of TINU. Amoxycillin, cephalosporines, azithromycin, and non-steroidal anti-inflammatory drugs have been reported in this regard.[4]
The related drugs include beta lactams, amoxicillin, cephalosporins, azithromycin etc.[4]
TINU syndrome has been documented in the following individuals-
Reactivation of the herpes zoster virus
Infection with Epstein–Barr virus
Systemic toxoplasmosis
Positive PPD skin tests
Along with systemic conditions such as hyperthyroidism, hypoparathyroidism, and rheumatoid arthritis.[2,4]

Clinical Presentation
Systemic Features[2,4]
Fever
Weight loss
Fatigue, malasie
Weakness
Abdominal / flank pain.
Arthralgia, myalgia, headache
Polyuria, nocturia

Ocular Featrues
(Usually Bilateral And Non Granulomatous Uveitis)[2,4]
Eyepain, redness
Blurred vision
Photophobia
ANTERIOR SEGMENT: Ciliary congestion (CCC), keratic precipitates, anterior chamber cells, flare.
There are evidences supporting intermediate, posterior and pan uveitis.

Complications[2]
Posterior synechiae
Optic disc swelling
Cystoid macular edema , macular pucker and chorioretinal scar
Retinal detachment
Cataract formation

Diagnosis
A comprehensive eye examination can lead to a clinical diagnosis of ocular involvement. Additionally, urinalysis and serum tests for elevated beta-2 microglobulin, along with proteinuria, may reveal the presence of eosinophils, pyuria or hematuria, urinary white cell casts, and normoglycemic glucosuria.[2,6]
An increase in blood urea nitrogen and creatinine indicates renal impairment.
A renal biopsy is necessary to establish a definitive diagnosis of tubulointerstitial nephritis (TIN).
The pathology report will show infiltrates of eosinophils and mononuclear cells while sparing the glomeruli.

Differential Diagnosis[2,5]
Conditions where uveitis and renal involvement is seen are the main differentials for TINU. These include non-infective causes such as Systemic lupus erythematosus , Sjogren's syndrome, Granulomatosis with polyangiitis (formerly Wegener's), Behcet's disease. Infective causes include Syphilis, EBV infectious mononucleosis, TB and Toxoplasmosis.

Treatment
Topical steroids are typically effective for treating anterior uveitis.[5]
Given the recurrent nature of the condition, it is advisable for these patients to have ongoing follow-up.[5]
If kidney function doesn't restore quickly, a brief period of high-dose intravenous or oral steroids is commonly administered.
It may be beneficial to collaborate with nephrology.
For cases of severe inflammation, immunomodulatory therapy that spares steroids might be necessary (azathiorpine, methotreaxate, cyclosporin, mycophenolate mofetil)[2]

Prognosis
Uveitis may need a prolonged course of treatment and is known to recur in nearly 40% of those affected.[2,5]
Nephritis resolves spontaneously or with minimal treatment in most cases, with recurrences being rare.[5]
Overall, the prognosis is good with only occasional instances of renal failure or ocular complications.

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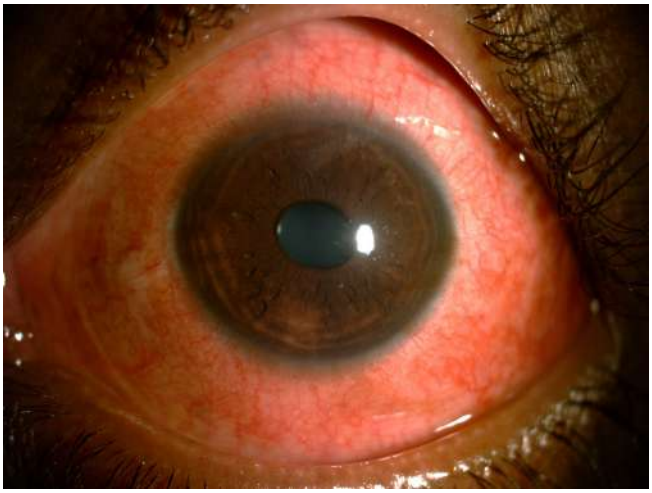

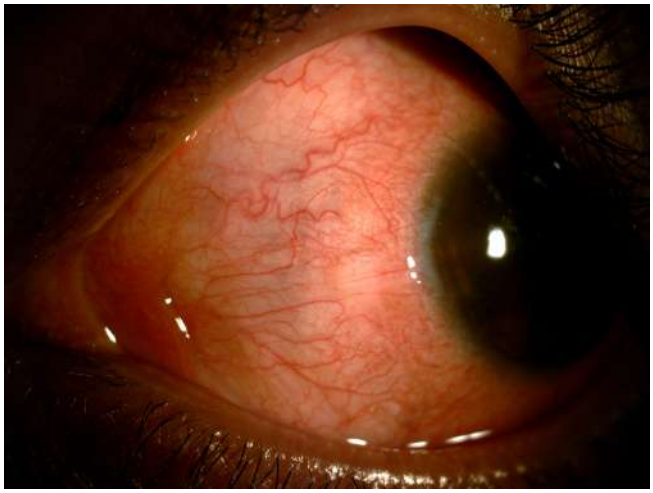

Figure 1 and 2: *Slit-lamp photograph of the eye showing circumcorneal congestion and anterior chamber inflammation in a biopsy confirmed case of tubulointerstitial nephritis and uveitis.*
Image courtesy: *Dr. Parthopratim Dutta Majumder, Sankara Nethralaya, Chennai.*

Trematode Granuloma

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Introduction

Infectious uveitis is the common cause of uveitis in developing countries like India. The occurrence of infectious uveitis has different geographical distribution in different parts of the country and knowledge towards these specific etiologies is important to make a definitive diagnosis and to give prompt treatment in these patients.

One such infectious disease is Trematode granuloma. Years of effort have been spent by ophthalmologist around the world to make an etiological diagnosis of this entity. Few decades back, children were presenting in clusters from localized geographical location with granuloma in the anterior chamber. They were being treated with anti -tubercular therapy with no improvement in the clinical picture. Such occurrence was established not only in our country but also in localized geographical belts all over the world with tropical climate. These children usually presented either with anterior chamber granuloma or sub-conjunctival granuloma. There was a temporal history of recent exposure to water bodies among these children. With the scientific developments in last few decades, an etiological diagnosis was made with the help of histopathological and molecular diagnostics. It was established that these granulomas may be secondary to trematode parasites.

Life cycle

This disease is caused by exposure to murky water infested with snails. The lifecycle of the trematode begins with birds. The adult worms are found in the conjunctival sac of the birds and are released when they come down in contact with the waterbodies. The eggs laid by these worms become miracidia while in water. They then get matured into cercariae in the intermediate host, the snails and again end in birds to complete

their cycle. Humans or usually children are accidental hosts and get infected when they play in these waterbodies infested with infected snails. The inflammation caused by the entry of cercariae leads to a granular reaction particularly in the eye.

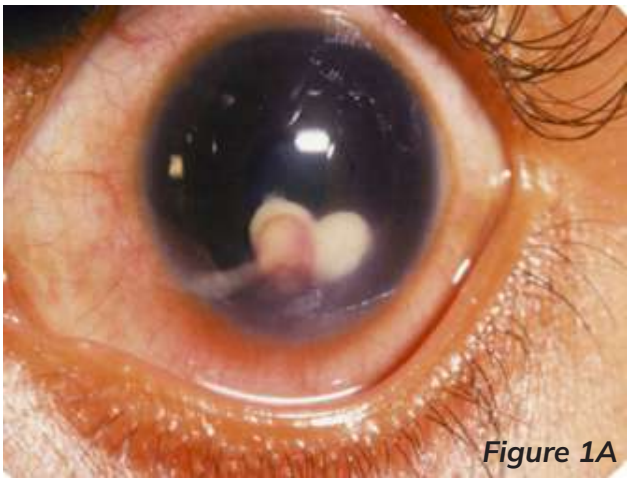
Clinical presentation

These are young children from particular geographical belt presenting with pain, redness or swelling in the eye. On detailed questioning, history of exposure to a water resource in the recent past can be established. They may have generalized itching or itching localized to the perioral area.

Signs:

Articles by Rathinam et al, have established that the clinical presentation may be unilateral or bilateral.

It may be chalazion like swelling in their lids, sub conjunctival granuloma and/or anterior chamber granuloma (Figure 1 and Figure 2).



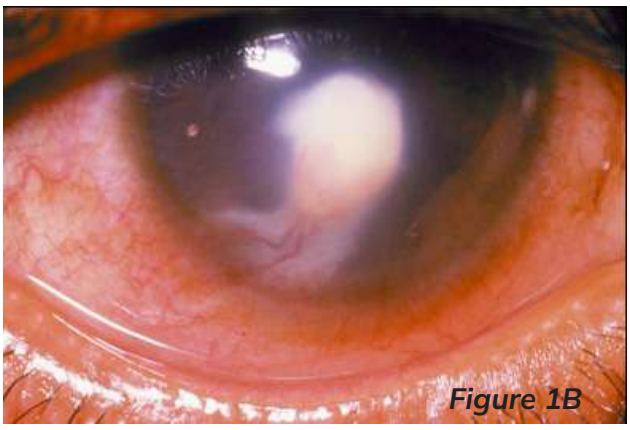


Figure 1A and 1B: *showing anterior chamber granuloma with retro-corneal membrane*

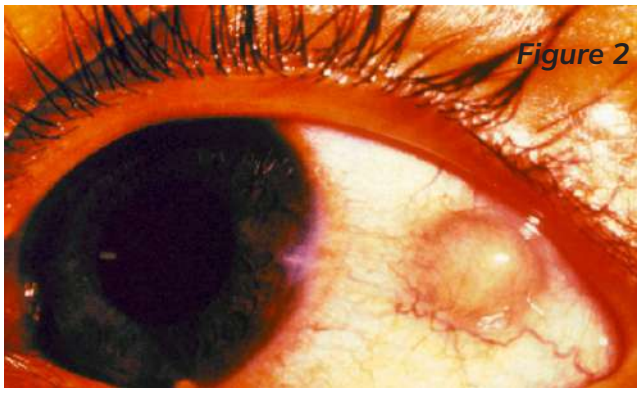


Figure 2: *showing subconjunctival granuloma*

When left untreated or when it is chronic they may present with

Cataract

Glaucoma

Retro corneal membrane

And even pthisis bulbi.

Few other studies have even discussed ciliary body granuloma and intermediate uveitis secondary to this disease.

Investigation

It is usually diagnosed clinically in these patients, particularly when the child presents from a geographical belt known to have the incidence of the disease. Ultrasound bio-microscopy has been done in few clinical studies which again confirms the existing clinical picture.

But the gold standard is confirmation with histopathological or molecular diagnostics. Histopathology in the excised granuloma shows Splendore – Hoeppli phenomenon. The granuloma may exhibit teguments of parasite in the center surrounded by inflammatory cells. Polymerase Chain Reaction is the investigation of choice in this era to confirm the diagnosis.

Systemic evaluation

Even in a clinical setting where the geographical location makes trematode granuloma as the primary etiological diagnosis in a patient, investigation to rule out other infectious and non -infectious causes should be done for completion.

The basic investigations are Complete blood count, Mantoux, Erythrocyte Sediment Rate and Serum ACE. Systemic imaging is done when appropriate.

Treatment:
Smaller lesions can be treated with topical and systemic steroids, while larger lesions may need surgical intervention.

Posterior sub-tenon steroid injection and cryotherapy has been tried in few studies. Oral Anti-helminthic medications were not proven to cause much of clinical improvement.

Above all its important to improve the knowledge and the awareness in general public to reduce the incidence and to prevent recurrence of the disease.

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Blinding Storm: A Case of Devastating Seasonal Hyperacute Panuveitis in a Young Child

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Introduction

Seasonal Hyperacute Panuveitis (SHAPU) is a rare ocular emergency unique to Nepal, with a seasonal outbreak in odd years, association with exposure to female white moths of the genus Gazalina (Lepidoptera)[1] and rapid progression resulting in blindness in ≤ 72 hours in a healthy person with subsequent eye shrinkage.[2,3] It is preferably found in children and more than 50% of SHAPU cases result in severe visual impairment or blindness with a great impact on the individual, families and society.[2] In Nepal, Pokhara Valley has been the place of the first report of SHAPU and has become the hotspot in every SHAPU outbreak. But herein we report a case of a 4-year-old boy from the south-eastern belt of Kathmandu with sudden onset of redness and decreased vision ultimately leading to unilateral blindness despite aggressive medical and surgical treatment. This case is an example of the ongoing scenario of SHAPU blindness in Nepal.

Case Presentation

A 4-year-old boy from Dhulikhel (southeast to Kathmandu) presented to us on 9th November 2023 with a sudden onset of right eye redness without discharge for 5 days. There was no history of trauma, foreign body entry, discharge, or eye pain. The child was comfortable but the mother noted red eye and whitish eye reflex so brought him to the local pharmacy and was finally referred to us for further management. On enquiry, the mother gave a history of exposure to her son to the white moths in their field, especially in the evening time.

Ocular examination revealed that he could only perceive light in his right eye, while his left eye had normal vision. He had a congested conjunctiva, a clear cornea, 4+ cells, and 4+ flares in the anterior chamber,

with fibrin tissue settling inferiorly. The lens was clear, but dense exudate was behind it, following the characteristic feature of "Red Eye with White Pupil," as shown in Figure 1. The posterior segment view was obscured for further evaluation.

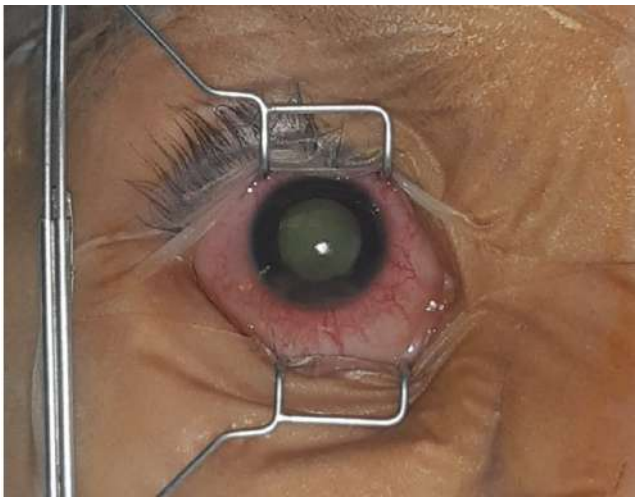

Figure 1: *Clinical photograph of the right eye under speculum with a classic presentation of the Red Eye with Leukocoria*

The ultrasonography B scan confirmed the presence of dense vitritis in the anterior and mid-vitreous with a flat retina. The right eye was digitally soft on palpation. The left eye examination revealed no abnormality. He was diagnosed with severe stage of Seasonal Hyperacute Panuveitis (SHAPU) and was admitted and blood investigations sent. He was immediately started on frequent dosing of topical antibiotics with steroids. His baseline blood investigations were all normal. On the next day, he underwent right eye diagnostic aqueous and vitreous tap followed by core vitrectomy with intravitreal injection (vancomycin 1 mg/0.01 ml+ ceftazidime 2.25 mg/0.01 ml, and dexamethasone 400 µg/0.01 ml) and subconjunctival gentamycin (40 mg/0.4 ml) and dexamethasone (4 mg/0.4 ml).

The ocular sample analysis was negative for Gram stain and KOH mount and yielded no growth in bacterial and fungal culture media. The residual ocular samples were stored at -40°C for the genomic study and cytokine analysis in future.

After a week, the vision was still perception of light but anterior chamber inflammation lowered, and anterior vitreous haze slightly decreased but retinal glow was still not visible. The eye was in a state of hypotony. USG B scan (Figure 2) showed high hyperechogenicity in the posterior vitreous suggestive of the possible inflammatory exudates but the retina appears relatively flat.

Figure 2: *Clinical Photograph of showing decrease in the congestion but presence of white pupillary reflex (left) and USG A+B scan showing the hyperechoic shadows in the posterior vitreous characteristic of* ***severe vitritis*** *(right)*

So repeat intravitreal injection was given, but this time, it was a 0.1ml cocktail regimen was preservative-free triamcinolone acetonide (4 mg/0.1 ml), dexamethasone (0.4 mg/0.1 ml) and of moxifloxacin (0.6 mg/0.1 ml) using a 30-gauge needle.

By the 10th week, the right eye had vision of only hand movement with onset of esotropia and atrophic bulbi and difficult to record IOP. Despite medical and surgical interventions, the sight and globe architecture were not able to be preserved.

Discussion

SHAPU is still a difficult and mysterious type of uveitic condition that remains a nightmare with potentially catastrophic consequence, particularly in children. Although surgery and vigorous anti-inflammatory plus antimicrobial treatment are essential, long-term ocular prognosis is guarded if the presentation is delayed by 48 hours like in this case. The predominance among children and painless nature of the disease and unilateral involvement are responsible for the delayed presentation of SHAPU.

It is necessary to distinguish this SHAPU case history from Ophthalmia Nodosa and HLA B27 arthritis, where mild forms of vitritis have been more common but dense vitritis is quite uncommon. It should also be distinguished from cases of exogenous or endogenous endophthalmitis by the absence of a history of trauma or surgery in individuals who appear healthy and do not exhibit noticeable eye pain.

With anecdotal links to female white moths of the genus Gazalina (Lepidoptera)[1]as

reported in this instance, the seasonal and regional pattern points to a potential environmental or vector-borne aetiology. Numerous white moths in the patient's surroundings raise interesting concerns about their possible function as carriers of microbiological pathogens or transmitters of the moths's toxins/chemicals that induce hyperacute inflammatory cascades within the eye.[2,3] Several chemicals, including histamine, acetylcholine, and formic acid, as well as numerous enzymatic components, including trypsin-like proteins, chymotrypsin-like proteins, serine protease, phospholipase, and esterase, have been reported in the Gazalina moth's setae.[4]

This case also highlights the importance of moth migration to the neigbouring regions of Kathmandu due to ongoing climate change crisis.

Even the slightest delay in presentation by 48-72 hours can guard the patient's visual prognosis due to the rapid intraocular tissue insult secondary to the cytokine cascades. And our case had presented after 5days, thus already inflammatory insults had happened within his eyes which could not be controlled with medical and surgical interventions.

Recent studies have suggested the use of long-acting and short acting steroids directly into the vitreous cavity as a powerful tool to fight the inflammatory cascade and halt the ciliary shutdown with improvement in vision and the rise in IOP.[5] But even this therapy could not help to reduce the inflammatory load within the child's eye probably due to delayed in presentation.

Prospects for the Future

We believe potential causal agent identification, genetic research and cytokine analysis can enhance the early diagnostic tool, and treatment regimen optimization—including potential preventive measures during peak seasonal occurrences—should be the main goals of future research in SHAPU.

Thus, future studies should concentrate on the following areas to enhance SHAPU diagnosis and treatment:

1. Finding possible causative agents (microbiological factors, moth toxins).
2. Using cytokine and genetic analysis to find early diagnostic signs
3. Improving treatment plans, including preventative actions during busy times
4. Research on how moth groups are affected by climate change
5. Evaluating the psychological effects of children's SHAPU-induced blindness
6. Assessing the Quality of Vision and life in the affected individuals

Conclusion

This article presents an acute presentation of SHAPU in a paediatric patient that necessitates urgent core vitrectomy and aggressive antimicrobial with anti-inflammatory therapy. This example underlines the need to spread awareness on the aggressive character of SHAPU in the various regions of Nepal and urge the need for early intervention. To pinpoint the precise aetiology, risk factors, and best management practices, more study is required including the influence of the climate on these moth habitats.

Moreover, future studies should also concentrate on the wider effects of SHAPU on patients' quality of life in addition to therapeutic and technological developments, especially in youngsters, who are the group most impacted by this illness. Research on the psychological effects of vision loss in SHAPU patients may help create more comprehensive treatment strategies.

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Diffuse Infiltrating Retinoblastoma Masquerading as Panuveitis

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Introduction

In ophthalmic literature, the term "masque rade syndrome" was first used in description of intraocular inflammation for conjunctival malignancy by Theodore. Retinoblastoma is the most common primary intraocular malignancy of childhood. It usually occurs in children below 5 years of age with most common presentation being leukocoria. Less common presenting signs include secondary glaucoma, hyphema and intraocular inflammation. Intraocular inflammation is associated with advanced cases of retinoblastoma or those with tumor necrosis and the Diffuse Infiltrative variety. Diffuse infiltrative retinoblastoma is seen in 1 to 2 percent of all the cases of retinoblastoma. It can present with anterior segment seeding termed as pseudo-hypopyon, hyphema or vitreous hemorrhage, endophthalmitis. Often, a complete dilated fundus examination suffices for diagnosis of a typical

retinoblastoma. Atypical presentations require additional information to establish the diagnosis.

Case Report

A 5-year-old systemically healthy boy and a non-contributory perinatal history with a 3-month duration of white reflex in the right eye was referred to our service with an office diagnosis of ruling out Behcet's disease in the background of total cataract, vitritis and secondary glaucoma. He was initiated on topical steroids and anti-glaucoma medications elsewhere. There was no history of trauma or TORCH complex association. On evaluation, the unaided Visual acuity was perception of light, accurate projection of rays confined only to superior quadrant in the involved eye with other eye acuity being 20/25 (Snellen). External examination ruled out facial asymmetry or obvious mass in periorbital area. Ocular exam under anesthesia revealed high IOP (32mmHg) despite being on anti-glaucoma medication, diffuse corneal edema, endothelial deposits, pseudo – hypopyon(2mm), total cataract (Figure 1A) and no regional lymphadenopathy. There was no view of the fundus in the involved eye while that of the other eye was unremarkable. Baseline evaluation for metastasis was negative. Ultrasound B – scan revealed low to medium density echoes in the mid, posterior vitreous cavity and an ill-defined echogenicity in the infero-temporal quadrant (Figure 1B). Ultrasound Bio-microscopy (UBM) showed ciliary body thickening with tumour deposits in the anterior chamber (Figure 1C). A contrast enhanced MRI of the orbits confirmed the presence of 7mm x 5mm, plaque like mass (Figure 1D) in the infero-temporal quadrant of uncertain etiology with no evidence of optic nerve involvement, choroidal invasion or extraocular extension. Factors such as age at presentation and clinico – radiological evaluation leaned in the favor of intraocular malignancy with high possibility of atypical presentation of retinoblastoma. In view of poor visual potential, rationale of life salvage superseding eye salvage, child underwent a primary enucleation with implant followed by histopathological evaluation. A systematic bread – loafing of the enucleated specimen confirmed diagnosis of moderately differentiated retinoblastoma with anterior chamber, angle, multifocal ciliary body infiltration, focal choroidal invasion (<3mm). However, resected optic nerve was free of malignant cells. Child was treated with protocol-based adjuvant chemotherapy with Vincristine, Etoposide and Carboplatin for 6 cycles on 3 – weekly basis followed by restoration of cosmesis with a custom fit ocular prosthesis. At 3 month follow up, the child is doing well.

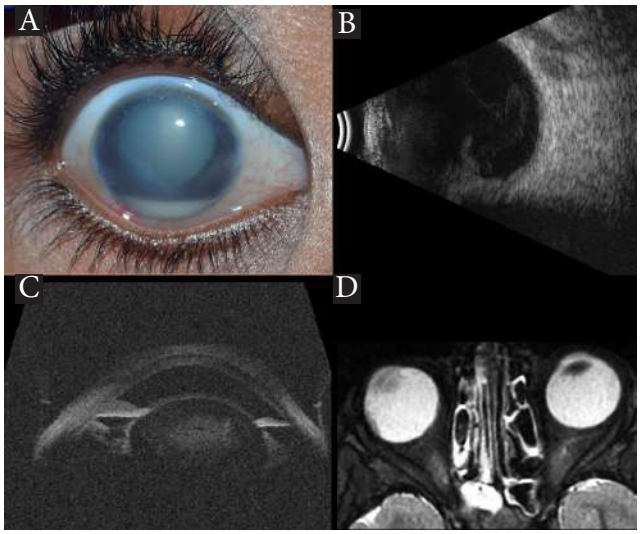

***Figure 1A**. Top left Right Eye of the child presenting with corneal edema, pseudo-hypopyon and total cataract, **Figure 1B**. Top right B-scan showing ill defined, low to medium echoes in the mid and posterior vitreous cavity, **Figure 1C**. Bottom left Thickening of the ciliary body with tumor deposits in the anterior chamber, **Figure 1D**. Bottom right T2 weighted image showing a plaque in the infero-temporal quadrant of the right eye.*

Discussion

Retinoblastoma is the most common pediatric intraocular malignancy[1]. It arises within the retinal layers and is known to have the endophytic, exophytic, mixed endo-exophytic, diffuse infiltrating pattern of growth or has been reported to show spontaneous arrest of growth[2]. In 1958, Ashton was the first to introduce the term 'diffuse infiltrative retinoblastoma' to describe a tumor with relatively flatter configuration and infiltrating the retinal tissue in the absence of a well-defined mass. Since then, many similar cases have been reported in the literature wherein the tumor tissue infiltrates the retinal layers without forming a typical white nodular or discernible mass in the vitreous cavity. Cases reported so far have known to involve one eye in contrast to a typical retinoblastoma

wherein bilateral involvement has been noted in 25-30% of the cases. In terms of laterality, our case also had unilateral involvement from the available literature. Clinically, most common presenting sign in a typical case of retinoblastoma is leukocoria, reported in 56 percent of the cases[3] while strabismus, hyphema, intraocular inflammation has also been documented[4]. In a Diffuse retinoblastoma, one of the initial presenting signs is an intraocular inflammation, often misdiagnosed and treated as uveitis[.]. Intraocular inflammation usually presents with signs of conjunctival injection, chemosis, cells in the anterior chamber, hypopyon and vitreous cells. In our case, absence of conjunctival signs was noteworthy. Nicholson et.al[6] have emphasized the importance of intraocular inflammation in an otherwise quiet eye be viewed with caution and retinoblastoma as a diagnosis be considered. Involvement of the anterior segment with presence of tumor cells in the anterior chamber in a preexisting case of retinoblastoma which is on or having completed treatment can be considered as a tumor extension. However, such a group of tumor cells when present on baseline evaluation can complicate diagnosis and subsequent decision making. Such cases have been primarily treated either as uveitis or endophthalmitis.[7] The mechanism for formation of the pseudo-hypopyon has been explained by Nicholson to be due to the non-cohesive nature of tumor cells and is pseudo-inflammatory. Although uncommon, it is likely to occur in cases of Diffuse Infiltrative retinoblastoma. Diffuse infiltrative retinoblastoma can involve the iris, ciliary body, trabecular meshwork and present with features of secondary glaucoma.[8]

In the absence of an optimal visualization of the tumor due hazy media or when additional information is needed, ocular imaging can be useful in not only establishing a diagnosis but also differentiating it from other simulating conditions. In typical retinoblastoma, an intralesional calcification is evident. This does not hold true with many cases of the diffuse infiltrative variant[9]. There was no evidence of intralesional calcification in this case. Other sonographic findings like retinal detachment, thickening of the retina and vitreous echo densities have been reported.[10] Our case showed the presence of hypo and hyper intense echoes in the vitreous cavity which was not consistent with calcium and could have been vitreous debris. A contrast enhanced MRI with low signal intensity, in T2 weighted, fat suppressed images maybe useful in better examination of the retinal leaflets.[11]

In a unilateral, diffuse infiltrative variant primary enucleation remains the treatment of choice and the need for adjuvant chemotherapy like any other case of unilateral retinoblastoma, depends on the presence of histo-pathological risk factors such as invasion of the anterior segment structures inclusive of trabecular meshwork, retrolaminar invasion of optic nerve, massive choroidal invasion(>3mm) and scleral extension.[12]

Conclusion

In summary, this pattern of growth is relatively rare. A child with features suggestive of panuveitis or endophthalmitis must be dealt with a high index of suspicion for a possible intraocular malignancy and treated on lines of retinoblastoma until proven otherwise.

Informed Consent: Parents' consent taken for pictures to be displayed or published.

Financial Disclosures: None.

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Imaging in Paediatric uveitis: Importance and Practical Guide

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Introduction

Paediatric uveitis accounts for approximately 5% to 10% of all uveitis cases, though the exact incidence in infants remains unknown. It is the third leading cause of blindness in children.[1] Diagnosis is often delayed due to the absence of verbal complaints or noticeable symptoms. Typically, a mother may observe a white spot in her child's eye, or the condition may be incidentally detected during a routine checkup. In children, concerns such as redness, leukocoria or strabismus

often prompt evaluation, by which time inflammation has usually been present for some duration. Uveitis in children is rare but can lead to severe visual impairment if not diagnosed and managed early. Its varied presentation and the difficulty of performing conventional clinical examinations present significant diagnostic challenges.

Recent advancements in wide-field digital fundus imaging and handheld optical coherence tomography (OCT) have improved early detection of uveitis in younger children, while multimodal imaging plays a crucial role in older children. Multimodal imaging aids in diagnosis, management, follow-up, and prognostication in all paediatric uveitis cases.

Wide-Field Fundus Imaging

Various wide-field digital fundus imaging systems, both contact and non-contact, are available. The most commonly used contact-based systems include RetCam™ (Clarity Medical System, Pleasanton, CA, USA) and 3Nethra Neo™ (Forus Health, Bangalore, India), which effectively detect anterior and posterior segment abnormalities in infants. These cameras capture approximately 120-130 degrees of the retinal field, and with careful scleral indentation and pupil dilation, even peripheral lesions can be identified. Importantly, these systems allow imaging in infants under topical anesthesia in a supine position, without requiring sedation in an outpatient setting. The ability to adjust color and contrast further enhances the detection of subtle vascular changes.

Non-contact fundus cameras, such as the MII RetCam (smartphone-based) and Optos™ Panoramic 200Tx imaging system (Optos PLC, Dunfermline, Scotland, UK), provide alternative options. Smartphone-based cameras have a restricted field of view, capturing a maximum of 90 degrees with an inverted image, whereas Optos captures approximately 200 degrees in a single, erect, pseudocolor retinal image. (Figure 3A and Figure 3B). The modified "flying baby position," where one arm supports the chest and chin while the other supports the head, has been demonstrated to facilitate the acquisition of ultra-wide-field images.[2]

A pioneering pilot study by Vinekar et al. utilized wide-field digital imaging to screen 1021 full-term neonates, revealing that 0.9% of otherwise healthy infants had vision- or life-threatening conditions requiring medical or surgical intervention. The study detected anterior and posterior segment abnormalities such as retinal vasculitis, salt-and-pepper retinopathy, and posterior synechiae.[3] Similarly, a 2011 case report highlighted how the detection of peripheral retinal vasculitis in a premature infant led to the early diagnosis of systemic candidial abscesses, prompting timely antifungal treatment and preventing severe complications.[4] Further evidence from Jayadev et al. in 2015 reinforced the role of wide-field imaging in detecting neonatal uveitis of infectious etiology, including toxoplasmosis, (Figure1A and Figure 1B), fungal infections, bacterial infections, tuberculosis, rubella, cytomegalovirus, and varicella retinitis.[5]

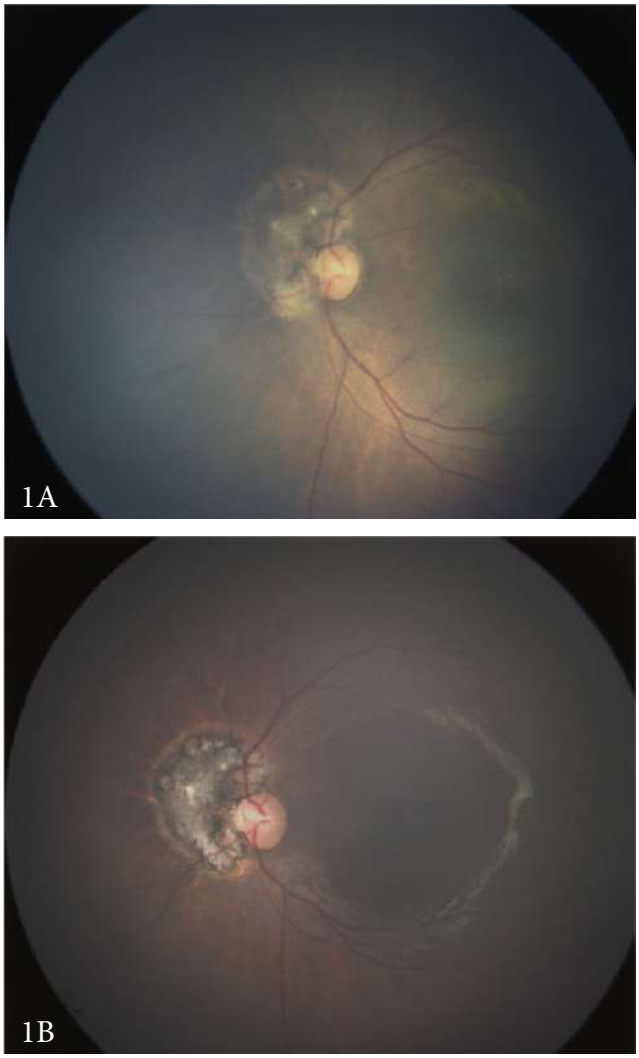


Figure 1: *RetCam™ colour fundus photograph images of the left eye of an infant showing peripaillary Jensens Retinochoroiditis (1A pre treatment and 1 B post treatment).*

Fundus Findings

Congenital Toxoplasmosis: Characterized by chorioretinal scars with reactivation at the lesion's edge, often involving macular, peripapillary, or peripheral regions with vitritis. Other ocular complications may include retinal detachment, optic nerve atrophy, cataracts, microphthalmia, microcornea, and nystagmus.[6,7] Congenital Rubella Syndrome presents with cataracts, glaucoma, microphthalmia, and stationary pigmentary retinopathy. The characteristic "salt-and-pepper" fundus appearance results from rubella virus interference with retinal pigment epithelium (RPE) development during embryogenesis.[8] CMV Retinitis may present with subtle flecks, retinal scars, optic atrophy, optic nerve hypoplasia, or coloboma, though active retinochoroiditis is rare.[9] Congenital ocular syphilis is typically manifests with vitritis, optic neuritis, and a "ground-glass" retinal appearance with vasculitis. Early stages may show multifocal chorioretinitis that gradually becomes confluent, leading to a bilateral "salt-and-pepper" fundus pattern. Endogenous endophthalmitis presents with unilateral or bilateral loss of the red reflex, corneal haze, hypopyon, and vitreous opacities. Fundus imaging and B-scan ultrasonography aid in diagnosis and treatment monitoring. Given its association with systemic infections, routine ocular examination should be integrated into neonatal care protocols for high-risk infants.[10]

Optical Coherence Tomography (OCT)

OCT is a non-invasive, non-contact imaging modality that provides high-resolution cross-sectional visualization of the retina and choroid, offering critical structural insights in uveitis. Spectral-domain OCT (SD-OCT) and swept-source OCT (SS-OCT) have significantly shorter acquisition times than time-domain OCT, making them particularly beneficial for imaging young children. The Bioptigen/Leica Envisu C2300 (Bioptigen Inc, Research Triangle Park, NC) is a portable SD-OCT system with a handheld probe, allowing flexible imaging. Proper pupil dilation, ocular surface lubrication, and manual focus adjustments are necessary for optimal image quality. Additionally, age-adjusted axial length reference tables should be used to ensure accurate imaging.[11] Optical coherence tomography (OCT) utilizes low-coherence interferometry to generate high-resolution cross-sectional images of the cornea, anterior chamber, retina, and choroid. Advances in OCT technology have significantly improved visualization of the posterior segment. However, traditional OCT and handheld OCT devices previously had limitations in adequately imaging the choroid. The introduction of enhanced depth imaging (EDI) in spectral-domain OCT and swept-source OCT, which allow for deeper tissue penetration, has made it possible to study choroidal changes in posterior segment pathologies associated with uveitis.[12]

OCT is well tolerated even in premature infants and plays a crucial role in diagnosing and managing uveitis, distinguishing it from masquerade syndromes.[13]Interpretation of infant OCT images requires an understanding of normal age-dependant changes. Unlike adults, infant OCT scans show a shallower foveal depression, persistence of inner retinal layers, attenuated photoreceptor layers, and absence of photoreceptor sublayers. Most of this thinning results from the centrifugal migration of inner retinal cells, which occurs between 31 and 42 weeks of postmenstrual age. Initially, the infant's PRL is thin, but as the infant matures, the photoreceptor subcellular structures undergo progressive centripetal growth, extending into the foveal center[14]

AS- OCT

Although juvenile idiopathic arthritis (JIA)-related uveitis predominantly affects the anterior segment, OCT has revealed macular edema and foveal detachment in some cases. Anterior segment OCT (AS-OCT) has also been instrumental in visualizing anterior chamber inflammation by detecting hyper-reflective cells[15]

A feasibility study demonstrated that AS-OCT is a reliable and well-tolerated tool for the quantitative evaluation of JIA-associated uveitis. A study by Akbarali et al. examined children with uveitis and healthy controls, showing that AS-OCT had a sensitivity of 91.7% and specificity of 85.7% in detecting anterior chamber cells when compared to slit-lamp examination.[16]

In Blau syndrome, where panuveitis can evolve from anterior uveitis, AS-OCT serves as a valuable non-invasive imaging tool for diagnosis and disease monitoring. A case report described two siblings, an 8-year-old girl and a 5-year-old boy, both genetically confirmed to have Blau syndrome. While the younger sibling was asymptomatic, AS-OCT revealed hyperreflective dots in the aqueous humour and on the posterior corneal surface in the older sibling, corresponding to anterior chamber cells and keratic precipitates.[17]

EDI-OCT

EDI-OCT has proven to be a precise, non-invasive tool for detecting and assessing choroidal granulomas (CGs), complementing indocyanine green (ICG) angiography. Increased transmission effects observed on OCT may aid in CG identification. (Figure 3F). Larger granulomas are typically full-thickness, round, well-defined, and display lower reflectivity compared to surrounding structures, often exhibiting an internal homogeneous pattern. The morphology and pattern of CGs can vary depending on the underlying disease. For instance, tubercular-related lesions often present with a lobulated shape and a nonhomogeneous internal pattern.[18] Choroidal thinning, resulting from inflammatory damage to the stroma and vasculature, can lead to choroidal atrophy and fibrosis, as seen in structural OCT imaging. This thinning is commonly observed in the chronic stages of disease (Figure 3E, Figure 3L and Figure 3K) and may indicate recurrent inflammation or inadequate inflammatory control. Late-stage choroidal thinning has been documented in conditions such as birdshot chorioretinopathy (BCR) and VKH, where choroidal inflammation is predominant. Interestingly, thinning has also been observed in conditions primarily affecting the anterior segment, such as Fuchs' uveitis.[19,20]

Balbaba et al. documented SD-OCT and FA findings in a cohort of 23 paediatric patients with Behçet's disease (BD) and ocular involvement, noting a significant increase in subfoveal choroidal thickness. This observation aligns with multiple studies in adults, where the thickening is attributed to choroidal effusion caused by an influx of inflammatory mediators during acute inflammatory episodes. Similarly, Ishikawa et al. analyzed 23 eyes from 13 patients with BD using EDI-OCT, finding a strong correlation between choroidal thickness and anterior, posterior, and overall inflammation scores. Following treatment with infliximab, a reduction in choroidal thickness was observed. Conversely, some studies have reported a decline in choroidal thickness, particularly in cases with prolonged disease duration and recurrent posterior uveitis. This reduction is believed to result from fibrosis within the choroid[21,22] Mahendradas et al have described the intraocular cysticercosis as hyperreflective dot surrounded by area of hyporeflectivity with hyperreflective margin by high-definition spectral-domain optical coherence tomography.[23]

OCT Findings in Congenital / Paediatric Uveitis: -

Toxoplasmosis: Active lesions show hyperreflective spots in the vitreoretinal interface, thickening of the posterior hyaloid, hyper-reflectivity of the neurosensory retina with posterior shadowing and choroidal thickening with hyporeflectivity. The scarring phase presents with retinal thinning and ellipsoid zone defects.[24] Preretinal round-shaped deposits as a potential indicator of toxoplasmic etiology, though other infectious causes, such as varicella-zoster virus (VZV) and syphilis, remain important differentials.[25]

Rubella: Resolution phase shows outer retinal atrophy with photoreceptor layer defects.[26]

Ocular Syphilis: Features include epiretinal membrane (ERM), cystoid macular edema (CME), and outer retinal layer loss. Post-resolution changes include retinal thinning, inner retinal disorganization, and secondary choriocapillaritis.[27]

CMV Retinitis: Inner retinal disorganization, hyperreflective deposits, and subsequent outer retinal atrophy post-treatment.[27]

Congenital Zika Syndrome: Findings include neurosensory retinal thinning, ellipsoid zone defects, hyperreflectivity beneath atrophic RPE, and coloboma-like excavation of the retina and choroid.[28]

Although OCT use in neonates is still evolving, it provides an objective assessment of treatment response and holds predictive value for visual recovery and prognosis.

Ultrasound Biomicroscopy (UBM)

Ultrasound biomicroscopy (UBM) utilizes high-frequency transducers, typically ranging from 50 to 100 MHz, to capture images of deeper structures up to 4 mm from the surface. This technique requires a coupling medium, such as saline or methylcellulose, which is placed over the eye in a customized cup while the transducer is immersed in it. UBM is particularly valuable for imaging the ciliary body in cases of uveitis and ocular trauma. However, unlike conventional ultrasound (USG), UBM often requires general anesthesia for paediatric patients.[29] UBM scanning is instrumental in assessing the ciliary body in uveitic eyes, aiding in the diagnosis of conditions such as atrophic ciliary processes and cyclitic membranes, particularly in uveitic cataracts.[30] In cases of presumed trematode-induced granulomatous intermediate uveitis (PTIGIU) that did not respond to medical treatment, surgical intervention was necessary, and UBM proved useful in evaluating the ciliary body region.[31]

Fundus Autofluorescence

Fundus autofluorescence (FAF) is a non-invasive imaging technique used to study diseases of the retinal pigment epithelium (RPE).[32] (Figure 3C, Figure 3D, Figure 3I and Figure 3J). Mahendradas et al. reported autofluorescence changes in unilateral acute idiopathic maculopathy, characterized by distortion of the normal foveal hypoautofluorescence in the left eye.[33] A trizonal pattern of autofluorescence has been observed in a 13-year-old boy with epilepsy and acute zonal occult outer retinopathy (AZOOR)[34]. Zaheer et al. demonstrated autofluorescence changes in four cases of relentless placoid chorioretinitis. Initially, the lesions exhibited hypoautofluorescence surrounded by hyperautofluorescence at the edges. Over time, the lesions progressively increased, with an appearance of hypoautofluorescence in the healed stage.[35]

Fundus Fluorescein Angiography

Fundus fluorescein angiography (FFA) is a critical diagnostic tool in the management of paediatric uveitis, particularly in identifying retinal vasculitis and assessing disease severity. FFA is invaluable in detecting retinal vascular abnormalities and inflammatory changes, which are essential for tailoring therapeutic strategies.

FFA is a powerful tool for confirming or detecting retinal vasculitis. Even when vascular sheathing is not visible, FFA can unveil inflammation by revealing leakage along the vessels, particularly in exudative vasculitis, such as in cases of sarcoidosis. Additionally, in occlusive vasculitis, like tubercular vasculitis or Eale's disease, FFA can identify capillary non-perfusion areas. Additionally, FFA can uncover unexpected vasculitis, as reported in a case of sympathetic ophthalmia.[36] Wide-field fluorescein angiography can reveal peripheral vascular leakage that might go unnoticed with standard imaging techniques[37] Apart from vascular pathology, FFA can also highlight choroiditis. In cases of choroiditis, FFA shows early hypofluorescence and late hyperfluorescence, although it may not be as sensitive as indocyanine green (ICG) angiography in detecting choroidal lesions. In serous retinal detachment, such as in Vogt-Koyanagi-Harada disease, FFA may show pinpoint leakage and pooling of dye in the late phase.

Additionally, FFA is useful in differentiating active inflammatory vitreous cells from old cells or non-inflammatory cells. In cases of active vitritis, FFA may show capillary leakage, as seen in intermediate uveitis (Figure 2A), whereas no vascular leakage will be observed in the presence of non-inflammatory cells in the vitreous cavity. A study by Hossain et al. characterized FFA features in paediatric uveitis, demonstrating that a standardized quantitative FFA scoring system can be useful in the characterization of uveitis in paediatric patients. The study found that the mean FFA score in anterior uveitis was lower than that in other categories, and the mean FFA score in the clinically active group was higher than that in the clinically inactive group. Worse visual acuity was associated with retinal vascular staining/leakage, retinal staining/pooling, and neovascularization elsewhere. Non-infectious uveitis more often demonstrated optic disc hyperfluorescence, retinal vascular staining/leakage, capillary leakage,

and pinpoint leaks, while infectious uveitis more often demonstrated retinal staining/pooling.[38] Beyond diagnosis, FFA is pivotal in assessing treatment responses. The ability to visualize the extent and nature of retinal inflammation through FFA allows clinicians to make informed decisions regarding the aggressiveness of treatment require. Quantification of vascular leakage may help in deciding whether to increase or decrease the medication to optimize the therapy.[39,40]

The application of FFA in paediatric patients presents unique challenges, primarily due to the need for patient cooperation during the procedure. Paediatric patients often struggle with remaining still, leading to suboptimal imaging results. This challenge is compounded by the need for mydriasis, which can be difficult to achieve in uncooperative young children. Recent advancements in imaging technology, such as ultra-widefield fluorescein angiography (UWFFA), have addressed some of these challenges. UWFFA allows for the capture of a larger area of the retina in a single exposure, reducing the need for patient repositioning and minimizing the time required for the procedure[41] Moreover, the use of oral fluorescein as an alternative to intravenous administration has been explored, which may reduce the anxiety associated with needle insertion and intravenous access[42] Studies have indicated that oral fluorescein is well tolerated in paediatric patients and can provide adequate imaging quality for clinical assessments.Intraoperative FFA has been utilized to guide treatment in children, allowing for the identification and treatment of retinovascular abnormalities that may not be visible through standard examination techniques.[43]

For fundus fluorescein angiography (FFA) in children, fluorescein dye is typically prepared by diluting 10% sodium fluorescein to minimize the risk of adverse reactions. The dosage is calculated based on body weight, with a standard recommendation of 5 mg/kg. In neonates and infants, further dilution may be necessary, and a slow intravenous (IV) push is advised to reduce the risk of nausea or anaphylaxis. The recommended IV dose is approximately 7.7 mg/kg, with a maximum limit of 500 mg.[44] For oral FFA, the recommended sodium fluorescein dosage is 7.5 mg/kg body weight, administered as either 20% fluorescein solution at 0.0375 ml/kg or 10% fluorescein solution at 0.075 ml/kg. To improve palatability, the dye is mixed with a small amount of liquid (e.g., juice or water) before administration. Fluorescence typically appears in the retinal circulation within 10–15 minutes post-ingestion. While oral FFA is generally well-tolerated and effective in paediatric patients, it produces slower and less intense fluorescence compared to IV administration.[45] (Figure 2B). While performing FFA in paediatric patients presents several challenges, advancements in imaging technology and techniques have significantly improved the feasibility and effectiveness of this diagnostic tool in managing paediatric uveitis. The integration of UWFFA and alternative administration routes for fluorescein has enhanced the ability to obtain critical diagnostic information while minimizing discomfort and anxiety for young patients. The use of a standardized quantitative FFA scoring system can further aid in the characterization of uveitis in paediatric patients and may prove valuable in assessing and managing these patients

Indocyanine green angiography (ICG)

Indocyanine green angiography is the gold standard imaging technique to evaluate, diagnose and follow up choroidal inflammatory lesions. It helps clinicians accurately identify the type and extent of choroidal vasculitis in the two key choroidal layers: the choriocapillaris and the choroidal stroma. Choroidal vasculitis is seen in nearly all cases of inflammatory choroidal involvement. In choriocapillaritis, it presents as vessel occlusion, while in stromal choroiditis, it appears as leaky vessels, leading to hyperfluorescence, blurred choroidal vessel outlines, and late diffuse stromal hyperfluorescence on ICGA. Systemic vasculitis conditions, on the other hand, tend to cause occlusive vasculitis affecting the larger choroidal vessels.[46,47]

Indocyanine green angiography (ICGA) is defined by two key properties of the ICG molecule used in this technique:[1] its fluorescence at approximately 830 nanometers (nm) in the near-infrared spectrum and its macromolecular nature. Indocyanine green (ICG) is a water-soluble dye that attaches to plasma proteins and

is injected intravenously. Unlike fluorescein angiography, it penetrates deeper, making it especially valuable for evaluating choroidal circulation and detecting inflammatory changes When the choroidal blood vessels are inflamed or damaged, they appear brighter than expected on imaging. In contrast, areas of inflammation within the choroidal stroma show up as darker spots because ICG dye spreads around these lesions instead of filling them[48,49] ICG angiography is a valuable imaging tool for diagnosing and monitoring paediatric uveitic conditions particularly choroidal inflammatory diseases. (Figure 4A-4E). The procedure involves injecting a weight-based dose of ICG (0.5-1.0 mg/kg, upto a maximum of 25mg) into a vein usually in the arm or hand. The dye is mixed with sterile water or saline and injected quickly over 3-5 seconds, followed by a 5-10ml saline flush to ensure it circulates properly. Before the test, it is important to explain the procedure to the child and their care givers. One must also check for iodine or shellfish allergies as ICG contains iodine. Imaging is performed using a confocal scanning laser ophthalmoscope (cSLO) or an ICG compatible fundus camera that captures how the dye moves through the choroidal blood vessels. Imaging begins immediately, recording different phases of the circulation-early choroidal filling (10-30 seconds), mid-phase staining (1-3 minutes) and late phase wash-out (10-30 minutes). After the test, caregivers should be aware that mild greenish urine discolouration can occur as the body clears the dye through bile. While allergic reactions are rare, monitoring for immediate side effects is essential. Proper hydration helps to flush the dye out faster.

However, like fluorescein angiography, ICGA can be challenging in children due to its invasive nature. Using orally administered ICG could help make the procedure more comfortable and easier for paediatric patients. In paediatric uveitis, ICGA plays a crucial role in detecting choroidal inflammation that might not be visible during a clinical exam or with fluorescein angiography. It helps identify hypofluorescent dark spots, which can indicate granulomas or reduced choroidal blood flow. This imaging technique is particularly useful for tracking inflammation in conditions like Sympathetic ophthalmia, Vogt-Koyanagi-Harada (VKH) disease and tubercular uveitis. By guiding diagnosis and treatment monitoring, ICGA supports timely intervention and helps optimize immunosuppressive therapy in children.

Inflammatory choriocapillaris non-perfusion or reduced perfusion appears as irregular, geographic regions of hypofluorescence. This pattern is observed in both primary and secondary choriocapillaritis, as well as in inflammatory choriocapillaropathies.

Knecht PB et al identified four key ICGA patterns associated with choriocapillaritis.[50]

Extension of hypofluorescence beyond the hypofluorescence of the actual infectious focus seen on fundus photography or FA that indicated perilesional choriocapillaris nonperfusion.

Small dark dots around the infectious focus that are termed ‘satellite dark dots’ (SDDs).

Multiple ‘confetti-like’ hypofluorescent areas or confluent hypofluorescent areas.

Widespread areas of nonperfusion involving large parts of the posterior pole and midperipheral retina.

Herbort, C.P. et al described the ICG angiographic signs in stromal choroiditis.[51]

Hypofluorescent dark dots (HDDs)

Indistinct choroidal vessel (Fuzziness of choroidal vessels)

Diffuse late choroidal hyperfluorescence (partially hiding HDDs)

ICGA disc hyperfluorescence (in severe choroiditis)

On ICG angiography, both active and healed lesions can continue to show hypofluorescence. Healed lesions may appear smaller and more irregular in shape, whereas active lesions will be larger, rounder, and more confluent.[52] ICG angiography has been found to closely correlate with visual function, particularly in visual field testing, unlike fundus examination or fluorescein angiography. It can serve as a highly sensitive tool for monitoring inflammatory choriocapillaropathies, providing valuable insights into disease progression and treatment response when intervention is needed.[53] Although ICG angiography is primarily used for diagnosing primary choroidal inflammatory diseases, it has

also been utilized in retinal conditions such as acute retinal necrosis (ARN). In these cases, it offers valuable insights into choroidal vascular involvement, helping to better understand the extent of the disease. Bissig A et al identified several distinct angiographic patterns, including [1] a characteristic triangular zone of reduced perfusion, [2] hypofluorescent lobular patches accompanied by areas of blurred choroidal vascular hyperfluorescence, and [3] isolated hypofluorescent lobular patches in the contralateral eye. Indocyanine green angiography can offer valuable insights into choroidal vascular involvement in acute retinal necrosis (ARN) and may help in the early detection of subtle, subclinical changes in the unaffected eye.[54] Gedik S et al investigated the ICG angiographic characteristics in active ocular Behçet's disease and found that ICG and FFA serve as complementary diagnostic tools. [10] While FFA is generally a reliable guide, some ICG findings are not detectable with FFA. However, these findings are neither specific nor pathognomonic. Despite their combined usefulness, the study did not recommend performing both procedures routinely for diagnosing Behçet's disease.[55]

Optical coherence tomography – Angiography (OCT- A)

OCTA is a non-invasive imaging technique used to analyze the retinal and choroidal blood vessels by assessing phase decorrelation within vessels across sequential images. This process captures changes in vascular flow over time5. OCTA creates maps that illustrate how pixel intensities in OCT images change, reflecting the structure of the vascular system after adjusting for various artifacts. Specifically, this technique relies on multiple OCT scans of the same region, conducted at speeds of up to 100 kHz, under the assumption that no structural changes occur between scans6. Any differences observed between the scans are interpreted as "movement" or blood flow. Typically, OCTA images are analyzed in an en face orientation after segmenting the volumetric data according to the selected tissue layer. The reference layer is chosen based on the specific types of lesions being studied.[1]

Acquisition and Analysis of Optical Coherence Tomography Angiography Images:-

OCTA images are acquired using software based on the split-spectrum amplitude decorrelation angiography (SSADA) algorithm. A built-in software grades the image qualities automatically from Q1 (worst) to Q10 (best). Automated layer segmentation of the superficial capillary plexus (SCP) ranging from internal limiting membrane to 10 μm above the internal plexiform layer (IPL), and the deep capillary plexus (DCP) ranging from 10 μm above the IPL to 10 μm below the outer plexiform layer is done· 3 × 3 scanning pattern, which is centered on the macular fovea, cross line mode, and/or enhanced HD line mode are commonly used The qualitative image parameters include the image quality grades and automatic segmentation accuracy.Tthe quantitative measurements included the foveal avascular zone area (FAZ),SCP vascular density (SCP VD), DCP vascular density (DCP VD) and subfoveal choroidal thickness (SFCT).

OCTA can depict changes in the vessel density of superficial or deep capillary in vasculitis but is not able to detect leakage like FFA. Previous studies of uveitis have demonstrated reduced capillary density.[56] Kim et al found that the density of parafoveal capillaries in the superficial retinal plexus was significantly lower in eyes with retinal vasculitis compared to healthy eyes. Furthermore, ocular inflammation was linked to a loss of parafoveal capillaries in the superficial capillary plexus, regardless of whether macular edema was present. OCTA can potentially be used to quantitatively measure the effects of intraocular inflammation.[57]

OCTA has recently been used to evaluate patients with various inflammatory diseases, such as Behcet's disease and Vogt–Koyanagi–Harada disease (VKH).[58,59] The non-invasive nature of OCTA renders it suitable for use in paediatric patients. Reports on optical coherence tomography angiography (OCTA) imaging in paediatric intermediate uveitis are limited. In adult patients with intermediate uveitis, OCTA imaging reveals a reduction in vascular density within both the superficial and deep retinal layers. Additionally, there is increased variability in choriocapillaris perfusion, which suggests that the microvasculature

of the macula is impaired.[60]

In a study by Soberon et al that involved five paediatric and four adult subjects with idiopathic intermediate uveitis, Optical Coherence Tomography Angiography (OCTA) successfully identified neovascularization and structural changes in blood vessels. However, it was unable to quantify the foveal avascular zone or detect inflammatory changes,such as vascular leakage[61] In a recently published review by Khochtali et al 14, the OCTA findings of a paediatric patient with pars planitis and macular edema showed an enlarged foveal avascular zone, dilated capillaries, and disorganization of the normal architecture in the capillary network at the deep capillary plexus.[62]

Qu et al recently conducted a retrospective study involving 32 paediatric patients with uveitis, with a mean age of 11.1 ± 2.2 years, alongside 30 matched normal controls whose mean age was 10.7 ± 2.4 years. The study aimed to assess the utility of Optical Coherence Tomography Angiography (OCTA) in paediatric uveitis. The findings revealed that the vascular densities of both the superficial capillary plexus and the deep capillary plexus were reduced in the uveitis patients compared to the normal controls. Findings confirm the persistence of subclinical inflammation in the posterior segments, along with a reduced vessel density and increased SFCT during a recurrence of anterior uveitis. The VDs in the SCP and DCP were significantly decreased in uveitic eyes, suggesting that these parameters may be sensitive indicators of inflammation in the posterior segments.[63]

B scan

Ocular ultrasound has gained space within the evaluation of ophthalmic lesions due to its characteristics as non-invasive method, easy reproducibility, low risk of complications to the patient and because it is more easily accessible than other imaging methods. In general, ophthalmic equipment is set to a frequency close to 8 MHz or above, which allows penetration into ocular tissues. The use of a high-frequency transducer (ranging in the studies reported from 7.5 to 20 MHz) seems to be the most suitable for better visualization and morphological analysis of the structures. [64]

Posterior scleritis

Posterior scleritis may be classified into diffuse posterior scleritis or rarely nodular posterior scleritis. The diffuse form causes generalised increased eye wall thickness, while the nodular subtype causes a scleral nodule. The latter usually causes an amelanotic subretinal mass, with adjacent subretinal fluid and chorioretinal folds. Nodular posterior scleritis can be misdiagnosed as an intraocular tumour or posterior uveitis. Misdiagnosis may lead to aggressive treatment methods such as with radiotherapy or chemotherapy. One of the cases reported had been misdiagnosed as choroidal melanoma and was referred for enucleation Shields *et al*. reported that posterior scleritis represented 1.5% of 400 lesions mimicking choroidal melanoma

B-scan ultrasonography revealed subretinal fluid and hyperechogenic nodular scleral thickening with underlying diffuse edema in Tenon's space.[65,66]

VKH

Consistent echographic findings included: diffuse, low to medium reflective thickening of the choroid posteriorly, serous retinal detachment, located inferiorly or in the posterior pole, mild vitreous opacities with no posterior vitreous detachment, thickening of the sclera and/or episclera posteriorly. Resolution of these findings occurred with systemic corticosteroid therapy. [67]

The applicability of ultrasound as a method of investigation, particularly in paediatric uveitis, for diagnosis, and follow-up, due to its characteristics such as fast exam time, being reliable, safe, low cost, free from radiation, providing excellent real quality images on time, allow dynamic evaluation, makes it a suitable option of choice in a rural set-up.

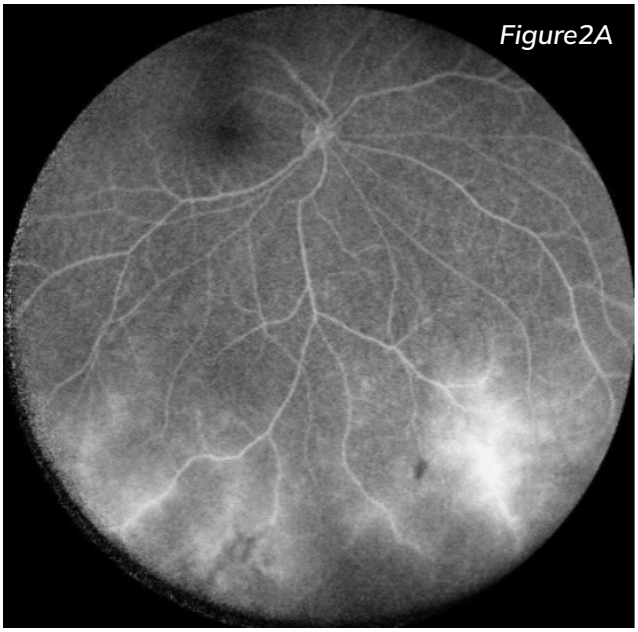
Morphological changes such as the presence of punctate echogenicities in the vitreous cavity and thickening of the choroid are important parameters to be analyzed for the diagnosis of uveitis, as well as association with inflammatory joint diseases as well as other uveitic entities.[68,69]

Conclusion

Early diagnosis is crucial, as untreated inflammation can result in severe complications, potentially leading to

permanent vision loss. It can also prompt systemic evaluations for congenital infections. Identifying inflammatory uveitic conditions may require a multidisciplinary approach involving ophthalmologists, paediatricians, infectious disease specialists, and rheumatologists.

Multimodal imaging is an invaluable tool for the early detection and management of paediatric uveitis. Wide-field imaging helps document fundus changes, while fluorescein angiography (FFA) remains the gold standard for diagnosing retinal vasculitis. Optical coherence tomography (OCT) is essential for assessing retinochoroidal diseases, and OCT angiography (OCTA) is particularly useful for detecting paediatric choroidal neovascular membranes (CNVM)



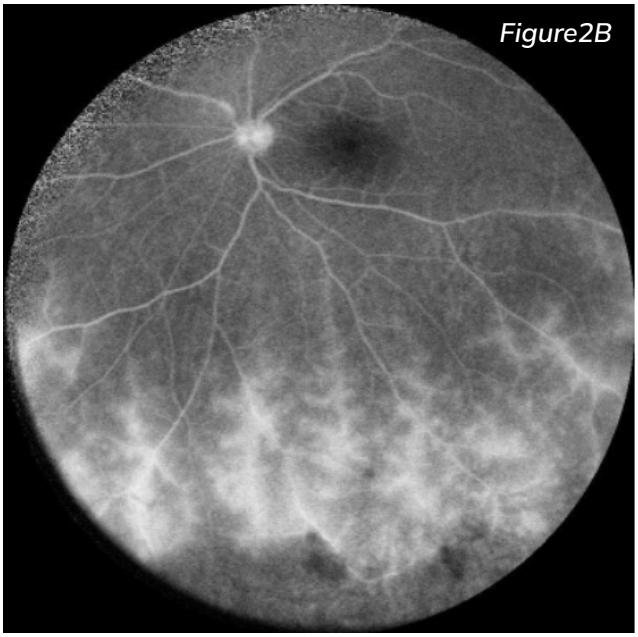
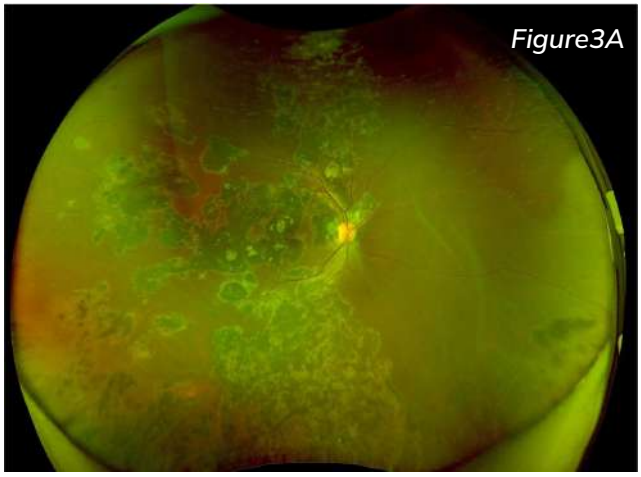
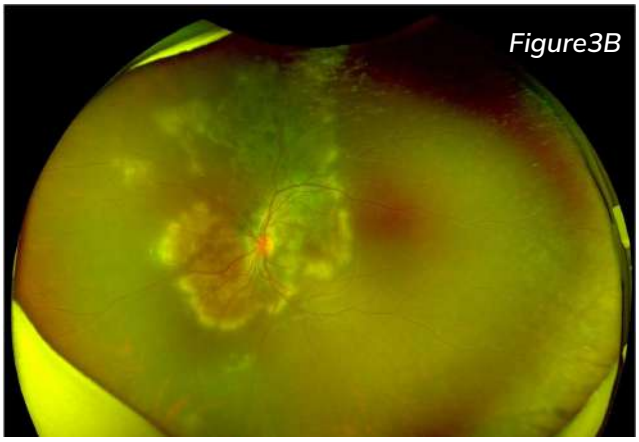
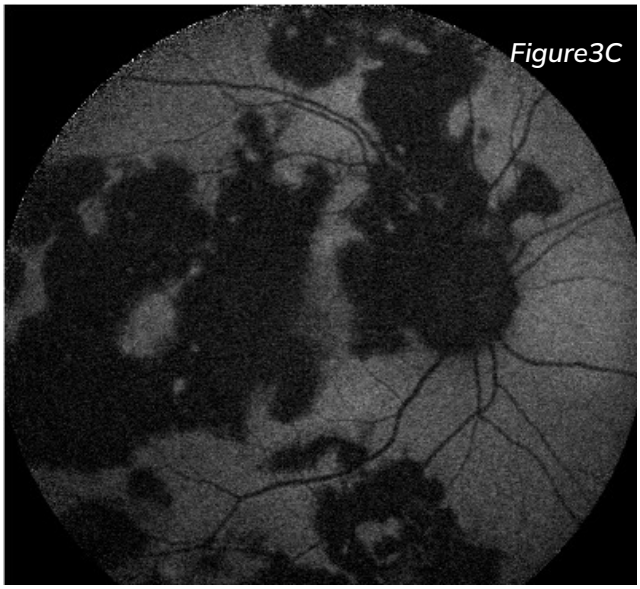


Figure 2: *A 13-year-old male presented for routine eye check-up. He was diagnosed with intermediate uveitis. His FFA shows inferior peripheral vascular leakage in both the eyes with disc hyperfluorescence and capillary non-perfusion areas in the left eye*







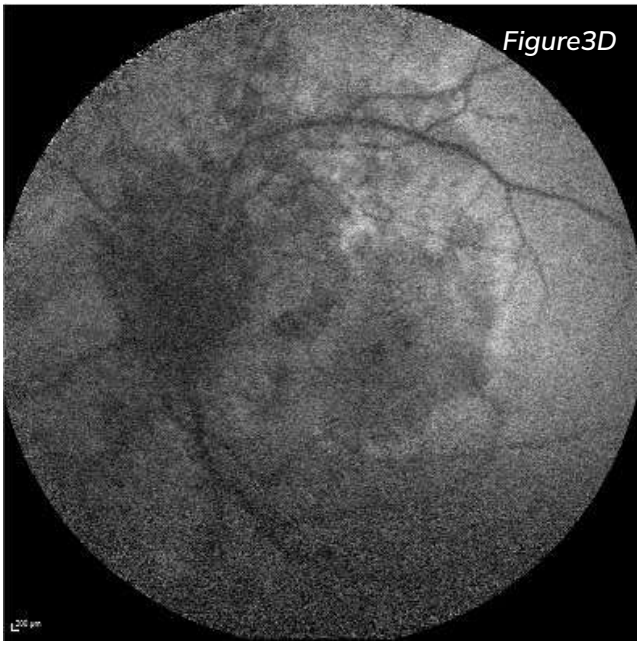
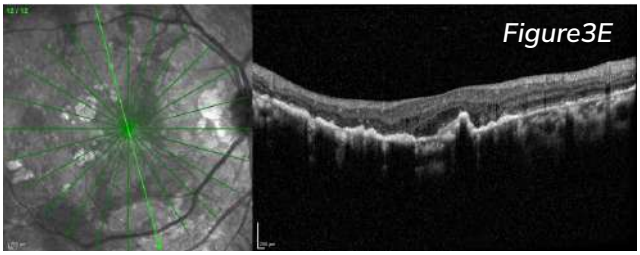


Figure3D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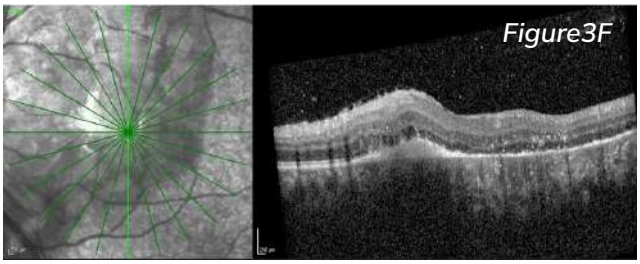
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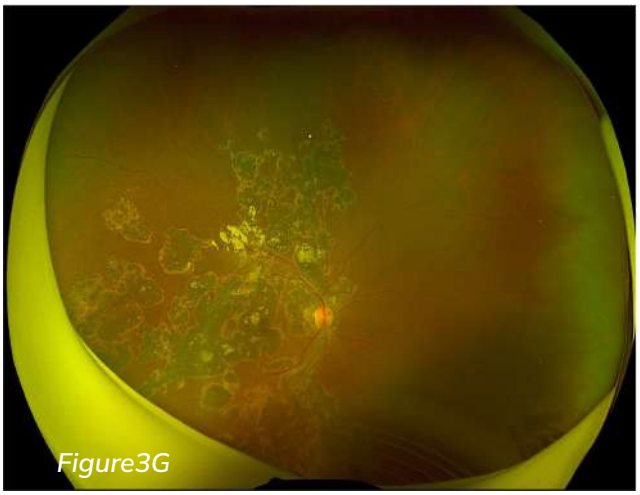


Figure3G


Figure3H

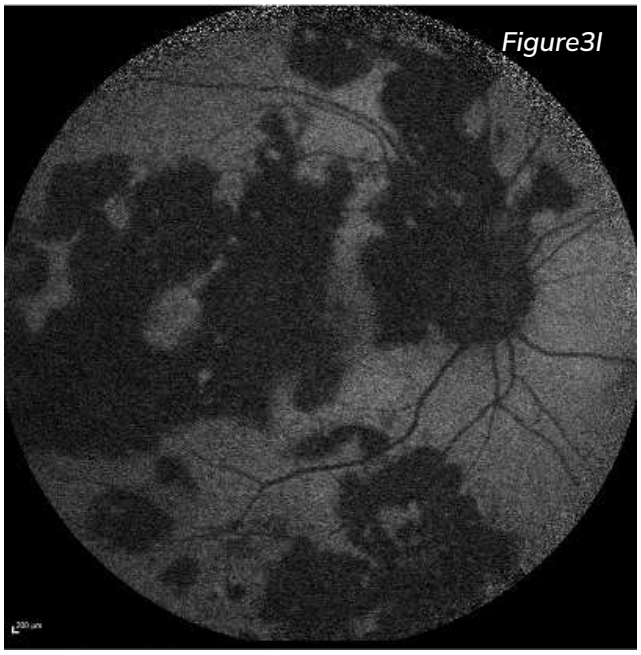
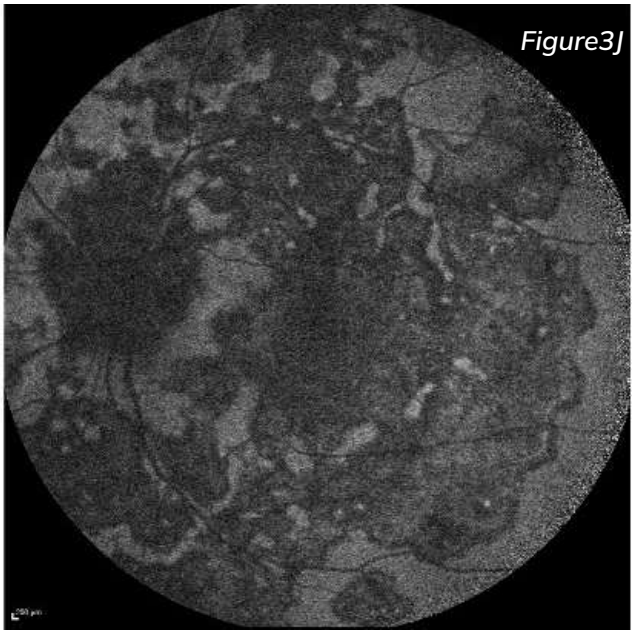


Figure3I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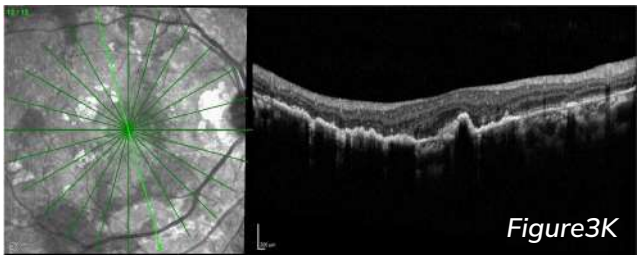


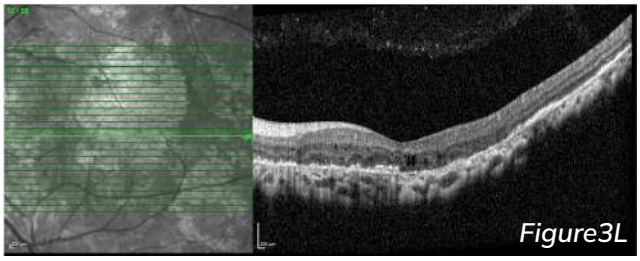
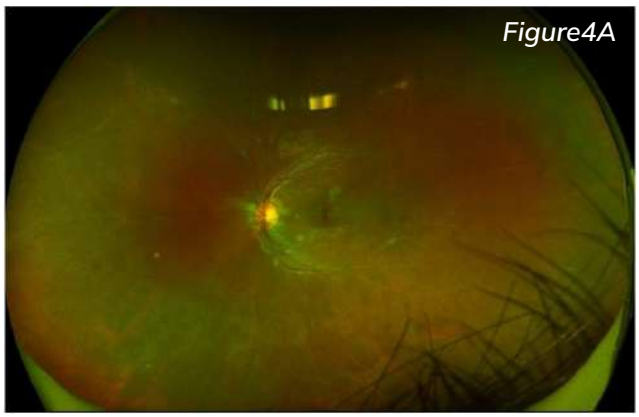
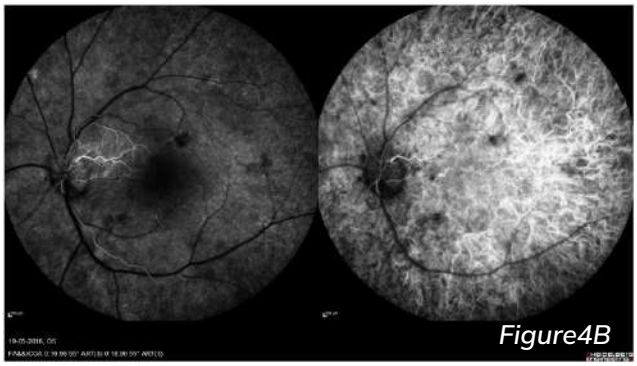
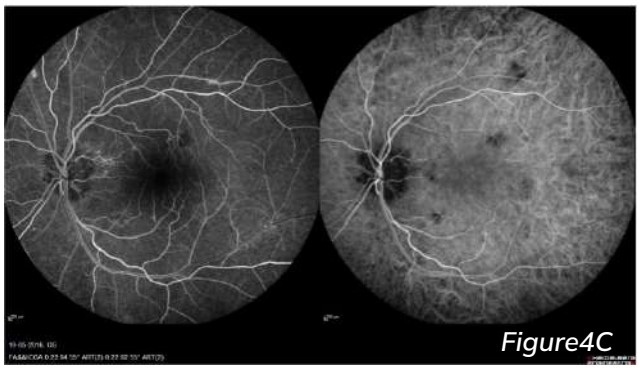
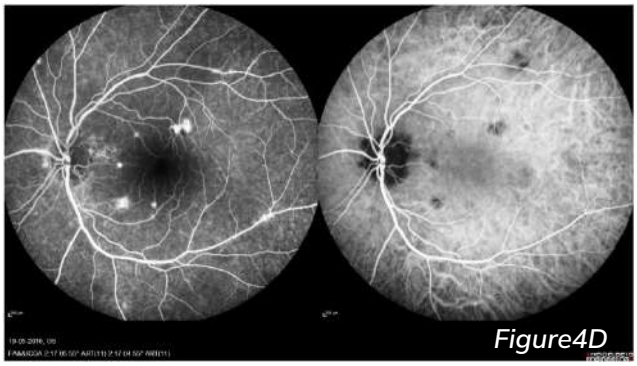


Figure 3**. A 12 years female child presented with the history of blurring of vision in the left eye. Optos TM colour fundus photograph revealed multiple healed chorioretinal scars in the right eye **(Figure3A)** and active choroiditis lesions along the margins of the lesions in a case of serpiginous like choroiditis in the posterior pole and midperiphery of the left eye **(Figure 3B)**. **Figure 3C**. Areas of hypoautofluorescence in the right eye. **Figure 3D**. Areas of hypoautofluorescence surrounded by areas of hyperautofluorescence in the left eye. **Figure 3E**. SDOCT right eye radial scan revealed outer retinal distorsion with irregular hyperreflectivity in the retinal pigment epithelium. **Figure 3F.** SDOCT of the vertical scan revealed hyperreflective dots in the posterior vitreous cavity, retinal and choroidal layers, with focal area of hyperreflectivity in the outer retinal layer suggestive of subretinal hyperreflective material (SHRM) with area of hyporeflectivity in the choroid. On follow up, OU hypoautofluorescence lesions in both eyes RE> LE **(Figure3I and 3J)**. OU hyerreflectivity in the outer retinal layers in both eyes with distorsion of ELM and ellipsoid zone. **(Figure 3K and 3L)









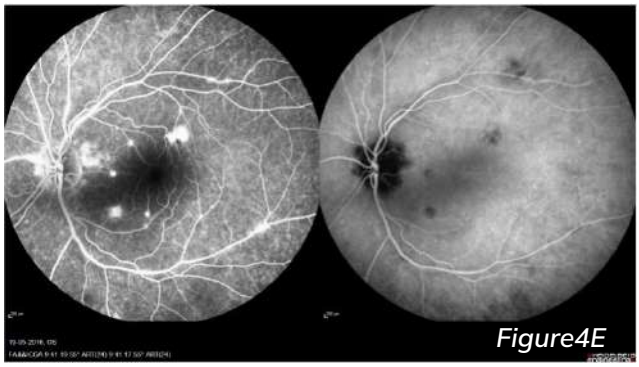


***Figure 4:** ICGA findings in a 10 year old boy who had right eye traumatic bacterial endophthalmitis leading to a blind eye following which he developed sympathetic ophthalmia. He developed choroidal granulomatous lesions with shallow retinal detachments on fundus examination **(Figure 4A)**. ICGA revealed multiple hypofluorescent dark dots (HDDs) in early **(Figure 4B)** to late phases **(Figure 4C)** indicating choroidal granulomatous inflammation. There is evidence of delayed or patchy choroidal perfusion suggestive of areas of ischemia. Late phase images show diffuse choroidal hyperfluorescence consistent*

with ongoing choroidal vessel leakage. There is peripapillary hypofluorescence highlighting optic disc involvement. These findings align with typical sympathetic ophthalmia (SO) features that are useful in monitoring response to systemic immunosuppressive therapy, as decreased HDDs ***(Figure 4D and Figure 4E)*** *and improved choroidal perfusion is often observed with treatment.*

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Blau Syndrome: A Diagnostic and Therapeutic Challenge in a Young Child

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1

Abstract

This case report highlights a young child with Blau syndrome presenting atypically as isolated uveitis. The patient, initially managed with corticosteroids and methotrexate, was later diagnosed through whole genome sequencing. Subsequent treatment with adalimumab and surgical interventions led to significant improvement. The case emphasizes the importance of early diagnosis and the role of immunosuppressive agents in managing Blau syndrome.

History

A 2-year-old boy was referred for bilateral uveitis and complicated cataracts. He had been treated with oral and topical corticosteroids, which provided partial improvement. Visual acuity at presentation was 20/800 in both eyes. Over the course of follow-up, the patient developed febrile episodes, joint pain, and maculopapular skin rashes. A referral to pediatric rheumatology and subsequent genetic testing confirmed Blau syndrome. A heterozygous missense mutation in the NOD2 gene was identified, consistent with the diagnosis.

Clinical Features

At presentation, the child exhibited signs of chronic anterior uveitis, including band-shaped keratopathy, posterior synechiae, and complicated cataracts. Fundoscopy

revealed sago grain-like retinal lesions in all quadrants. Initially, there were no systemic features such as arthritis or dermatitis, delaying the diagnosis. During follow-up, the patient developed joint pain with swelling, involving the wrists and ankles, alongside skin rashes characteristic of Blau syndrome. These findings completed the classic triad of arthritis, dermatitis, and uveitis.

Investigation

Blood tests revealed mildly elevated serum angiotensin-converting enzyme (ACE) levels, with slightly positive antinuclear antibody (ANA) titres. These findings were nonspecific and inconclusive. Whole genome sequencing confirmed a pathogenic NOD2 mutation, which provided a definitive diagnosis. Imaging, including ocular ultrasonography and rheumatologic assessments, further supported the diagnosis by excluding alternative conditions such as juvenile idiopathic arthritis.

Treatment

The patient's initial treatment regimen included topical and systemic corticosteroids, which temporarily controlled the uveitis. Methotrexate was introduced as a steroid-sparing agent, but inflammation recurred despite dose escalation. Progressive cataract formation necessitated surgical intervention. Pars plana vitrectomy and lensectomy were performed sequentially in both eyes after controlling inflammation for one month. The eyes were left aphakic to minimize the risk of postoperative inflammatory reactions, and the child was fitted with scleral contact lenses for visual rehabilitation.

The onset of scleritis and recurrent uveitis prompted the initiation of adalimumab, a tumour necrosis factor (TNF) inhibitor. The biologic agent resulted in significant improvement, with resolution of active inflammation and prevention of further relapses. The patient's corticosteroid dosage was gradually tapered and eventually discontinued. Regular follow-ups ensured compliance with immunosuppressive therapy and allowed for early identification and management of minor inflammatory episodes, which were treated with short courses of topical steroids and antiglaucoma medications.

Discussion

Blau syndrome is a rare autosomal dominant disorder caused by gain-of-function mutations in the NOD2 gene, leading to heightened NF-kB signalling and chronic inflammation. The syndrome is classically characterized by a triad of arthritis, dermatitis, and uveitis, but atypical presentations are increasingly recognized. In this case, the absence of systemic features at presentation delayed the diagnosis, emphasizing the importance of considering Blau syndrome in children with chronic uveitis.

Ocular involvement is the most significant cause of morbidity in Blau syndrome, often presenting as bilateral anterior uveitis that progresses to panuveitis. Complications such as cataracts, band keratopathy, and secondary glaucoma are common. Early and aggressive management is crucial to preserving vision. This patient's case highlights the challenges of managing chronic uveitis, particularly in pediatric patients, where compliance with treatment and monitoring are critical.

Methotrexate and corticosteroids are commonly used as first-line therapies in Blau syndrome. However, TNF inhibitors such as adalimumab have shown superior efficacy in controlling inflammation and preventing relapses. Adalimumab binds to TNF-α, inhibiting its interaction with cell surface receptors and disrupting the inflammatory cascade. This case demonstrates the effectiveness of adalimumab in achieving sustained control of ocular inflammation and highlights its role as a cornerstone of therapy in Blau syndrome.

Surgical intervention is often necessary to address complications such as cataracts and vitreoretinal involvement. In this case, pars plana vitrectomy and lensectomy significantly improved visual outcomes. Preoperative control of inflammation was critical to minimizing the risk of postoperative complications. Post-surgical rehabilitation with scleral contact lenses and amblyopia therapy further optimized the patient's visual potential.

This case underscores the importance of a multidisciplinary approach to managing Blau syndrome. Collaboration between ophthalmologists, rheumatologists, and

geneticists facilitated accurate diagnosis and effective treatment. Early recognition of atypical presentations and timely initiation of immunosuppressive therapy are essential to improving outcomes in this rare condition.

Conclusion

Blau syndrome can present atypically, posing significant diagnostic challenges. This case emphasizes the need for a high index of suspicion in pediatric patients with chronic uveitis. Genetic testing is crucial for confirming the diagnosis, and TNF inhibitors like adalimumab play a pivotal role in managing inflammation and preventing complications. Surgical interventions, when necessary, should be carefully timed to ensure optimal visual outcomes. A multidisciplinary approach is vital in achieving long-term success in managing Blau syndrome.

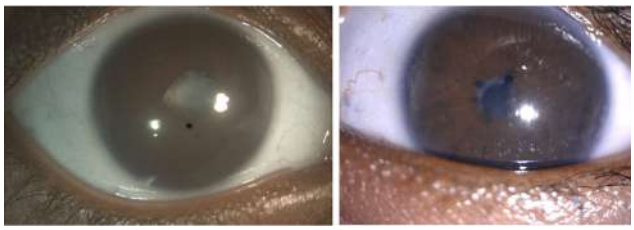

Figure 1: *At presentation*

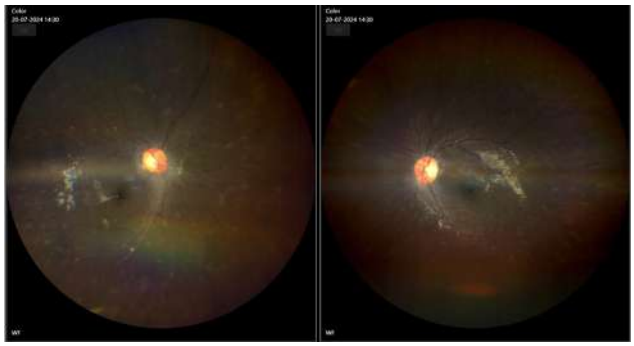

Figure 2: *Fundus appearance after lensectomy and vitrectomy*

The Sinking Eye: A case of Acute Retinal Necrosis with hypotony in a five-year-old child

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2

History

A five-year-old girl presented with complaints of redness in her left eye for two weeks. She had been receiving topical antimicrobial treatment elsewhere for conjunctivitis. But when her vision began to deteriorate, she sought a consultation with us.

Clinical features

On presentation, her best corrected visual acuity (BCVA) in right eye was 6/6 and 6/36 in the left eye. Intraocular pressure (IOP) in right and left eye were 14 and 16mm Hg respectively. Slit lamp and fundus examination of the right eye was within normal limit. Slit-lamp examination of the left eye revealed endothelial dusting with fine pigments, cells 4+, flare 3+ posterior synechiae and plenty of cells in the anterior vitreous. (Figure 1A) Fundus examination of the left eye showed dense vitritis. Dilated fundus examination revealed hazy media with hazy view of the disc. There was presence of coalescing tongue shaped retinitis lesions associated with vasculitis affecting 270 degrees of peripheral retina with retinal detachment in the inferior and inferotemporal quadrant. (Figure1A) A preliminary diagnosis of acute retinal necrosis (ARN) with retinal detachment was made and the child was investigated further.

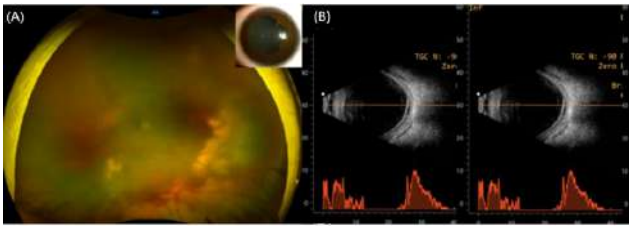

Figure 1A *Fundus picture of the left eye on presentation showing media haze along with retinitis patches and retinal detachment in the ITQ; Inset showing festooned pupil indicating inflammation.* ***Figure 1B****. Ultrasound B scan revealing reflective membranous echoes in ITQ suggestive of retinal detachment.*

Investigations

An ultrasonography B scan (USG) was done which revealed moderate vitreous opacities along with the presence of localized hyperechoic membrane in the inferior and infero-temporal quadrant persisting in low gain indicating localized retinal detachment. The presence of shifting fluid however could not be determined. (Figure 1B)

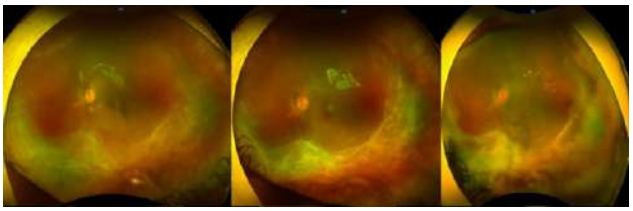

Figure 2: *Fundus pictures of the left eye following one month of treatment showing clear media, healed retinitis patches and re-attachment of the retina*

Treatment

The child was further evaluated by pediatric neurologist who ruled out central nervous system involvement and was admitted for intravenous acyclovir (500 mg/m^2). Four days later, the patient was taken up for left eye intravitreal ganciclovir (0.1mL) along with aqueous tap under general anesthesia. The aqueous aspirate was sent was for polymerase chain reaction for herpes simplex (HSV), Varicella zoster (VZV) and cytomegalovirus (CMV) analysis which detected 12,94,992 copies/ml of DNA of HSV genome. The patient was continued on intravenous acyclovir and gradually started on oral steroids (0.7 mg/kg/day). The patient was serially followed up and was continued on 21 days of intravenous antivirals along with oral corticosteroids. Successive ocular examination indicated reduction in the retinal detachment with successful control of inflammation. One month later, the retinitis lesions healed, and the retinal detachment settled (Figure 2) and the child maintained a vision of 6/36. She was continued on oral antivirals along with tapering oral steroids. At this time, her IOP in the left eye was recorded 2 mm Hg. She was started on intense topical steroids.

On further visits, the patient maintained a vision of 6/60 along with healed fibrotic areas of retinitis in the periphery. An optical coherence tomography revealed foveal thinning. (Figure 3) The hypotony persisted even after the use of difluprednate (0.05%) eye drops. Also, the patient had developed complicated cataract. Hence, she was taken up for left eye lens aspiration with vitrectomy, endolaser and silicon oil injection under guarded visual prognosis.

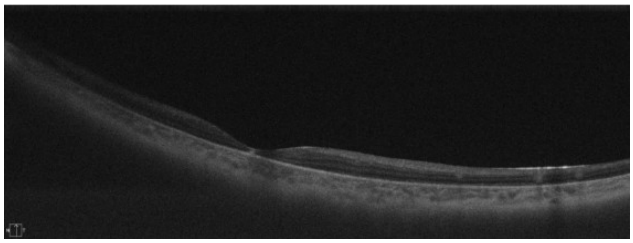

Figure 3*: Swept source optical coherence tomography (SSOCT) passing through the centre of macula revealing foveal thinning. The foveal thickness here was reduced to 45microns.*

One-month post-surgery, the patient maintained a distant vision of 6/60 with aphakic correction. Unfortunately, the hypotony still persisted with IOP of 2mm Hg.

At the final visit, the visual acuity and the retinal status were both maintained, and the patient was continued on topical difluprednate for hypotony.

Discussion

ARN is relatively a rare cause of viral retinitis in children and presents with multiple yellow confluent retinitis lesion in the periphery. Gradually these lesions coalesce 360 degree and progress eventually to the posterior pole if left untreated. In the initial stages, vision is not significantly affected and may go unnoticed unless a careful and meticulous fundus examination is performed. In children, the risk of misdiagnosing ARN increases severalfold, as they often cannot recognize early visual disturbances. Additionally, examining the fundus, including the peripheral retina, in

children can be challenging and requires skill and expertise. As a result, ARN can be misdiagnosed in its early stages, as seen in this case, and may present late to the uvea clinic. Chances of complications such as retinal detachment, secondary glaucoma, cataract formation are very high in children with ARN. The risk of involvement of other eye is also high in such cases which warrants systemic anti-viral treatment. Hypotony in one of the dreaded complications of any chronic uveitis including ARN . Persistent hypotony ultimately leads to pthisis causing complete loss of vision. Management of hypotony, which can occur after surgical intervention in ARN, is extremely challenging. The use of locally injected corticosteroids carries the risk of reactivating the viral infection, while the long-term use of systemic corticosteroids is limited due to their harmful effects in children. As a result, treatment options for managing hypotony in these cases are very limited.

A Case of Recurrent Choroidal Neovascular Membrane in a Child with Multifocal Serpiginoid Choroiditis

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3

History

A 12-year-old female child presented with diminution of vision in her left eye for 10 days duration. She had history of defective vision in her right eye since the age of 6 years and was treated as multifocal choroiditis earlier. She was investigated elsewhere and found to be positive for Mantoux and Quantiferon TB Gold. She was started on Anti-tubercular therapy (ATT) and has received 2 doses of intravenous (i.v) methyl prednisolone followed by which oral steroids were started.

Clinical Examination

At the time of presentation, her visual acuity was 6/60 in right eye and 6/18 in left eye. Intraocular pressure was 16mmHg in both eyes. Right eye had predominantly healed choroiditis lesions with 1+ vitreous cells. Left eye had mutton fat keratic precipitates, anterior chamber 1+ cells, vitreous 2+ cells with hyperemic disc and active lesion encroaching macula [Figure 1, A-F].

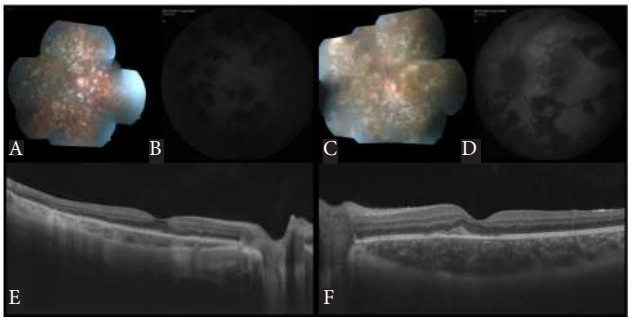

Figure 1A** shows OD Montage fundus picture with healed greyish white lesions involving the posterior pole and the peripheries with corresponding hypoautofluorescent patches in **Figure 1B.

Figure 1C *shows OS Montage fundus picture with healed greyish white lesions involving the posterior pole and the peripheries with few active lesions involving macula and the corresponding faint hyperautofluorescent lesions noted in autofluorescence* ***Figure 1D****.* ***Figure 1E*** *and F shows SSOCTA pictures of OD and OS respectively with formation of CNVM in OS*

Investigations

The PCR analysis for Mycobacterium tuberculosis done in aqueous sample was found to be negative. Color vision was defective in both eyes and visual field analysis showed scattered defects in right eye and superior defects with few inferior spill over in left eye. Based on the workup, she was diagnosed as bilateral multifocal serpiginoid choroiditis.

Treatment & Follow up

After paediatric consultation, she received full course of ATT and i.v steroids, followed by Mycophenolate Mofetil (MMF) and oral steroids. Two-month follow-up showed ocular activity in both eyes, requiring three doses of i.v steroids with increased dosage of oral steroids. MMF and ATT were continued. Subsequent review revealed 3+ vitreous cells in both eyes with active choroidal neovascular membrane (CNVM) in right eye, treated with two doses of intravitreal Anti-Vascular Endothelial Growth Factor (Anti-VEGF) injections. Five months later, left eye showed vision deterioration by 4 lines with 2+ vitreous cells and SSOCT showed presence of CNVM in both eyes [Figure 2].

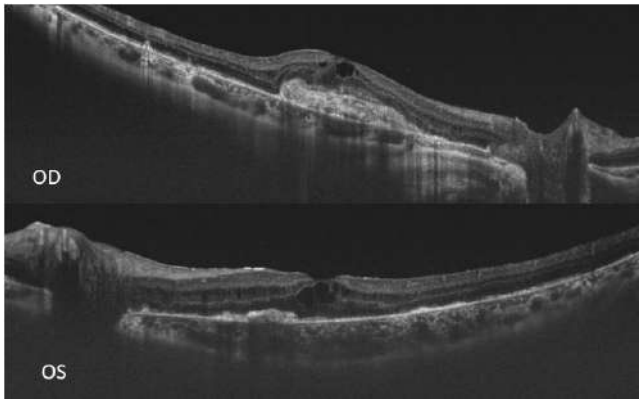

Figure 2: *SSOCT showing presence of CNVM in both eyes*

Hence, two doses of intravitreal Anti-VEGF injection were given in left eye. PSC in left eye necessitated cataract surgery. Four months post-surgery, OCTA done revealed compact fovea over scarred CNV in right eye and Chronic CME with subretinal fibrosis in left eye. FFA done showed late disc staining suggestive of inflammation [Figure 3] and was treated three doses of i.v steroids.

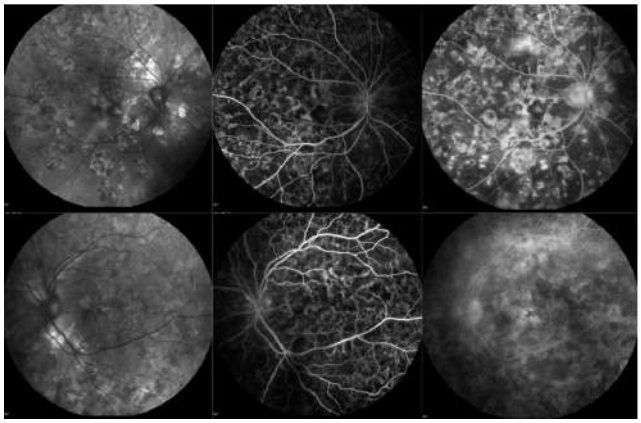

Figure 3: *OD shows central late foveal staining s/o scarred choroidal neovascular membrane. OS shows disc staining and leakage and cystoid pooling and staining in the late phase of the left eye*

T.MMF and Oral steroids were continued. On seven-month follow-up, both eyes were quiet with healed choroiditis and SSOCTA showed Regressed CNVM in both eyes [Figure 4].

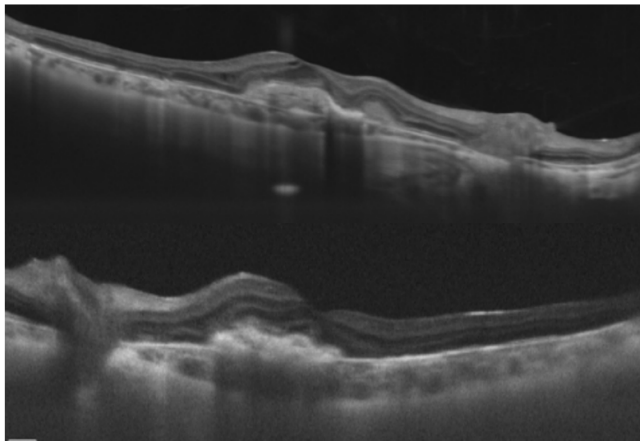

Figure 4: *showing OU regressed CNVM*

On the next follow-up two months later, vitreous haze with healed choroiditis was present. SSOCTA showed abnormal vascular network in right eye at the level of ORCC, requiring third dose of intravitreal Anti-VEGF. Patient was maintained on oral steroids. On follow-up 4 months later, inflammatory activity was more than CNV activity, prompting to restart T. MMF along with oral steroids. 6 months later on follow-up, visual acuity was stable and SSOCTA showed stable subretinal network in both eyes [Figure 5 a - h]. Oral steroids were stopped and T.MMF was continued. She is currently under observation and monitoring with Amsler chart.

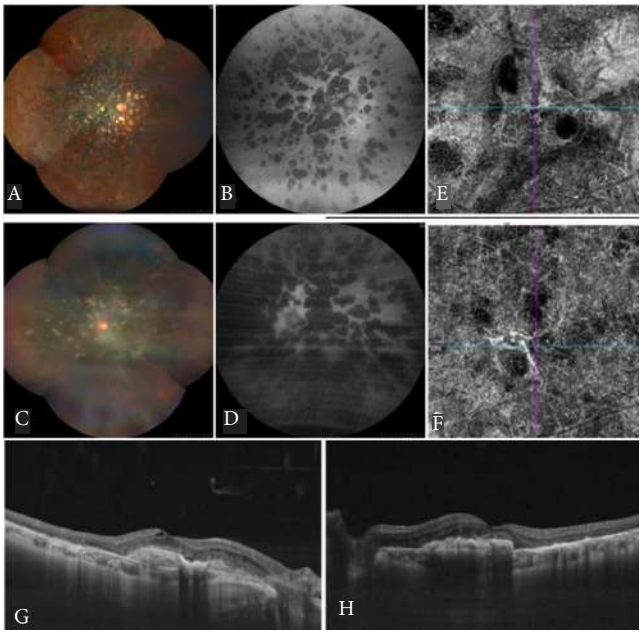

Figure 5A-D: *Montage fundus and autofluorescence pictures showing healed choroiditis.* ***Figure 5E-H****. SSOCTA OD shows stable subretinal network with compact retina over it with a few degenerative cysts and no subretinal fluid. OCTA OS shows stable subretinal network with minimal subretinal hyperreflective membrane over the scar and no subretinal fluid*

Discussion

Serpiginous choroiditis(SC) and Multifocal serpiginous choroiditis(MSC) are two entities which are part of the same spectrum but with phenotypic differences[1]. Multifocal serpiginous choroiditis is a chronic, progressive and recurrent disease with multifocality[2]. The ocular presentation in these cases of MSC is unilateral unlike our case which is bilateral. The median age of occurrence of MSC in Indian set-up is 30 years (range 18-57 years) [3]. Whereas our patient presented in her adolescence, which is a rare presentation. It is of utmost importance to differentiate SC from MSC in order to avoid unnecessary treatment with ATT in SC. The mainstay of therapy for MSC is systemic corticosteroids and ATT helps in reduction of recurrent attacks. In conditions of recurrent or relentless choroiditis like in our case, immunosuppressives are used[1,4].

Irrespective of whether its SC or MSC, the major complication impeding a good visual outcome is CNVM. Earlier study documented occurrence of CNVM in 13-35% of the study population[2]. The two-year incidence of CNV in patients with posterior uveitis is 2.7%. This risk increases in the presence of active inflammation and in bilateral posterior uveitis with presence of unilateral CNVM [5]. For evaluating and follow-up of the CNV areas in our patient, OCTA proved beneficial. The OCTA is helpful in obtaining high-resolution structural images of the retinochoroidal vasculature in MSC and the obtained information correlates well with other imaging modalities like Indocyanine green angiography[6,7]. Another study suggested that OCTA could even substitute ICGA during the subsequent follow-up visits owing to its excellence in reproducibility and non-invasive nature[8]. The investigative modalities are essential because once scarring sets in, the visual outcome is less satisfactory and affects the productive years of the patient[9]. The usage of Intravitreal Ranibizumab in our case contributed well to the regression of CNV. This therapeutic intervention is promising in terms of improvement in visual acuity and CNVM regression[10].

It is of utmost importance for prompt diagnosis of MSC, especially in a TB endemic country like India. Proper follow-up and monitoring of these cases with investigative modalities like SS-OCTA and ICGA proves helpful in identification of CNV early in its course, thereby providing appropriate treatment.

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Wrath of the Worms: Multimodal Imaging Depicting Disseminated Neuro-oculo-cysticercosis

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3

History

A 16-year-old girl presented to the ophthalmology clinic with complaints of progressive diminution of vision in her right eye for the past three months. There was no history of ocular trauma, prior ocular surgery, or any systemic illness. Her family history and past medical history was unremarkable. History of having contaminated food was uncertain.

Clinical Features

On examination, the best-corrected visual acuity (BCVA) in her right eye was reduced to hand movements, while the left eye had uncorrected visual acuity of 20/20, N6. Slit-lamp examination of the anterior segment in both eyes was unremarkable.

Fundus examination of the right eye revealed an inferotemporal cystic lesion accompanied by a combined retinal detachment. Surrounding the lesion, localized vitreous hemorrhage was noted, particularly in the inferior quadrant (Figure 1A). The left eye fundus appeared unremarkable with no focal lesions. Despite the absence of symptoms in the left eye, further imaging studies were warranted to rule out asymptomatic involvement.

Investigation

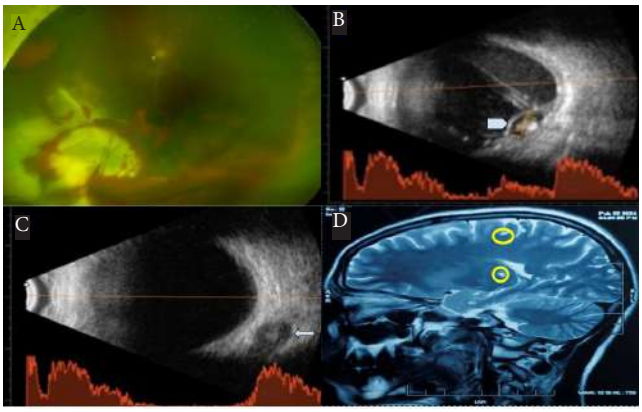
Ocular Imaging

B-scan Ultrasonography (Right Eye): The ultrasound B-scan revealed a well-defined intraretinal cystic lesion containing an enclosed scolex. Retinal detachment was noted, along with sub-membranous echoes suggestive of cysticercosis (Figure 1B).

B-scan Ultrasonography (Left Eye): Although asymptomatic, an orbital ultrasound was performed on the left eye, which revealed an intraconal cyst with a scolex (Figure 1C). The presence of a scolex was a significant diagnostic clue pointing toward ocular cysticercosis.

Neuroimaging

Magnetic Resonance Imaging (MRI) of the Brain: Given the red flag raised by bilateral ocular involvement, an MRI brain scan was advised to investigate possible systemic dissemination. MRI findings revealed multiple disseminated cystic lesions scattered throughout the brain parenchyma, suggestive of neurocysticercosis (Figure 1D).



Treatment

The patient was diagnosed with ocular cysticercosis in both eyes, with concomitant neurocysticercosis. A multidisciplinary approach was undertaken for management:

Ophthalmic Management

The patient underwent **surgical intervention** for the right eye to remove the cystic lesion. Surgical techniques such as pars plana vitrectomy (PPV) were employed to extract the intraretinal cyst and manage retinal detachment.

Postoperatively, the patient was closely monitored for any signs of inflammation or recurrence.

Systemic Treatment

Antiparasitic Therapy: Albendazole (15 mg/kg/day) was initiated for four weeks to eliminate any remaining parasites.

Corticosteroids: Oral prednisolone was prescribed to reduce the inflammatory response due to cyst degeneration.

Antiepileptic Therapy: Given the presence of multiple cysts in the brain, antiepileptic medications (levetiracetam) were started as a precautionary measure to prevent seizures.

Supportive Therapy: Nutritional counseling and hygiene education were provided to prevent reinfection.

Discussion

Ocular cysticercosis is a rare disease caused by infestation of *Taenia solium.* Disease contraction happens via consumption of contaminated food such as undercooked meat or even inadequately washed vegetables which may have egg of *Taenia solium. Taenia solium* gains access through circulation from the gut by penetrating gut wall. Once into circulation, it lodges at various spaces such as central nervous system, ocular structures such as vitreous, retina, subretinal space and orbit. Management includes mainly antiparasitic therapy, however that induces severe inflammation in surrounding tissue. Hence antiparasitic therapy needs additional systemic steroid treatment. If the inflammation by dying parasite is not controlled it can result in sequels of oedema such as convulsions, vitreous opacity, subsequent contraction and tractional complications in the eye. In the eye if exudative or inflammatory sequel have happened then surgical management needs to be undertaken.

Conclusion

This case highlights the pivotal role of ophthalmic manifestations in uncovering life-threatening systemic infections. The presence of bilateral ocular cysticercosis prompted further neuroimaging, leading to the diagnosis of disseminated neurocysticercosis. Early detection and timely intervention are crucial in preventing irreversible vision loss and systemic complications. Comprehensive evaluation and a multidisciplinary approach are essential in managing ocular cysticercosis effectively.

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Optimizing Treatment for Pediatric Occult Retinal Vasculitis

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3

Introduction

Paediatric retinal vasculitis is a challenging condition because of the children's inability to articulate their symptoms. Often diagnosis is missed especially in occult vasculitis where one does not find any features of vasculitis on fundus examination and FA is necessary to make a diagnosis. Reluctance to order FA in such subclinical vasculitis results in further delay in the diagnosis and treatment. Additionally, the longer potential duration of disease in children, compared to those with adult-onset uveitis, increases the likelihood of accumulating uveitic complications over a lifetime. Therefore, although uveitis occurs less frequently in children than in adults, it often presents with a more severe course, resulting in permanent vision loss.

In this case report, we present two pediatric cases of occult retinal vasculitis, each managed with different approaches: one with conventional immunosuppressants and the other with biologic immunosuppressants.

Case 1

History

A 16-year-old girl presented with redness and blurred vision in her right eye for one month, with no history of systemic illness.

Clinical feature

Visual acuity was 6/9 in the right eye and 6/6 in the left. Slit-lamp examination showed 2+ anterior chamber (AC) cells and vitreous

cells in both eyes (BE). Fundus examination of the right eye (RE) revealed grade 2 vitritis and optic disc edema, while the left eye (LE) showed no significant changes, except for anterior vitreous cells.

Investigations

Laboratory tests included a complete blood count, serum angiotensin converting enzyme, Mantoux test, Quantiferon TB Gold, RA, ANA, RPR, TPHA, ANCA, HLA-B27, and HLA-B51. All results were unremarkable. Widefield FA revealed significant vascular leakage with characteristic fern-like pattern in all quadrants in BE, along with a disc leak in the RE.

Treatment

Following treatment with Azathioprine and tapering oral steroids, there was good response with visual acuity improving to 6/6 in the RE. However, the vasculitis severity was unclear until repeat FA after four months, which showed reduction in leakage.

At six months review while she was on 10mg/day of steroids, there was reduction in vision in RE and OCT showed macular edema. Biologic therapy was recommended, but the patient declined. Her steroid dose was increased to 30mg/day, Azoran was continued, and a triple immunosuppressive regimen, including mycophenolate mofetil, was started after rheumatology consultation.

Case 2

History

A 15-year-old girl was referred with headache and scotoma for the past one month and a prior diagnosis of papilledema.

Clinical feature

Her BCVA was 6/6 in BE, and slit-lamp examination showed a normal anterior segment. Fundus examination revealed bilateral disc edema with inferior retinal hemorrhage in the RE. FA showed typical fern-like leakage and disc leaks in BE, with blocked fluorescence in the RE corresponding to the hemorrhage areas.

Investigations

Uveitis workup was unremarkable, and the patient was referred to a rheumatologist.

Treatment

She received intravenous methylprednisolone (750 mg/day) for three days, followed by oral steroids, adalimumab (40 mg every two weeks), and methotrexate (12.5 mg). Steroids were tapered and discontinued after 4 months with near-complete inflammation control. She is continuing adalimumab and methotrexate. Repeat FA after 4 months showed significant improvement in the vasculitis.

Discussion

Our case report highlights the concept of occult or subclinical retinal vasculitis, where the vasculitis is not visible clinically and is identifiable only on FA, making it a diagnostic challenge. [1] Nearly 80% of pediatric idiopathic uveitis patients exhibit retinal vasculitis, linked to lower inflammation control at 1 year and a poorer visual prognosis. [2]

Abraham et al emphasized the importance of FA in pediatric uveitis cases with posterior segment involvement in their study. Similarly, our case highlights FA's crucial role in detecting occult vasculitis, monitoring disease progression, and adjusting treatment dosages. An interesting similarity observed in both cases was the absence of macular edema despite significant vascular and disc leakage. The reason for the lack of macular edema remains unclear and difficult to explain. However, our first case developed macular edema on the later course of the disease.

Studies on experimental models of autoimmune uveitis have shown that TNF-α plays a crucial role in the pathogenesis of intraocular inflammation, and inhibiting this factor helps control uveitis. Adalimumab is a fully human monoclonal antibody, engineered through gene technology with site-directed mutagenesis to enhance its binding efficiency to TNF-α. The Sycamore study demonstrated the efficacy of adalimumab combined with methotrexate in treating JIA and refractory uveitis cases.[3] Similarly, one of our cases was successfully managed with this combination therapy, allowing for rapid steroid tapering while ensuring effective inflammation control. In contrast, the other case relapsed when the steroid was tapered, requiring the initiation of triple immunosuppressive therapy and a longer duration with higher dose of steroid therapy.

Although both cases had the same diagnosis, the first patient declined biologic treatment due to the cost. It is crucial to counsel parents about the duration and approximate cost of therapy before starting treatment. The unpredictability of the disease course and treatment response is also a significant challenge.

Previous clinical trials have highlighted the serious adverse effects of adalimumab. To date, our patient has not experienced any side effects. However, long-term follow-up is essential for patients receiving adalimumab to monitor for potential adverse events.

Conclusion

This case report highlights the often-missed condition of subclinical or occult vasculitis in the pediatric population. Adalimumab combined with methotrexate can be considered as first-line treatment to achieve disease remission and enable the withdrawal of systemic corticosteroids. However, the cost-effectiveness of this approach, particularly in the Indian population, remains a concern.

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2. *Yang P, Zhong Z, Su G, Ye X, Tan S, Li F, Du L, Zhou C, Cao Q, Wang Y, Kijlstra A. RETINAL VASCULITIS, A COMMON MANIFESTATION OF IDIOPATHIC PEDIATRIC UVEITIS? Retina. 2021 Mar 1;41(3):610-619.*
3. *Ramanan AV, Dick AD, Jones AP, McKay A, Williamson PR, Compeyrot-Lacassagne S, Hardwick B, Hickey H, Hughes D, Woo P, Benton D, Edelsten C, Beresford MW; SYCAMORE Study Group. Adalimumab plus Methotrexate for Uveitis in Juvenile Idiopathic Arthritis. N Engl J Med. 2017 Apr 27;376(17):1637-1646.*

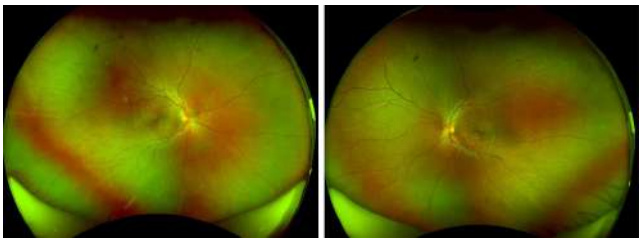

Figure 1: *Optos both eyes: No significant features of vasculitis noted*

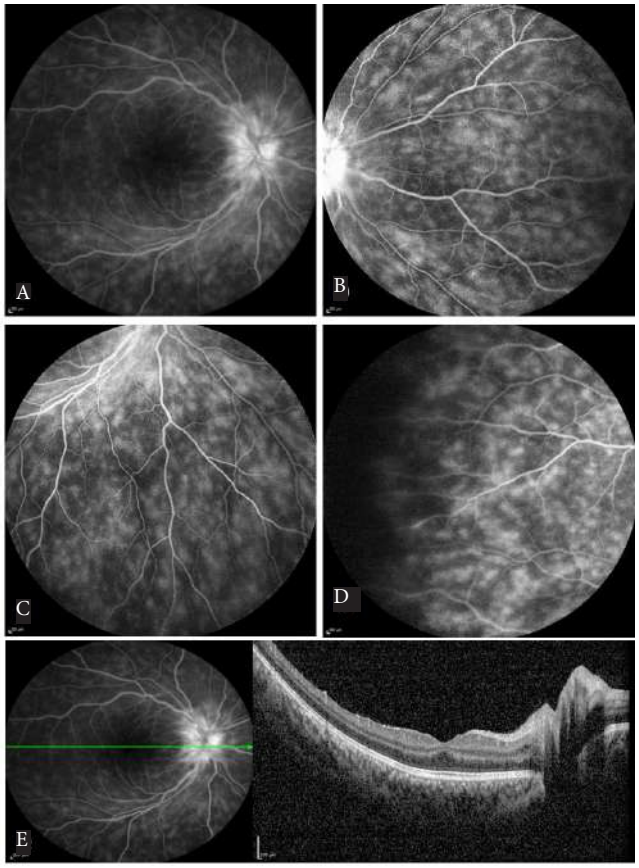

Figure 2A*-D. FA showing disc leak and diffuse capillary leak. Note the typical fern pattern.* ***Figure 2E****. OCT showing no macular edema.*

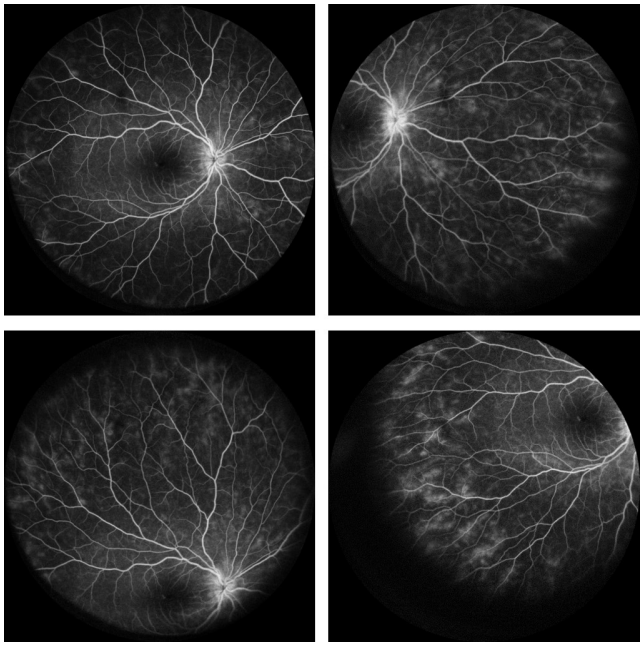

Figure 3: *Follow up FA showing improvement in vasculitis following treatment.*

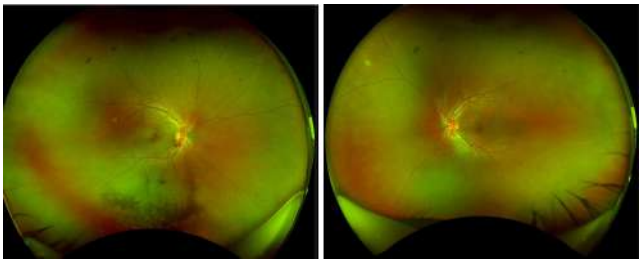

Figure 4: *Optos of both the eyes showing hyperemic disc and retinal haemorrhage of the right eye.*

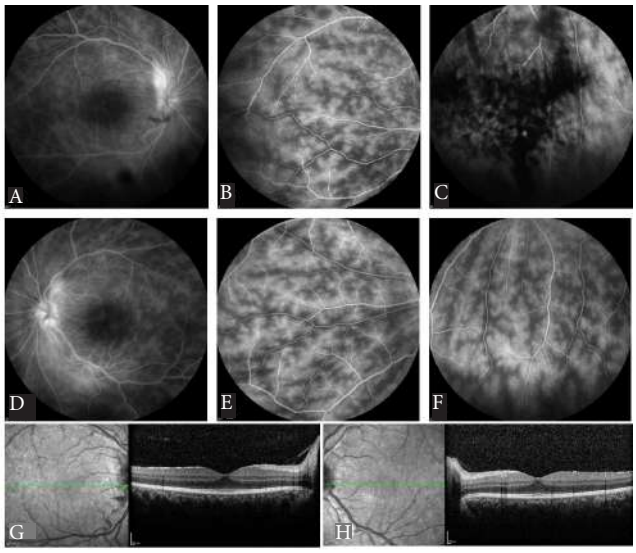

Figure 5A-F. *FA showing diffuse capillary and fern like pattern of both the eyes.*
Figure G-H *Normal OCT in both the eyes.*

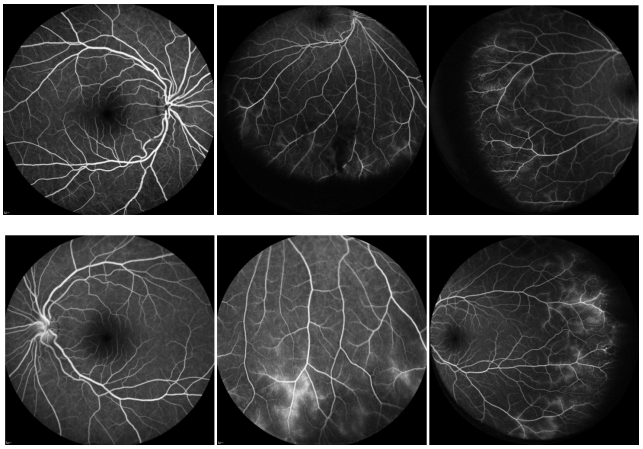

Figure 6: *Follow up FA showing improvement in vascular leak.*

Get on Board: Uveitis Fellowship Opportunities

Details of Uveitis fellowship programs offered at various institutes

Name of Institute: Sankara Nethralaya - C U Shah Ophthalmic PG training center

Location with address: Sankara Nethralaya (Medical Research Foundation) New No: 41, College Road, Chennai - 600 006.

Number of seats per year: 4 years per year, There are two sessions in a year. Two candiates is selected for each session.

Chief mentor(s): Dr. Jyotirmay Biswas, M.S , Director of Uveitis

Duration of the course: 18 months program

Highlights of the program: Goals and Objectives:
1. To give scientific and logical training to help trainees diagnose and treat intraocular inflammations, retinal vasculitis and scleritis
2. To provide proper exposure to all kind of common and rare uveitis which will help them in their future practice.
3. To make them able to manage all kinds of uveitis conditions independently and confidently.

Duration & commencement of program: 18 Months
Program commences in January and July every year

Minimum qualifications: MS / DO / DNB in Ophthalmology

Age Limit: Upto 40 years

Application procedure: Same as for other fellowship programs

Requirements:
1. Interest in Uveitis/Immunology
2. Capability to do indirect ophthalmoscopy
3. Willingness to participate in research activities/ projects

Selection procedure: Through interview in UVEA specialty, after qualifying in the written examination which is common for all the anterior segment fellowship programs

Clinical exposure: In initial months, fellows will be given rotational postings in Glaucoma, Medical Retina and Diagnostics. This will give them adequate exposure in these subspecialties to help them in managing common and related conditions. A thorough exposure in anterior, intermediate and posterior, pan uveitis, scleritis and retinal vasculitis will be given in subsequent months of training. In the last six months fellows will work as senior resident and manage uveitic cases independently.

They will also gain exposure to ocular pathology in pathology lab during their fellowship.

Surgical exposure:

Fellows will be given sufficient opportunities for minor invasive procedures like posterior sub tenon injections, anterior chamber tap and intra vitreal injections.

They will get enough chance to learn cataract surgery. They will be properly trained by experts to perform cataract operation (Extra capsular, small incision, Phaco emulsification) independently.

Fellows will be given opportunity to observe and give proper pre and post operative treatment for complicated cataracts under expert supervision of consultants.

They will also get chance to operate such cases.

Research possibilities: Fellows will get chance to work on various clinical and basic science projects under senior consultants. They will get enough guidelines and opportunities to work for publications in various journals.

Suggested reading:
1. Atlas of Uveitis and Scleritis by Ganesh SK, Agarwal M, George AE, Dr. Biswas J, Jaypee Medical Publishers, 1st Edition, 2003.
2. Uveitis: An Update, J Biswas, Parthopratim DM, Springer, 2015.
3. Basic and clinical science course: Intraocular inflammation and uveitis-American Academy of ophthalmology 2020-2021.

Contact: 044- 4227 1500 , 28271616

Get on Board: Uveitis Fellowship Opportunities

Details of Uveitis fellowship programs offered at various institutes

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Name of Institute: **Aravind Eye Hospital**

Location with address: Aravind eye hospital
Cuddalore main road, Thavalakuppam, Pondicherry 605007

Number of seats per year: 2

Chief mentor(s): Dr. S Bala Murugan

Duration of the course: 6 months and 1.5 years

Highlights of the program: 1.Comprehensive coverage of hands on Uveitis training 2.Guaranteed Phacoemulsification and SICS training of minimum number of cases stipulated as 100 and 500 respectively

3.Assured publication in international journal as first author with collaboration efforts

4.Diabetic retinopathy and medical retina management with assured laser training

5.Friendly learning atmosphere

6.Training of surgeries supervised with videos compulsorily

Contact: 9360384382, 9080518580

Name of Institute: **Aravind Eye Hospital, Madurai**

Duration of the course: 18 months

Highlights of the program: Fellows get to train in one of the world's largest Uvea clinics which has treated over 1,20,000 + patients over the past 33 years. They can discuss about cases with experienced senior faculty members under Dr Rathinam Shivakumar and expertise in treating infectious & non-infectious uveitis, ocular inflammatory diseases along with exposure to advanced multimodal diagnostics.

Fellows will also get simulator training followed by hands-on microsurgical SICS training with weekly OT turns. Phaco training will be provided for post-fellowship Medical Officers.

Medical Retina with Uvea fellowship: You can also opt for medical retina one year followed by uvea fellowship 18 months.

Get on Board: Uveitis Fellowship Opportunities

Details of Uveitis fellowship programs offered at various institutes

Name of Institute: Narayana Nethralaya

Location with address: 121/C West of Chord Road
1st 'R' Block. Rajaji Nagar, Bengaluru - 560 010

Number of seats per year: 02 (01 Every six months)

Chief mentor(s): Dr. Padmamalini Mahendradas

Duration of the course: 18 Months (15 Months Uvea + 3 Months Medical Retina)

Highlights of the program: Uvea Clinical evaluation, complete work-up and management of uveitis cases, Basic immunology, anterior chamber paracentesis, vitreous tap and diagnostic biopsies, ocular pathology and molecular diagnostic tests, multimodal imaging, targeted drug therapy, periocular and intraocular steroid injections and implants, antimicrobial therapy (intraocular and systemic), systemic immunosuppressive therapy, biologics and JAK inhibitors. Interdisciplinary postings with good exposure to infectious diseases, pulmonology and rheumatology. Training in the management of complications of uveitis. Evaluation of paediatric uveitis with hand-held slit lamp examination and indirect ophthalmoscopy. Evaluation of systemic autoimmune diseases and to monitor the side effects of the drugs with good academics and research support

Medical Retina Indirect ophthalmoscopy with Amsler Dubois drawings, B scan ultrasonography (performance and reporting), FFA and ICGA (procedure-learning and reporting), Lasers (both adult and pediatric) including PRP, Targeted laser, Focal laser, PDT, TTT, Intravitreal injections, Ozurdex injections, Wetlab training, Simulator training for anterior vitrectomy and Suprachoroidal injections, ROP Screening, diagnosis and Lasers

Contact: 9513144766

Name of Institute: LV Prasad Eye Institute

Location with address: LV PRASAD EYE INSTITUTE
Near Sai International, Patia, Bhubaneswar 751024,

Number of seats per year: 2

Chief mentor(s): Dr. Anup Kelgaonkar, **Dr.** Mudit Tyagi, **Dr.** Soumyava Basu

Duration of the course: 3 years

Highlights of the program: 1. Hands on experience on uveitic and complicated cataract surgeries. 2. Medical retina 3. Intravitreal injections 4. Laser photocoagulation 5 exposure to electrophysiology tests and retina diagnostics 6. SICS training program of three months 7. Phaco training program by Alcon 8. Hands on phaco and cataract surgery in secondary centre for one year. 9. Leadership skills development - managing secondary centre for one year. 10. Rheumatology posting 11. Opportunity to work in laboratory for molecular and immunology tests. 12 research and publications opportunity with faculty.

Contact: 8087540324

Name of Institute: **LV Prasad Eye Institute**

Location with address: LV Prasad Marg, Banjara Hills Hyderabad, Telegana

Number of seats per year: 4

Chief mentor(s): Dr. Soumyava Basu, **Dr.** Mudit Tyagi, **Dr.** Shabtab Nasir

Duration of the course: 3 years

Highlights of the program: Structured training in uveitis and medical retina, including lasers and retinal imaging;

Expertise in complex cataract surgeries, including high-volume cataract surgery in secondary centers.

Rheumatology rotation for systemic evaluation skills.

Contact: 040-68102167

Name of Institute: **Prabha Eye Clinic and Vittala Eye Hospital**

Location with address: 504, 40th cross, 8th block, Jayanagar, Bengaluru

Number of seats per year:2

Chief mentor(s): Dr. Kalpana Babu

Duration of the course: 1.5 years

Highlights of the program: Get to see variety of uvea cases including rare cases,clinical and academic oriented programme

Contact: 9448260189

Get on Board: Uveitis Fellowship Opportunities

Details of Uveitis fellowship programs offered at various institutes

Name of Institute: Sadguru Netra Chikitsalaya

Location with address: Sadguru Seva Sangh Trust, Jankikund, Chitrakoot, Madhya Pradesh

Number of seats per year: 2 Years

Chief mentor(s): Dr. Alok Sen, Dr. Sachin Shetty, Dr. Priyansha Multani

Duration of the course: 2

Highlights of the program: Candidates will see a wide variety of uveitis and medical retina cases. They will have the opportunity to work with state-of-the-art imaging devices and will gain valuable exposure to retinal lasers and cataract surgery, including phacoemulsification

Contact: 7898201605

Name of Institute: Christian Medical College, Vellore

Location with address: Department of Ophthalmology
Christian Medical College, Schell Campus, Arni Road
Vellore, Tamil Nadu -632001, India

Number of seats per year: 1

Chief mentor(s): **Dr. Sheeja Susan John**, Senior Professor & Head, **Dr. Smitha Jasper**, Professor, Ophthalmology-Unit 3, Uvea & Medical Retina, Christian Medical College, Vellore

Duration of the course: Two-year Postdoctoral Fellowship course in Uvea and Medical Retina

Highlights of the program: The Post-doctoral fellowship course in Uvea and Medical Retina offers comprehensive training in the diagnosis and management of ocular inflammatory diseases, and the medical management of retinal diseases. The candidate will get exposure to a wide variety of clinical cases, and be trained in the performance and interpretation of various investigative modalities, such as Optical coherence tomography (OCT), OCT-Angiography, Fundus fluorescein angiography (FFA), Indocyanine green angiography (ICGA), Electroretinography (ERG), Visual evoked potential (VEP), B scan ultrasonography and Automated perimetry, required for the evaluation of these patients. The candidate will also be trained in surgery for complicated cataract in uveitis, periocular and intravitreal injections of steroids and anti-VEGF drugs, laser photocoagulation, and in the planning and monitoring of various systemic immunomodulatory and other therapeutic regimens. The course will include clinical and laboratory-based postings in the Departments of Clinical Immunology and Rheumatology, Paediatric Rheumatology, Infectious diseases (Adult and Paediatric), Clinical Microbiology, Clinical Virology, Parasitology (The Wellcome Trust Research Laboratory), General Pathology, Transfusion Medicine and Immunohematology (HLA lab), and Endocrinology, Diabetes and Metabolism. The fellowship aims to give the candidate a comprehensive, well-rounded training experience, with exposure to the various clinical and laboratory aspects, as well as the multidisciplinary approach required for the evaluation and management of patients with ocular inflammatory and medical retinal diseases, with ample opportunity for research.

Contact: 09003938547

Get on Board: Uveitis Fellowship Opportunities

Details of Uveitis fellowship programs offered at various institutes

Name of Institute: B P Koirala Lions Centre for Ophthalmic Studies, Institute of Medicine

Location with address: Maharajgunj, Kathmandu, Nepal

Number of seats per year: 2-4

Chief mentor(s): Dr. Ranju Kharel Sitaula

Duration of the course: 6-12 months

Highlights of the program: Multi-department tertiary level hospital with inter-department collaboration and clinical posting

Contact: +977 9841314495

Name of Institute: Singapore National Eye Centre

Location with address:11 Third Hospital Avenue, Singapore 168751

Number of seats per year: 5

Chief mentor(s): Dr. Anita Chan

Duration of the course: 12 months

Highlights of the program: The objective of this sub specialty fellowship is to achieve competency in managing a wide variety of inflammatory eye conditions including immunosuppressive therapy and surgical management. The fellowship program also includes participation in clinical research projects.

Contact: 67157091

Name of Institute: Sankara Eye Hospital

Location with address: Bengaluru, Varthur main Road, 560037

Number of seats per year: 2

Chief mentor(s): Dr. Minija CK, Dr. Nidhi Dubey

Duration of the course: 18 months

Highlights of the program: Medical Retina, Uvea and Cataract surgeries

Contact: 9448881500

Get on Board: Uveitis Fellowship Opportunities

Details of Uveitis fellowship programs offered at various institutes

Name of Institute: iRetina Centre

Location with address: B-232/233, Money Plant High Street, Jagatpur Road, Ahmedabad

Number of seats per year: 2

Chief mentor(s): Dr. Nimesh Patel

Duration of the course:15 months

Highlights of the program:*Get mentorship from former LVPEI Faculty
*Exposure to wide filed imaging system on Mirante UWF FA/ICGA and OCTA
*Learning basics of uveitis with scientific logic
* 1 case report and 1 paper have to publish during the program
*Exposure to Medical Retina and ROP
*To learn and perform Retinal Lasers and Intravitreal Injections

Contact: 9428352489

Name of Institute: Dr. Natasha's Retina Care, Kochi

Location with address: Kochi

Number of seats per year:1 every 3 months

Chief mentor(s): Dr. Natasha Radhakrishnan

Duration of the course:3 months short-term

Highlights of the program: Wide variety of Uvea cases with hands on experience from management and treatment

Contact:94963 89999

To care beyond eye care: CUBS Childhood Uveitis Blindness Support

Childhood Uveitis Blindness Support (CUBS) is a trust envisaged to provide financial aid to children with Uveitis.

It was inaugurated during IGNITE 2025 by Actor Kunchacko Boban and Editor of a leading newspaper, Manorama, Mr Philip Mathew, in the presence of USI, KSOS and COC office bearers. The Trust was founded by Dr. Natasha Radhakrishnan and 4 friends from different walks of life with a common goal.

It is registered as a charitable Trust with 80 G exemption with the aim,"To care beyond eye care". In four months, the Trust has been able to help 5 families and is forging ahead with good support from benefactors.

You can also contribute and help CUBS be a small lighthouse in the sea of Paediatric Blindness.

For contributions,
Name of account : CHILDHOOD UVEITIS BLINDNESS SUPPORT
Account Number: 10217443625
IFSC : IDFB0080514
Branch : KOCHI MG ROAD
Type.of account : TASC- SAVINGS ACCOUNT
For receipts, please contact Dr. Natasha Radhakrishnan, 94963 89999.

Uveitis Society (India)

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26th Annual Conference of Uveitis Society (India)

3rd | 4th | 5th October

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