

**A REVIEW OF GRANULOMATOUS ANTERIOR UVEITIS:
CLINICAL PRESENTATION AND MANAGEMENT**

ABSTRACT

Background: Inflammation of the uvea is called uveitis. Iris, ciliary body, and choroid are parts of the uvea. It is anatomically classified into Anterior, Posterior, Intermediate, and Pan-uveitis. Prevalence of Anterior uveitis is more common when compared to another type of inflammations, with varied rates of occurrence within the broader population of different countries. The severe implications of untreated or recurring anterior uveitis are often underestimated. Anterior uveitis is characterized by Iritis, which is inflammation of the iris, the anterior region of the ciliary body pars plicata (anterior cyclitis), or both components (iridocyclitis); it is the most common cause of uveitis. Also, based on its cause, Uveitis is classified into Granulomatous and No granulomatous uveitis. Non-infectious and infectious causes may cause it. **INFECTIOUS:** Tuberculosis, Syphilis, Leprosy, Herpes viruses, Cytomegalovirus, Trematodes, Toxoplasmosis, Post-streptococcal infections. **NON-INFECTIOUS:** Sarcoidosis, Multiple sclerosis, Lymphoma, Lens-induced. Pain, impaired vision, redness, watering, and photophobia are common symptoms of anterior uveitis. The treatment of uveitis should be evaluated according to the disease's signs and symptoms.

Objective: The purpose is to review the articles related to clinical features and management of granulomatous anterior uveitis.

Methodology: The data were collected from various electronic databases like google scholar, PubMed, etc.

Result: After reviewing the patient from OPD and given articles, granulomatous anterior uveitis can be managed by the given treatment and also reduces further diminution of vision

Conclusion: After reviewing the articles, we conclude that a given treatment can manage the signs and symptoms of granulomatous anterior uveitis.

Keywords: Uveitis, Anterior Uveitis, Iridocyclitis, Granulomatous Uveitis, Infectious uveitis, Non Infectious uveitis.

INTRODUCTION

Inflammation of the uvea is called uveitis. Parts of the uvea are Iris, ciliary body, and choroid, resulting from various causes. During an examination, cells or cellular clumps in the anterior chamber are symptomatic of anterior uveitis in a person. One of the most prevalent types of ocular inflammation that eye care professionals may face is anterior uveitis^[1]. Depending on where the inflammation is present, it can be classified as anterior, intermediate, posterior, or panuveitis; etiologically, it can be classified as infectious or non-infectious uveitis; and histopathological, It might be granulomatous or non-granulomatous uveitis in nature, depending on the body's immunological response to the underlying cause of uveitis^[2].

The most prevalent type of inflammation of the eye is Anterior uveitis, with varied rates of occurrence within the broader population of different countries. The severe implications of untreated or recurring anterior uveitis are often underestimated.

The pathophysiology of anterior uveitis might be granulomatous or non-granulomatous. Granulomatous inflammations are related to large, mutton-fat keratic precipitates (KPs), mainly consisting of epithelioid cells on the corneal epithelium. Granulomatous uveitis is a chronic illness frequently linked to systemic diseases and immunological reactions^[3].

In acute episodes of herpes, non granulomatous uveitis is common; in chronic cases, granulomatous uveitis is common^[4].

The underlying disease must be detected and treated to relieve the symptoms and save sight and may reveal systemic issues causing it. Suppose it is not treated or inadequately managed. In that case, acute inflammation can turn into Inflammation that is causing permanent vision loss, highlighting the importance of the ophthalmic primary care provider in handling these patients effectively and efficiently.

CAUSE:

Many causes, both infectious and non-infectious, can cause granulomatous inflammation of the uveal tract. **INFECTIOUS:** Tuberculosis, Syphilis, Leprosy, Herpes viruses, Cytomegalovirus, Trematodes, Toxoplasmosis, Post-streptococcal infections. **NON-INFECTIOUS:** Sarcoidosis, Multiple sclerosis, Lymphoma, Lens-induced.

Infectious cause includes-

Bacterial- Cat-scratch disease (*Bartonella*), Lyme disease (*Borrelia*), Syphilis (*Treponema pallidum*), Tuberculosis (*Mycobacterium tuberculosis*).

Viral- The most prevalent cause of anterior uveitis is infections. Varicella-zoster virus (VZV) or human herpesvirus 3, Cytomegalovirus (CMV) or human herpesvirus 5, HIV (retrovirus by which CD4+ T-Lymphocytes are infected).

Fungal- Suspected ocular histoplasmosis syndrome is characterized by atrophy of vessels around papillary, chorioretinal atrophy of retina "punched out histo spots," and without vitreous, maculopathy occurs.

Parasitic- Toxoplasmosis (*Toxoplasma gondii*), Toxocariasis (*Toxocara canis*).

Drug-induced uveitis- Uveitis caused by drugs is virtually always recoverable in weeks after the medication is stopped and topical treatment is started. Rifabutin, Cidofovir, Bisphosphonates (e.g., zoledronate and pamidronate), and Inhibitors of Tumor Necrosis Factor-alpha (i.e., adalimumab and etanercept) are some of the medications that cause uveitis.

CLINICAL FEATURES

Pain, redness, impaired vision, photophobia, and watering are common symptoms of anterior uveitis^[5]. Acute, chronic, or repeated bouts of anterior uveitis can occur. The most frequent intraocular inflammation is anterior uveitis, which manifests as unilateral discomfort or photophobia, anterior chamber cells, circumglobal redness, and flare. Pain, impaired vision, redness, watering, and photophobia are common symptoms of anterior uveitis. Most of the patients sought counsel from several ophthalmologists who would have had many attacks and utilized topical medications and systemic medications on and off. The most common symptom is blurring vision, produced by aqueous turbidity. Ciliary muscular spasm is the most prevalent cause of photophobia; however other factors such as cellular infiltration of the anterior chamber, corneal epithelial oedema, and involvement of pupillary muscle can also play a role. Spasm of the ciliary muscle is responsible for the varying degrees of pain reported in anterior uveitis. It usually feels like a dull aching pain or a throbbing sensation. Raised intraocular pressures have been related to severe pain.

The most common clinical features of granulomatous anterior uveitis are:^[6]

- keratic precipitates (KPs) are present on the corneal endothelium as cellular deposits.
- Granulomatous inflammation is linked to large and very fat KPs. The last occurrences of anterior uveitis are indicated by colored or pigmented KPs. KPs are an aggregation of lymphoplasmacytic inflammatory cells under the microscope, with epithelioid cells seen in granulomatous KPs^[7].
- At the pupillary margin, Koeppe's nodules can be detected.
- Signs of granulomatous inflammation- Iris nodules come in two varieties: Busacca nodules present on the anterior stroma and Koeppe's nodules present at the pupillary border. Both are formed up of leukocytes and should not be mistaken with nodules that have been infected^[8].
- Although in granulomatous anterior uveitis, Busacca nodules are more common, Koeppe's nodules can be detected in both granulomatous and non granulomatous forms^[8].
- Patients can have raised intraocular pressure^[9].
- Posterior synechiae —Iris and Lens adhesion – can eventually stretch 360 degrees, blocking aqueous flow through this pathway^[10].
- Granulomatous uveitis patient may have a ciliary injection, angle granulomas, anterior chamber flare cells, phakoanaphylactic uveitis cataract surgery, and inspection of the anterior segment anterior vitreous cells are present^[10].
- Some signs, such as herpetic uveitis corneal scars and atrophy of iris, roseola in syphilis (iris nodules are vascularised), trematode uveitis, an anterior chamber granuloma, may also be present^[11].
- Circumlimbal injection, anterior chamber cells, and flare are all classic symptoms of acute anterior uveitis. The expansion of episcleral arteries next to the inflammatory ciliary body causes circumglobal injection. Proteins and Inflammatory cells in the anterior chamber cause cells and flare inside the aqueous. The presence of anterior chamber cells, which does or does not be associated with a flare, indicates anterior uveitis. A hypopyon, which would be a mass of inflammatory cells gathering inside the anterior chamber inferiorly, can occur if the cells are dense enough.

Laterality is another factor to consider when evaluating and, eventually, contemplating a systemic checkup for anterior uveitis cases. Bilateral appearances, like granulomatous versus

nongranulomatous inflammation, are more likely to be related to chronic, systemic diseases, while unilateral presentations are more likely to be acute, infectious, or idiopathic.

The indications and symptoms you're experiencing can help you figure out what's causing the problem. Blurred vision is the most prevalent patient symptom caused by cells and flares in the aqueous. Ciliary muscular spasm is the most prevalent cause of pain and photophobia; however, anterior chamber infiltration, pupillary muscle involvement, and corneal epithelial edema can also cause light sensitivity.

Pain in the temple or periorbital region is typically dull, aching, or throbbing. If you have increased intraocular pressure (IOP), your pain will be more localized and acute. There seems to be no mucopurulent discharge, which can distinguish this illness from other types of anterior segment inflammation. The patient could be utterly symptom-free in cases of chronic uveitis, although the inflammation may be detected during a routine examination.

IOP can be affected in patients having anterior uveitis. There seem to be a variety of methods that can play a role in these shifts. The first is Intra Ocular Pressure reduction, which is the most prevalent. This happens when the ciliary body gets inflamed, causing the ciliary body to produce less aqueous fluid. Intra Ocular Pressure rises when aqueous humor outflow via the trabecular meshwork (TM) is blocked, as in trabeculations, and when pigment inflammatory cells block the Trabecular Meshwork. It is a more severe problem when the Intra Ocular Pressure increases because of peripheral anterior synechiae blocking the Trabecular Meshwork or when posterior synechiae cause pupillary obstruction; it is a more severe problem. Lengthy neovascularisation or steroid treatment, which could also happen at the angle and induce a spike in Intraocular pressure because of secondary angle closure, are two other reasons for elevated IOP. Luckily, iris rubeosis during uveitis is less severe and reversible than ischemic neovascularization, and it usually clears up with treatment ^[12].

INVESTIGATIONS

The underlying disease must be detected and treated to relieve the symptoms and save sight and may reveal systemic issues causing it. Suppose it is not treated or inadequately managed. In that case, acute inflammation can turn into Inflammation that is causing permanent vision loss, highlighting the importance of the ophthalmic primary care provider in handling these patients effectively and efficiently.

Investigations required for diagnosis are:

Ocular investigations:

Optical coherence tomography, B-scan ultrasonography, and fluorescein angiography for posterior segment evaluation are used. In cases in which there are small pupils and hypotony, ultrasound biomicroscopy could be used to determine the state of the ciliary body and the presence of cyclic membranes ^[13].

Laboratory investigations :

To confirm the diagnosis, investigations should be "tailored." For the first time, a patient with anterior uveitis will be investigated using the history and examination. The research should be focused on excluding systemic illness and infectious uveitis as causes of uveitis ^[14].

In other circumstances, the following examinations may be recommended:

Leucocytosis in viral etiology, Complete Blood Count:-Baseline

ESR stands for erythrocyte sedimentation rate, and it is a nonspecific indicator for systemic disease.

The Mantoux test is a general assessment. This means you've already been exposed to tubercle bacilli. The VDRL (venereal disease research laboratory test) is a syphilis screening test that is not specific.

The TPHA (Treponema pallidum hemagglutination test) is a particular syphilis test.

HLA B27: In patients with episodes of relapsed anterior uveitis, being positive for HLA B27 assists the doctor in counseling the patient for more severe and frequent recurring attacks of uveitis.

Collagen vascular disease and antinuclear antibodies.

As measured by the serum angiotensin-converting enzyme assay, active sarcoidosis measures the amount of angiotensin-converting enzyme in the blood.

However, it can be expected in sarcoidosis patients while physiologically excessive in children and chronic smokers. The results of the serum ACE test should be read along with the clinical findings.

In Sarcoidosis, a chest X-ray shows calcified hilar lymphadenopathy and tuberculosis.

Ankylosing Spondylitis: X-ray Sacroiliac joint is taken.

A high-resolution CT scan of the chest reveals sarcoidosis.

Any atypical uveitis manifestation. Tridot analysis for HIV:

The tests listed above must be done individually, and not all of them are usually needed in all people who have anterior uveitis.

The primary care physician can establish a precise diagnosis indicative of an infectious or noninfectious underlying cause by classifying uveitis as posterior or anterior, chronic or acute, nongranulomatous or granulomatous, bilateral or unilateral, and mentioning essential clinical manifestations. Additionally, they can design a tailored systemic diagnostic procedure that will save the patient money and time. Finally, it enables them to begin a careful treatment plan targeted to specific patient clinical manifestations characteristics. The first step in treating a patient with anterior uveitis is making an accurate and complete diagnosis.

Finally, a dilated fundus examination must be included in every assessment of patients with anterior uveitis. Uveitis can induce secondary lens damage or spillover inflammation and suggest panuveitis in the posterior segment, a different and much more severe illness that necessitates rapid diagnosis and a different treatment method. Whether there is evidence of true intermediate or posterior uveitis, a dilated fundus examination can help.

MANAGEMENT

Topical corticosteroids are used to manage anterior uveitis at first. Prednisolone acetate % has been the most commonly given topical corticosteroid for managing anterior uveitis, second with dexamethasone 0.1 % then prednisolone sodium phosphate %. When an individual appears with anterior uveitis acute, the vision care professional should give corticosteroids per hour until at least one week when the patient is awake. Difluorinated

prednisolone derivative Difluprednate 0.05 % emulsified can be taken four times a day, which is as effective as prednisolone acetate 1% when taken eight times per day.

Local (ocular) and systemic treatment of granulomatous uveitis, as well as treatment of complications:

OCULAR TREATMENT:

Topical non-specific anti-inflammatory medications such as topical steroids and cycloplegics are employed ^[15]. With sufficient antimicrobial protection, steroid injections are given periocular and intravitreal, and steroid implants can be used to reduce inflammation in non-infectious and infectious disorders [16] promptly.

To produce high intraocular concentrations and a more effective treatment response, intravitreal antibacterial injections such as clindamycin can be used to treat Toxoplasma, and antifungals such as voriconazole it's possible use to manage candida. ^[17]. Non-infectious uveitis can also be treated with intravitreal immunosuppressants like sirolimus ^[18]. In lens-induced situations, surgical aspiration may be beneficial ^[19].

SYSTEMIC TREATMENT:

Systemic treatment is required to regulate the systemic condition associated with uveitis, directed at the underlying etiology. This has also been linked to a reduction in eye illness. In non-infectious situations, immunomodulatory and systemic steroids drugs such as azathioprine, Mycophenolate mofetil, methotrexate, cyclosporine, and azathioprine are used ^[20].

Antituberculous medications are used to treat tuberculosis, penicillin is used to treat syphilis, and acyclovir is used to treat herpetic uveitis. On the other hand, it is used to treat infectious disorders ^[21].

TREATMENT OF COMPLICATION:

Extraction of Cataracts can solve problems where an intraocular lens could be implanted, or the extraction may proceed without implantation of the lens. Glaucoma is treated medically using a variety of topical and systemic medicines and surgically if necessary ^[22].

Glaucoma can be treated surgically by trabeculectomy, iridectomy, and glaucoma drainage devices. Some research suggests that in the long run trabeculectomy is not as effective as glaucoma drainage devices for uveitic glaucoma, while others found no difference ^[23]. Treatments for macular edema cystoids and neovascularization of the choroids associated with granulomatous uveitis include bevacizumab or ranibizumab, which are drugs of anti-vascular endothelial growth factor are given in intravitreal injections ^[24].

DISCUSSION

After reviewing various articles from sources like Pubmed, Google scholar , etc. on Granulomatous Anterior Uveitis, the most prevalent type of inflammation of eye is Anterior uveitis, with varied rates of occurrence within the wider population of different countries. It can be granulomatous and non-granulomatous, Granulomatous inflammations are related with large, mutton-fat keratic precipitates (KPs) which on the corneal epithelium mostly consists of epitheloid cells . Granulomatous uveitis is a chronic illness that is frequently linked to systemic diseases and immunological reactions. Many causes, both infectious and

non-infectious, can cause granulomatous inflammation of the uveal tract. INFECTIOUS: Tuberculosis, Syphilis, Leprosy, Herpes viruses, Cytomegalovirus, Trematodes, Toxoplasmosis, Post-streptococcal infections. NON-INFECTIOUS: Sarcoidosis, Multiple sclerosis, Lymphoma, Lens-induced. Pain, redness, impaired vision, photophobia, and watering are common symptoms . Keratic precipitates, Koeppe's nodules, Busacca nodules, Posterior synechiae, raised intraocular pressure are some other clinical findings of anterior uveitis. Ocular and laboratory investigations are done for diagnosis. It can be managed by use of topical steroids and cycloplegics. Intravitreal antibacterial injections may be employed to produce higher intraocular concentrations and a better therapeutic response .[25-29]

CONCLUSION

After reviewing the articles, we come to the conclusion that ocular symptoms can be treated by use of topical steroids and cycloplegics. Intravitreal antibacterial injections may be employed to produce higher intraocular concentrations and a better therapeutic response .

To relieve systemic symptoms associated with anterior uveitis, systemic treatment is required such as steroids and immunomodulatory drugs .

REFERENCES:

1. Rao NA, Forster DJ. Basic principles. In: Podos SM, Yanoff M, editors. *The Uvea, Uveitis, and Intraocular Neoplasms*. Vol 2. New York: Gower Medical Publications; 1992:1–17.
2. Tsirouki T, Dastiridou A, Symeonidis C, Tounakaki O, Brazitikou I, Kalogeropoulos C, Androudi S. A Focus on the Epidemiology of Uveitis. *Ocul Immunol Inflamm*. 2018;26(1):2-16.
3. Agrawal RV, Murthy S, Sangwan V, Biswas J. Current approach in diagnosis and management of anterior uveitis. *Indian J Ophthalmol*. 2010;58(1):11–19.
4. Whitley W, Sheppard J. The basics of uveitis. *Rev Optom*. 2011. Available at: http://www.reviewofoptometry.com/continuing_education/tabviewtest/lessonid/107773/.
5. Hogan MJ, Kimura SJ, Thygeson P. Signs and symptoms of uveitis. *Am J Ophthalmol*. 1959;47:155–70.
6. Weinberg RS. Anterior uveitis. *Ophthalmol Clin North Am*. 1993;6:23–8.
7. Das D, Biswas J, Ganesh SK. Pattern of uveitis in referral uveitis clinic in India. *Int Ophthalmol*. 1995;43:117–21.
8. Myers TD, Smith JR, Lauer AK, Rosenbaum JT. Iris nodules associated with infectious uveitis. *Br J Ophthalmol*. 2002;86:969–74.
9. Pavesio CE, Nozik RA. Anterior and intermediate uveitis. *Int Ophthalmol Clin*. 1990;30:244–51.
10. McCarron MJ, Albert DM. Iridocyclitis and an iris mass associated with secondary syphilis. *Ophthalmology*. 1984 Oct;91(10):1264-8.
11. Amin RM, Goweida MB, El Goweini HF, Bedda AM, Lotfy WM, Gaballah AH, Nadar AA, Radwan AE. Trematodal granulomatous uveitis in paediatric Egyptian patients: a case series. *Br J Ophthalmol*. 2017 Aug;101(8):999-1002.
12. Agrawal RV, Murthy S, Sangwan V, Biswas J. Current approach in diagnosis and management of anterior uveitis. *Indian J Ophthalmol*. 2010;58(1):11–19.
13. Tran VT, LeHoang P, Herbort CP. Value of high-frequency ultrasound biomicroscopy in uveitis. *Eye*. 2001;15:23–30.

14. Weinreb RN, Tessler H. Laboratory diagnosis of ophthalmic sarcoidosis. *Surv Ophthalmol*. 1984;28:653–64.
15. Hosoda Y, Hayashi H, Kuriyama S. Posterior subtenon triamcinolone acetonide injection as a primary treatment in eyes with acute Vogt-Koyanagi-Harada disease. *Br J Ophthalmol*. 2015 Sep;99(9):1211-4.
16. Kim M, Kim SA, Park W, Kim RY, Park YH. Intravitreal Dexamethasone Implant for Treatment of Sarcoidosis-Related Uveitis. *Adv Ther*. 2019 Aug;36(8):2137-2146.
17. Bienvenu AL, Aussedat M, Mathis T, Guillaud M, Leboucher G, Kodjikian L. Intravitreal Injections of Voriconazole for *Candida* Endophthalmitis: A Case Series. *Ocul Immunol Inflamm*. 2020 Apr 02;28(3):471-478.
18. Nguyen QD, Merrill PT, Sepah YJ, Ibrahim MA, Banker A, Leonardi A, Chernock M, Mudumba S, Do DV. Intravitreal Sirolimus for the Treatment of Noninfectious Uveitis: Evolution through Preclinical and Clinical Studies. *Ophthalmology*. 2018 Dec;125(12):1984-1993.
19. Nche EN, Amer R. Lens-induced uveitis: an update. *Graefes Arch Clin Exp Ophthalmol*. 2020 Jul;258(7):1359-1365.
20. Elnahry AG, Elnahry GA. Abdominal sarcoidosis presenting as bilateral simultaneous optic disc granulomas. *Neuroophthalmology*. 2019 Apr;43(2):91-94.
21. Gupta V, Shoughy SS, Mahajan S, Khairallah M, Rosenbaum JT, Curi A, Tabbara KF. Clinics of ocular tuberculosis. *Ocul Immunol Inflamm*. 2015 Feb;23(1):14-24.
22. Ganesh SK, Mistry S. Phacoemulsification with Intraocular Lens Implantation in Pediatric Uveitis: A Retrospective Study. *Ocul Immunol Inflamm*. 2018;26(2):305-312.
23. Bettis DI, Morshedi RG, Chaya C, Goldsmith J, Crandall A, Zabriskie N. Trabeculectomy With Mitomycin C or Ahmed Valve Implantation in Eyes With Uveitic Glaucoma. *J Glaucoma*. 2015 Oct-Nov;24(8):591-9.
24. Talat L, Lightman S, Tomkins-Netzer O. Ischemic retinal vasculitis and its management. *J Ophthalmol*. 2014;2014:197675.
25. Gajbhiye, Varsha, and Yeshwant Lamture. "Minoxidil a Youth Elixir for Eyebrow Hypotrichosis." *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH* 14, no. 2 (February 2020). <https://doi.org/10.7860/JCDR/2020/42801.13474>.
26. Kedia, Palak, and Bhushan Madke. "Unilateral Molluscum Contagiosum Following Eyebrow Grooming." *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH* 13, no. 11 (November 2019): WD01–2. <https://doi.org/10.7860/JCDR/2019/42600.13283>.
27. Khasbage, Suwarna Dangore, and Arvind S. Bhake. "Cervical Lymphadenopathy in a Dental Patient: An Eye Opener Case Report." *SPECIAL CARE IN DENTISTRY* 39, no. 1 (February 2019): 59–64. <https://doi.org/10.1111/scd.12336>.
28. Laad, Gaurish, Bhushan Madke, and Balkrishna Nikam. "Cirroid Aneurysm of Upper Eyelid." *JOURNAL OF DERMATOLOGY DERMATOLOGIC SURGERY-JDDS* 23, no. 2 (December 2019): 109–10. https://doi.org/10.4103/jdds.jdds_30_19.
29. Mahatme KG, Deshmukh P, Sable P, Chakole V. Ultrasonography: The Third Eye of Anaesthesiologist. *JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL*. 2021;33(37A):235–8.

UNDER PEER REVIEW