Review Article

A REVIEW OF GRANULOMATOUS ANTERIOR UVEITIS: CLINICAL PRESENTATION AND MANAGEMENT

ABSTRACT

Background: Inflammation of uvea is called uveitis. Iris, ciliary body and choroid are parts of uvea. It is anatomically classified into Anterior, Posterior, Intermediate and Pan-uveitis. Prevalence of Anterior uveitis is more common when compared to other type of inflammations, with varied rates of occurrence within the wider population of different countries. The serious implications of untreated or recurring anterior uveitis are often underestimated. Anterior uveitis is characterised 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 on the basis of its cause Uveitis is classified into Granulomatous and Non granulomatous uveitis. It may be caused by non infectious and infectious causes. 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 the various electronic data bases 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 come to the conclusion that the signs and symptoms of granulomatous anterior uveitis can be managed by given treatment.

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

INTRODUCTION

Inflammation of uvea is called uveitis. Parts of uvea are Iris, ciliary body and choroid , can result from a variety of causes. During an examination, the presence of cells or cellular clumps in the anterior chamber is 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 histopathologically, 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 eye is Anterior uveitis, with varied rates of occurrence within the wider population of different countries. The serious 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 with large, mutton-fat keratic precipitates (KPs) which mostly consists of epitheloid cells on the corneal epithelium. Granulomatous uveitis is a chronic illness that is frequently linked to systemic diseases and immunological reactions[3].

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

The underlying disease must be detected and treated not only to relieve the symptoms, but also to save sight and may reveal systemic issues causing it. If it is not treated or inadequately managed, 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 characterised by atrophy of vessels around papillary, chorioretinal atrophy of retina "punched out histo spots," and without vitritis, maculopathy occurs.

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

Drug induced uveitis- Uveitis caused by drugs is virtually always recoverable in a matter of 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 (ie, 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 kind of intraocular inflammation is anterior uveitis, which typically manifests as unilateral discomfort or photophobia, anterior chamber cells, circumlimbal 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, as well as utilising topical medications and systemic medications on and off . The most common symptom is blurring of vision, which is produced by aqueous turbidity. Ciliary muscular spasm is the most prevalent cause of photophobia, however other factors such as cellular infiltration of anterior chamber, corneal epithelial oedema, and involvement of pupillary muscle can also play a role . Spasm of 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. Prior occurrences of anterior uveitis are indicated by coloured or pigmented KPs. KPs are an aggregation of lymphoplasmocytic inflammatory cells under the microscope, with epitheloid 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 nongranulomatous 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 ciliary injection, angle granulomas, anterior chamber flare cells, in phakoanaphylactic uveitis cataract surgery, and on inspection of the anterior segment anterior vitreous cells are present[10].
- Some signs, such as in herpetic uveitis corneal scars and atrophy of iris, roseola in syphilis (iris nodules are vascularised), and in 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 circumlimbal 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 by a flare, is indicative of anterior uveitis. A hyopyon, which would be a mass of inflammatory cells gathering inside the anterior chamber inferiorly, can occur if the cells are dense enough .

Another factor to consider when evaluating and, eventually, contemplating a systemic checkup for anterior uveitis cases is laterality. Bilateral appearances, like granulomatous versus nongranulomatous inflammation, are more likely to be related with 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, which is caused by cells and flare 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 oedema can also cause light sensitivity .

Pain in the temple or periorbital region is typically known as dull, aching, or throbbing. If you have increased intraocular pressure (IOP), your pain will be much more localised and acute. There seems to be no mucopurulent discharge, which can assist distinguish this illness from other types of anterior segment inflammation. The patient could be completely symptom-free in cases of chronic uveitis, although the inflammation may be detected during 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 is when ciliary body gets inflamed, causing the ciliary body to produce less aqueous fluid. When aqueous humour outflow via the trabecular meshwork (TM) is blocked, as in trabeculitis, and when pigment inflammatory cells block the Trabecular Meshwork, Intra Ocular Pressure rises. 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 serious problem. Lengthy neovascularisation or steroid treatment, which could also happen at the angle and induce a spike in Intra ocular pressure because of secondary angle closure, are two other reason of elevated IOP. Luckily, iris rubeosis during uveitis is less serious and reversible than ischemic neovascularization, and it usually clears up with treatment [12].

INVESTIGATIONS

The underlying disease must be detected and treated not only to relieve the symptoms, but also to save sight and may reveal systemic issues causing it. If it is not treated or inadequately managed, 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:

For posterior segment evaluation, optical coherence tomography, B-scan ultrasonography and fluorescein angiography are used. Cases in which there is small pupils and hypotony, ultrasound biomicroscopy could be used to determine the state of the ciliary body and the presence of cyclitic membranes [13].

Laboratory investigations :

To confirm the diagnosis investigations should be "tailored". A patient with anterior uveitis for the first time 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 aetiology, Complete Blood Count:-Baseline

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

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 syphilis test that is particularly specific .

HLA B27: In patients in which there are episodes of relapsed anterior uveitis is there, being positive for HLA B27 assists the doctor in counselling the patientfor more severe and frequent recurring attacks of uveitis .

Collagen vascular disease and antinuclear antibodies .

Active sarcoidosis as measured by the serum angiotensin-converting enzyme assay ,is a test that measures the amount of angiotensin-converting enzyme in the blood .

However, it can be normal 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 on an individual basis, and not all of them are normally needed in all people who have anterior uveitis .

The primary care physician can establish a precise diagnosis that is 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 that is targeted to specific characteristics of the patient's clinical manifestations . The first step in treating a patient with anterior uveitis is to make an accurate – and full – 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 also suggest panuveitis in posterior segment, which is a separate and far more serious illness that necessitates rapid diagnosis and a different treatment method. Whether there are 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 the management of 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 that can be taken four times in a day which has been shown to be 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 given periocular and intravitreal, as well as steroid implants, can be utilised to reduce inflammation promptly and reliably in non-infectious and infectious disorders [16].

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 voriconazole it's possible to use it 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:

To regulate the systemic condition associated with uveitis, systemic treatment is required, and it is directed at the underlying aetiology . 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, are used to treat infectious disorders[21].

TREATMENT OF COMPLICATION:

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

Glaucoma can be treated surgically by trabeculectomy, iridectomy and glaucoma drainage devices . Some research suggests that in long run trabeculectomy is not as effective as glaucoma drainage devices for uveitic glaucoma, while others found no difference[23]. Treatments for macular oedema 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 it can be stated that 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 .

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