

Uveitis: Concepts & Mechanisms Underlying Uveal Inflammation with A Case Study

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ABSTRACT

Uveitis is an ocular disease that indicates inflammation in the Uvea which is the pigmented and vascular middle layer of the eyeball that is located between white sclera and inner retina. Uvea is also known as the vascular tunic which is crucial for focusing vision, regulating light and nourishing the eye. Uvea consists of three major interconnected structures: Iris, Ciliary Body and the Choroid. Uveitis causes eye pain, redness and blurry vision. Late treatment leads to severe eye pain and vision loss. Uveitis can occur from Autoimmune Diseases, Infections, Genetic predisposition and physical trauma to the eye. Uveitis can be classified as Iritis, cyclitis, choroiditis and panuveitis depending on the affected part. The first line of treatment is corticosteroids. In severe cases, ophthalmologists may prescribe Immunosuppressive Agents, Antibiotics, Antivirals and pupil dilating drops. This study is a narrative review and case study of Uveitis connecting it with Ankylosing Spondylitis, HLA B27, JIA and others. This study also addresses the wrong diagnosis, proper diagnosis, treatment and observation of Uveitis patients.

INDEX TERMS Ocular, Uveitis, Panuveitis, Iritis, Corticosteroids, Uvea, Retina, Iris, Ankylosing Spondylitis, Juvenile Idiopathic Arthritis, HLA-B27, Photophobia

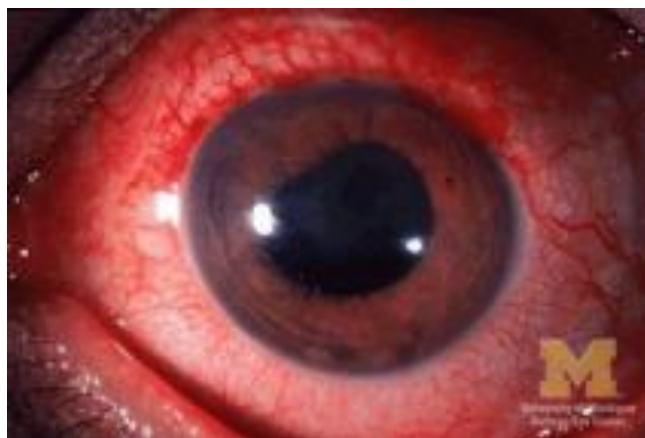


FIGURE 1. A uveitis-diagnosed eye showing severe uveal inflammation with characteristic redness, photophobia and vision loss. Source: J. Trobe, Wikimedia Commons, CC BY 3.0 [13].

INTRODUCTION AND OVERVIEW

Ocular infections and diseases are likely to arise from physical trauma. But many ocular diseases come from other existing problems. Uveitis is the greatest example in this regard [1], [2]. Most of the Uveitis cases are linked to Ankylosing Spondylitis (AS) [5]. Rheumatologists claim that regular Tofacitinib, Upadacitinib or similar dosage can save AS patients from Uveitis. Uveitis can also form from physical trauma. Eye infections particularly affecting Iris and Uvea can end up as Uveitis if remained neglected. The symptoms for Uveitis are marked as redness, reduced or blurry vision, eye pain, photophobia, floaters or dark spot in the vision [7] A uveitis-affected eye is illustrated in Fig. 1.

Uveitis is classified according to the part of the eye affected by inflammation. Anterior uveitis (iritis) is the most common form and affects the front portion of the eye. Intermediate uveitis (cyclitis) involves the middle part of the eye, particularly the ciliary body. Posterior uveitis (choroiditis) affects the back of the eye, including the choroid and retina. Panuveitis is the most extensive form, occurring when inflammation involves all layers of the uvea throughout the eye [3].

Research Objectives

1. Finding the history of Uveitis Diagnosis and Treatment
2. To highlight the existing treatment methods
3. To mention the correlation of Uveitis with Autoimmune Diseases
4. Using the case to address practical treatments and diagnosis
5. Addressing Immunological Mechanisms behind Uveitis

METHODOLOGIES

This Study was conducted as a narrative review of Uveal Inflammation known as Uveitis, data from several scholarly sources were added and analyzed. A case was added for study which included practical treatment of Uveitis, False and proper diagnosis seen among the patients were viewed and analyzed. The symptoms of Anterior Uveitis were properly introduced and analyzed.

(Note: The Author and the Patient are the same person. So, there is no legal or ethical issue behind the case study being published under the Author's name with his permission. If one wishes to use the information of this case, one must cite and refer to this paper. Otherwise, one must face legal charges. Patient Age: 15y (As of 2022), Date of Examination: December 2022).

Several figures, tables and diagrams provide enough information to analyze the previous research with the patient's case. The Literature Review consists of existing Uveitis theorems, treatment recommendations and other necessary information. The diagnosis mechanisms and Immunological Mechanisms have been addressed in this study. This Study is an all-in-one

Uveitis Study that ranges from reviewing Uveitis Research to addressing an actual Uveitis case that faced wrong diagnosis, decrease in vision, spotted vision and physical trauma in the eye.

This Research also addresses the Immunological mechanisms behind Uveal Inflammation and also analyze the co-relation of Uveitis with existing Autoimmune Diseases, especially Ankylosing Spondylitis and how the generational influence of them can be to more Uveitis cases.

This Research used IEEE citations to properly refer each of the articles, books and scholarly works. Every figure has proper source identified and referred.

LITERATURE REVIEW

Uveitis is a common eye disease that depends on sex, race, hygiene, genetics, environment and geographical location [4], [7]. Uveitis was known to ancient Egyptians and is marked as one of the oldest recorded ophthalmic diseases. In ancient Egyptian civilization, the recommended treatment for such ocular diseases was a lotion made of saltpeter and ebony wood shavings. Uvea is the Latin word for grape. It is known as the vascular middle layer of the eye. Iris is the most anterior part of the Uvea. Iris color varies from light blue to dark brown [2]. The sectional anatomy of the uveal tract is illustrated in Fig. 2.

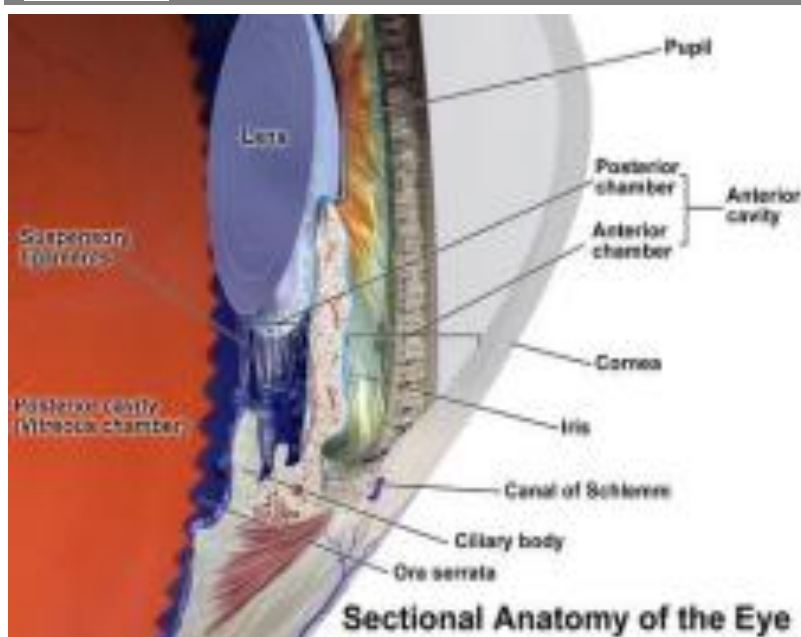


FIGURE 2. Sectional anatomy of a healthy eye showing the Uveal Tract including the Iris, Ciliary Body and Choroid. Source: Blausen Medical, WikiJournal of Medicine, CC BY 3.0 [12].

Previous Research

Previous research shows that Uveitis is closely associated with autoimmune diseases [1], [9]. Uveitis can start from Iris or different parts of Uvea and the infection can reach Retina. The retina can be found flattened in many cases which is a major reason behind blurry vision and spots in patients' vision [2]. An infected uvea with active anterior uveitis is shown in Fig. 3.

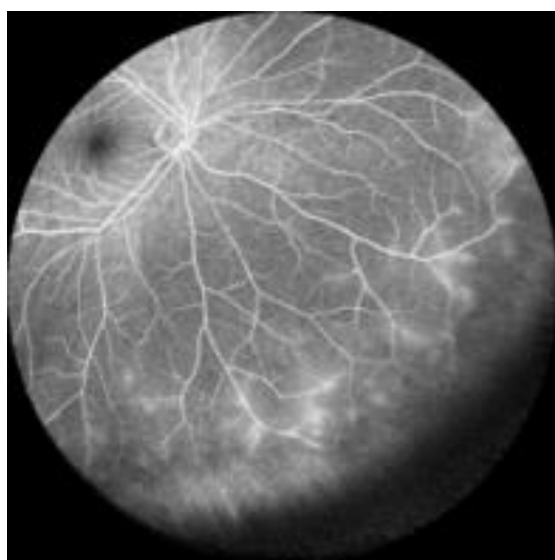


FIGURE 3. An infected Uvea demonstrating anterior uveitis with active disease. Source: Y. Chi et al., Wikimedia Commons, CC BY 4.0 [14].

Concept of Uveitis

Uveitis is not caused by a single virus or bacterium. It is an inflammation of the eye. Many ophthalmologists do not find the definite reason of Uveitis in many patients — this type is named idiopathic Uveitis [1], [8]. Most Uveitis cases are linked to Autoimmune Diseases but some viruses and bacteria can cause Uveitis too, such as: Herpes Simplex Infection, Herpes Zoster, Tuberculosis, and Syphilis [18]. A parasite named Toxoplasmosis can also cause uveitis. An eye injury can trigger Uveitis too. The common symptoms include:

eye pain, red eye, sensitivity to light, blurred vision, and excessive tearing [7].

Uveitis and Autoimmune Diseases

Research shows that Uveitis can be caused by previously existing Autoimmune diseases. Specialists call it the "Uveitis Attack." Ankylosing Spondylitis is the most prominent Autoimmune disease behind the cause of Uveitis [5], [10]. Several other Autoimmune Diseases can also cause uveitis [8].

Ankylosing Spondylitis

Known as the eclipse of bone, Ankylosing Spondylitis is a chronic autoimmune/autoinflammatory disease that primarily affects the spine and sacroiliac joints (where the spine meets the pelvis) [5]. It often comes along with the HLA-B27 antigen. HLA B27 is a common antigen found in 490 to 650 million people around the world. Only 8 to 9 percent of HLA-B27 positives get diagnosed with Ankylosing Spondylitis [5]. Even many Ankylosing Spondylitis patients do not have HLA-B27. But the combination of AS with HLA-B27 causes inheritance of the gene in children [10].

A true Mendelian chart can be made for HLA-B27 inheritance, but not for Ankylosing Spondylitis itself, because AS is influenced by many genes and environmental factors [5].

If we simplify and assume:

- Parent 1: HLA-B27 positive, no AS → genotype Bb
- Parent 2: HLA-B27 positive with AS → genotype Bb

(where B = HLA-B27 allele, b = non-HLA-B27 allele)

TABLE 1. Punnett square for two HLA-B27 positive heterozygous parents [5]

	B	b
B	BB	Bb
b	Bb	bb

TABLE 2. Expected inheritance frequencies of HLA-B27 assuming both parents are heterozygous (Bb × Bb) [5]

Outcome	Probability
BB (HLA-B27 positive)	25%
Bb (HLA-B27 positive)	50%
bb (HLA-B27 negative)	25%
Any HLA-B27 positive genotype	75%
Any HLA-B27 negative genotype	25%

TABLE 3. Key Features of Ankylosing Spondylitis [5], [10]

Feature	Description
Disease Type	Chronic inflammatory axial arthritis
Primary Sites	Spine and sacroiliac joints
Typical Age of Onset	Late teens to early 40s
Genetic Marker	HLA-B27 positive in most cases
Main Symptom	Chronic inflammatory back pain
Stiffness Pattern	Worse in morning, improves with activity
Extra-articular Features	Uveitis, IBD, psoriasis
Imaging Findings	Sacroiliitis on X-ray/MRI
Treatment	NSAIDs, physiotherapy, biologics (TNF/IL-17 inhibitors)

Juvenile Idiopathic Arthritis (JIA)

JIA is the most common reason behind childhood Uveitis. This combination is mostly seen in the female sex. Uveitis caused by JIA is a chronic anterior uveitis. It is often asymptomatic in the early stages, which is why regular ophthalmic screening is important [6].

TABLE 4. Key Features of JIA-Associated Uveitis [6]

Feature	Description
Associated Disease	Juvenile Idiopathic Arthritis
Type	Chronic anterior uveitis
Common Patients	ANA-positive children
Symptoms	Often asymptomatic initially
Complications	Cataract, glaucoma, vision loss
Treatment	Steroids, methotrexate, biologics

c: Psoriatic Arthritis

TABLE 5. Psoriatic Arthritis and Associated Uveitis [8], [11]

Feature	Description
Disease	Psoriatic Arthritis
Type	Chronic inflammatory spondyloarthropathy

Skin Association	Psoriasis (skin and nail changes)
Genetic Link	Often HLA-B27 positive (subset of patients)
Uveitis Type	Usually, anterior uveitis can be bilateral or chronic
Onset Pattern	Can be acute or insidious
Symptoms	Eye pain, redness, photophobia, blurred vision
Systemic Features	Arthritis, dactylitis, enthesitis
Treatment	NSAIDs, methotrexate, biologics (TNF/IL-17 inhibitors)

Inflammatory Bowel Disease (IBD)

Inflammatory Bowel Disease (IBD) is a group of chronic, lifelong autoimmune disorders that cause continuous inflammation in the digestive tract. It can cause Uveitis but the number of cases are relatively low. This includes Crohn's disease and ulcerative colitis [8].

TABLE 6. Inflammatory Bowel Disease and Associated Uveitis [8], [11]

Feature	Description
Disease	Inflammatory Bowel Disease (Crohn's, Ulcerative Colitis)
Type	Chronic immune-mediated gastrointestinal disorder
Genetic Link	Often associated with HLA-B27 (subset of patients)
Uveitis Type	Usually anterior uveitis can be bilateral or chronic
Onset Pattern	May occur independent of bowel flare-ups
Eye Symptoms	Pain, redness, photophobia, blurred vision
Systemic Features	Abdominal pain, diarrhea, weight loss
Pathogenesis	Immune cross-reactivity between gut and ocular tissues
Treatment	Steroids, immunosuppressants, biologics (anti-TNF agents)

TREATMENT

A. DIAGNOSIS

The diagnosis of Uveitis has changed significantly over the years [16], [17]. Optical coherence tomography (OCT) is one of the tests used for identifying Uveitis. OCT maps damage and inflammation that Uveitis leaves in the eye. OCT works by sending near-infrared light into the eye and measuring how long it takes to bounce back from different retinal layers. Different tissues reflect light differently, so the machine builds a cross-sectional image of the retina, almost like an optical biopsy without cutting anything [16]. The principle of frequency-domain OCT is illustrated in Fig. 4.

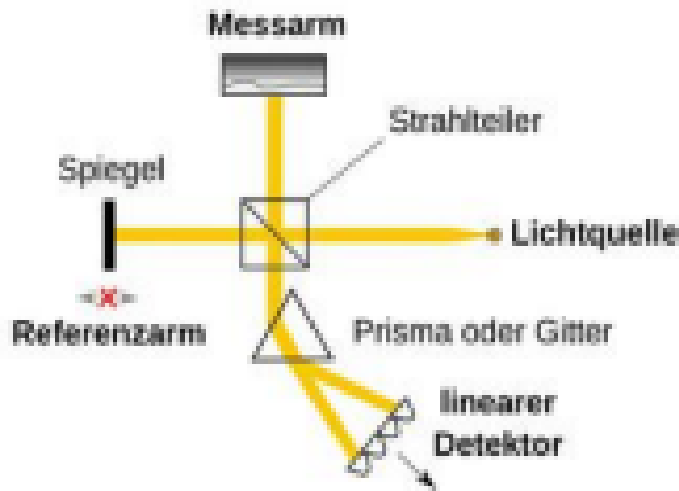


FIGURE 4. Principle of frequency-domain OCT (optical coherence tomography). Source: Muskid, Wikimedia Commons, CC BY-SA 3.0 [15].

MEDICATION

Treatment of uveitis depends on the aetiology, anatomical location and severity of the disease [9], [11]. The primary treatment options are summarized in Table 7.

TABLE 7. Medication Options for Uveitis [9], [11], [16]

Feature	Description
Topical corticosteroids	First-line for anterior uveitis; reduce inflammation rapidly
Systemic corticosteroids	Used in moderate to severe cases with posterior/panuveitis involvement
Periocular / intravitreal steroids	Targeted therapy for localized inflammation and macular edema
Cycloplegic agents	Relieve ciliary spasm, reduce pain, and prevent anterior synechiae formation
Immunomodulatory therapy	Methotrexate, azathioprine, mycophenolate for chronic or recurrent uveitis
Biologic agents	Anti-TNF drugs (adalimumab, infliximab) for refractory autoimmune uveitis
Antiviral therapy	Acyclovir or related agents for herpetic uveitis
Antibiotic therapy	Targeted treatment for infectious causes such as tuberculosis or syphilis
Adjunct therapy	Includes intraocular pressure control and management of complications like glaucoma or cataract

A CASE STUDY

Note: The Author and the Patient are the same person. So, there is no legal or ethical issue behind the case study being published under the Author's name with his permission. If one wishes to use the information of this case, one must cite and refer to this paper. Otherwise, one must face legal charges. Patient Age: 15y (As of 2022)

Date of Examination: December 2022

Sex: Male

Distance Vision Prescription (Before Uveitis):

OD (Right Eye): Sphere -1.25 D

OS (Left Eye): Sphere -1.50 D

Cylinder: Plano (0.00 D)

Axis: 180

Diagnosis:

Myopia (Nearsightedness)

Recommendation:

Single-vision distance spectacles for clear distance vision.

Distance Vision Prescription (After Uveitis):

OD (Right Eye): Sphere -3.00 D

OS (Left Eye): Sphere -1.75 D

Cylinder: Plano (0.00 D)

Axis: 180

Diagnosis:

Myopia (Nearsightedness)

Recommendation:

Single-vision distance spectacles for clear distance vision.

Diagnosis

The patient was diagnosed with A/P Intermediate Uveitis in his right eye in early December 2022. Intermediate Uveitis is an inflammatory eye disease localized to the vitreous cavity, ciliary body, and peripheral retina. In the UBM, the retina seemed flat. The media was hazy due to inflammation. Rhegmatogenous retinal detachments (RD), posterior vitreous detachments,

cyclitic membranes, and intraocular tumors were not seen. The Vitreous Opacity was seen to be within normal limits. Goldmann Applanation Tonometry (GAT) was 10| 10 HgC8.05A which indicates hypotony (abnormally low pressure), which can cause vision complications.

VA- Visual Acuity = 2/60: This indicates a **severe reduction in distance vision**. It means the patient must stand 2 meters away to see a large letter that a person with normal vision can see from 60 meters away.

PH (ePH)- Pinhole Acuity = NI: "NI" stands for No Improvement. Looking through the pinhole did not make the vision clearer. This strongly suggests that the vision loss in this eye is **not** just a simple refractive error that can be fixed with regular glasses.

- **VA = 6/24:** This represents a **moderate reduction in vision**. You can see at 6 meters what a person with normal vision can see from 24 meters away.
- **PH (ePH) = 6/9:** Looking through the pinhole **significantly improved your vision** to 6/9, which is nearly normal (normal baseline is 6/6).

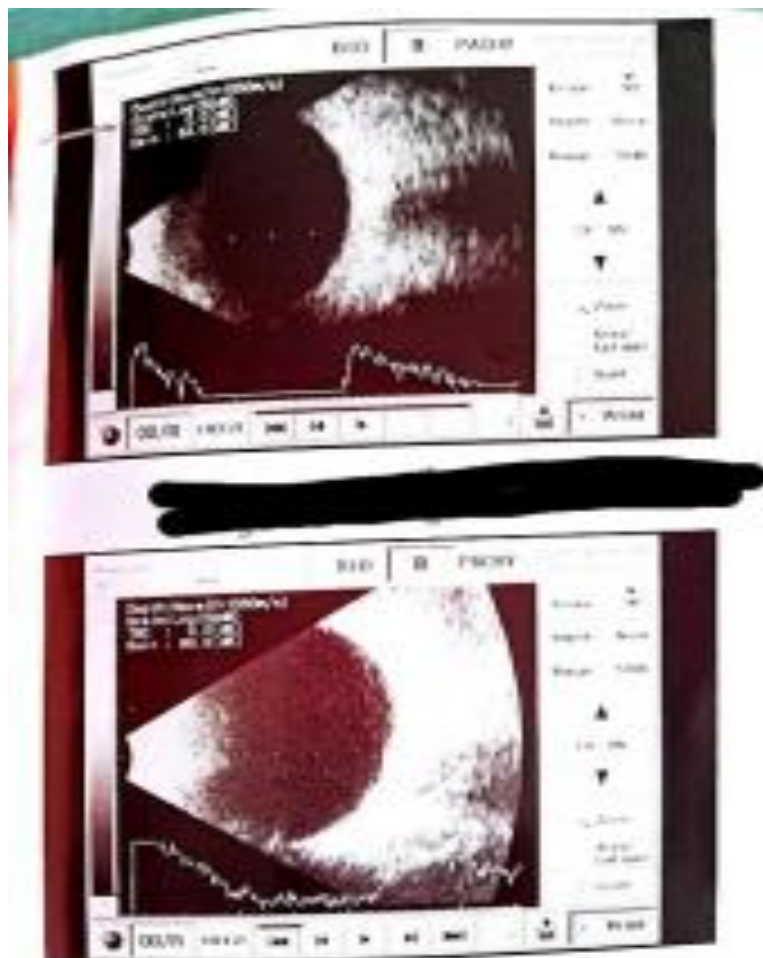


Figure 5: Ultrasound Biomicroscopy (UBM) of the patient's eye. It excels at detecting **snowballs** (inflammatory cell aggregates) and **snowbanks** (exudates over the peripheral retina/ciliary body).

Treatment:

- **Prednisolone 20 mg** – 1 month
- **Omeprazole 20 mg** – 1 month and 2 weeks
- Prednisolone- 3 weeks
- Prednisolone **Acetate 1%** - 2 weeks
- Moxifloxacin- 1 month and 2 weeks
- Calcium **Carbonate + Vitamin D3** – 1 month and 2 weeks
- Cefixime (most likely; strength needed for confirmation)- 2 weeks

Observation:

The patient was instructed to visit the doctor 1 time in a week for the 1st two weeks. Then he was instructed to visit again after a month and lastly, the regular six months visits are ongoing even after four years.

Words from the Patient:

The patient was first diagnosed with Conjunctivitis in late November 2022. He was prescribed fluoroquinolones for two weeks. But the redness, irritation started to increase after applying the eye drop. The patient stopped the treatment and rushed to a new hospital. The first doctor there identified it as Conjunctivitis but later changed her mind after seeing the treatment failure. The patient was transferred to a Uveitis specialist where he got proper diagnosis and treatment. Even after four years of recovery, the patient regularly visits the specialist (Each 6 months). The patient was later diagnosed with Ankylosing Spondylitis which marks the sudden occurrence of Uveitis.

Analysis of the Case with Previous Research:

Late Uveitis Diagnosis can lead to vision loss. The patient went to hospital on time, but the wrong treatment made the condition worse and decreased vision significantly. Most of the patients suffer the same path. Many doctors do not use UBM to save cost since countries like Bangladesh doesn't have proper insurance policy in health. **Corticosteroids are a must for Uveitis Treatment.** Ankylosing Spondylitis was the reason behind it since Uveitis did not make a reappearance after regular dosage of Tofacitinib 11 mg. Many AS patients take different types of medications which are Immune-repressive and can lower the risks of AS symptoms, Uveitis, IBD and others.

The post uveitis check ups are very important since it can come back anytime. Patients must maintain hygiene to keep the eye clean and try to visit a specialist in any case of physical trauma related to eye. Redness cannot be ignored, and proper precautions should be taken. Late diagnosis is not an option. Visiting properly trained and experienced Ophthalmologists is a must for any ocular disease. Medications can vary from patient to patient, but prescribing antibiotics and vitamin or calcium tablets is pretty common.

The infected eye cannot make any sort of contact with the healthy one. The patient's family must maintain distance from the patient just like in case of conjunctivitis. Usage of water is prohibited for a certain time (Usually, 2 weeks to 1 month). Uveitis is not pink eye. It is a far dangerous ocular disease that can lead to permanent vision loss.

Immunological Mechanisms of Uveitis:

T Lymphocytes play a central pathological role in the mechanisms of Immunology of Uveitis. Among the various T-cell subsets, T helper 1 (Th1) and T helper 17 (Th17) cells are particularly important in the development of uveal inflammation. Th1 cells secrete pro-inflammatory cytokines such as interferon-gamma (IFN- γ) and tumor necrosis factor-alpha (TNF- α), which promote the recruitment and activation of macrophages and other immune cells within ocular tissues. Th17 cells produce interleukin-17 (IL-17), a cytokine associated with chronic inflammation and tissue damage. Elevated levels of IL-17 have been reported in patients with active uveitis, suggesting a significant role in disease progression.

The migration of activated T cells across the blood-retinal barrier further amplifies inflammation. Once they are inside the immunological tissues, the T cells can change the system by releasing cytokines and chemokines that bring more immunological cells. This results in the episodes of Uveal Inflammation also known as Uveitis.

Uveitis Per Geographical Locations

The predominant causes of uveitis vary significantly by region, reflecting differences in genetic predisposition, infectious burden and environmental factors [4], [7].

TABLE 8. Predominant Causes of Uveitis by Region [4], [7]

Feature	Description
North America	HLA-B27, Sarcoidosis, HSV
Europe	HLA-B27, Sarcoidosis, Toxoplasmosis
South Asia	TB, HLA-B27, Behçet's
East Asia	VKH, Behçet's, TB
Middle East	Behçet's, HLA-B27, TB
Africa	HIV-related, TB, Onchocerciasis
Latin America	Toxoplasmosis, HLA-B27
Oceania	HLA-B27, Sarcoidosis

CONCLUSION

Ocular Diseases like Uveitis must be addressed in treatment or the result may end up in vision loss [7]. Uveitis can form from anything starting from Autoimmune diseases to physical trauma [1], [9]. Ophthalmologists must not diagnose Uveitis as Conjunctivitis or similar diseases. Uveitis must be treated with corticosteroid eye drops, oral steroids, targeted eye injections or implants, and immunomodulatory drugs for chronic or severe cases [11]. Ankylosing Spondylitis patients have the highest chances of Uveitis [5], [10]. Regular visits to experienced and specialist ophthalmologists must be made after recovery [16], [17].

DECLARATIONS

Ethics and Consent to Participate

The case study presented in this manuscript involves the author as both the researcher and the patient. The author has provided full consent for the publication of personal medical information. As the author and patient are the same individual, no separate ethics committee approval was required for this self-reported case. All information has been published with the full knowledge and consent of the individual concerned.

Consent to Publish

The author, who is also the patient described in the case study, provides full consent for publication of all personal medical information, clinical data, and findings presented in this manuscript.

Availability of Data and Materials

The data supporting the findings of this study are available within the manuscript. Clinical records pertaining to the case study are held by the author. Further data may be requested from the corresponding author on reasonable grounds.

Competing Interests

The author declares no competing interests.

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Authors' Contributions

K.N.B. conceptualized the study, conducted the literature review, compiled the case study, performed analysis, and wrote the manuscript in its entirety.

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