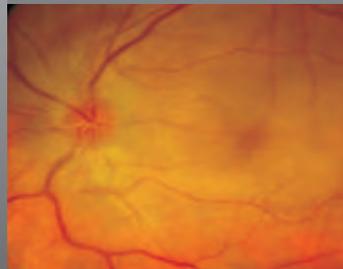
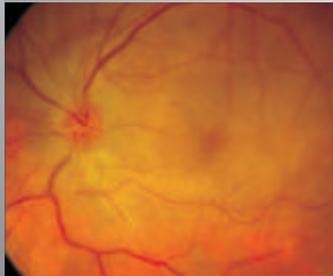
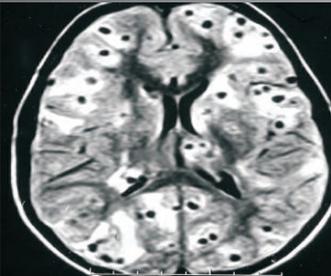


AIOS, CME SERIES (No.20)

Uveitis Made Simple

Workup & Management

S R Rathinam



ALL INDIA OPHTHALMOLOGICAL SOCIETY

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About CME

I know a lot of information is available on the net, in the books and journals. But the basic purpose of AIOS-CME series is to provide to the reader, concise up to date info on one particular topic, by an expert in the subject. The thrust is on presentation of the matter- so that it is easy to read and implement in your patient care.

Dr Rathinam`s CME on `Uveitis Made Simple` makes the topic look very simple. Very lucidly, Rathinam and his co-authors have detailed about `Workup in Uveitis`, What & How to investigate in Uveitis (always a tough and challenging decision) and what treatment to offer to the uveitis patient. Only after reading, you realize there is a lot more to Uveitis than just Steroids. Most interesting are the last 2 chapters-which gives Unusual case presentations & Differential diagnosis.

I hope all of you enjoy reading this nicely compiled CME series.

Any suggestions - please do write to us.

Lalit Verma

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Foreword

Dear Colleagues,

In ophthalmic practice, patients with vision-threatening uveitis come across as the most difficult patients to diagnose and treat. This is reflected in the dearth of “true uveitis specialists,” even at major medical centers, and the fact that many uveitis patients are cared for reluctantly by general ophthalmologists.

In this issue of AIOS CME series titled “Uveitis Made Simple”, Dr. S.R. Rathinam, Head of Uveitis Service, Aravind Eye Hospital & PG Institute Ophthalmology, Madurai, Tamil Nadu, and the co-authors have tried to simplify the approach towards managing a uveitis patient. They have touched upon the clinical workup, investigations and management strategies in a comprehensive but concise manner. Also few rare case scenarios have been discussed highlighting the varied nature of presentation of the disease.

This issue is valuable for post graduates as well as ophthalmologists and can be used as a reference for assistance in diagnosis and treatment of uveitis.

I would like to laud the efforts of Dr. S.R. Rathinam, Dr. N. Venu, Dr. Bala Murugan, Dr. Manohar Babu, Dr. Yoshish Kamath and Dr. T.R. Sathya in compiling a practical guide on uveitis.

Dr. S. Natarajan

Chairman, ARC

Introduction

Uveitis, facing the challenges in developing country

S R Rathinam

Uveitis is caused by disorders of diverse etiologies including wide spectrum of infectious and non infectious causes. The inflammatory process primarily affects the uveal tissues with subsequent damage to the retina, optic nerve and vitreous. On several occasions, it reflects diseases that are developing elsewhere in the body and uveitis may be the first evidence of such systemic diseases, generating a challenge for the ophthalmologist in reaching correct diagnosis. Besides several entities share common clinical symptoms and signs and hence the etiological diagnosis may prove to be a difficult task¹. Hence uveitis specialist needs to have through knowledge of all entities and his work up has to be complete including systemic and ocular examinations. In addition to the above mentioned challenges. India presents unique problems because of varying socio economic, demographic and morbidity patterns. The prevalence and severity of diseases in economically deprived population vary from those in rest of the world^{2,3} because of lack of good primary health care, poor affordability and poor compliance. Our ophthalmologist may also have to meet the added challenge of handling these problems in addition to managing uveitis.

Primary Medical Care

Although Government provides primary care largely free of cost, health services are often not used by poor people. Reasons include poor infrastructure, lack of sustainable care during critical circumstances, non availability of trained personnel and others⁴. India has one of the most highly privatized health care systems in the world with nearly 75% of Indian doctors based in cities, whereas about 70% of patients in this country are village-based and hence rural Indians lack access to basic health care facilities⁵. When the treatment for systemic ailment are not adequately covered, it accounts for higher incidence of ocular involvement. More importantly it is a great challenge indeed to manage rural and lower socioeconomic population in which infectious uveitis is much more common than the upper class urban patients. However these regional variations in the disease pattern are poorly addressed in the literature. Notably if systemic

work up is not already performed, systemic referrals may be needed, however it may not be accepted by the patient due to his economical constraints. At this juncture the challenge of uveitis person includes investigation and management on systemic problems as well.

Investigations

Despite the remarkable achievements in the analytical performance of investigations in standard laboratories, less attention is given in developing countries on building Evidence-Based Laboratory Medicine (EBLM) and on standardization. The lack of good quality research in this field contributes to lack of useful regional knowledge of EBLM. The diagnostic impacts of several tests are not clear in the eastern literature, resulting in inappropriate selection of laboratory tests by the ophthalmologist. The challenge still stays at ‘was the right test ordered and right interpretation derived?’ One of the best examples is the most frequently used serological test-ELISA. It is highly useful for various infectious diseases due to its simplicity, low cost and high sensitivity. But commercial ELISA tests developed in different countries demonstrate varying accuracies for different populations. It may be due to the vast molecular diversity in genes and encoded proteins among local isolates from different geographic regions, local isolates may be different from those used for the coating antigen preparations. In a study by Mohammadi ⁶, the degree of agreement varied on a home-made ELISA kit developed with local isolates against commercially used imported ELISA kits. Criteria to use imported kits include local laboratory standardization using true positive and negative sera of local population. New Receiver operating curves (ROC) in the country where they are going to be used should show the true sensitivity and specificity. But this crucial analysis is never done in any laboratory or in the hospital unless the patients are under some research project. It is not uncommon to see the ophthalmologist to be unaware of the antigens used in the kit or the cut off values of serological tests which has to be based on the baseline titer value of healthy population in his geographic location. Confirmatory diagnosis as well as the treatment unfortunately rely on tests which are not standardized for the population of developing country ⁶. Just like rigorous systems for approval of therapeutic drugs, diagnostic investigations can be subjected to systematic evaluation at local population before they are ready for commercial use. The evidence has to be collected and analyzed to ensure the diagnostic impact and clinical utility of laboratory investigations.

Sensible laboratory utilization assists in accurate diagnoses and in monitoring the prognosis. However inappropriate investigations or wrong interpretation of results in a situation similar to the interesting discussion by Rang on Ulysses syndrome. The author talks on patients getting trapped in a web of false positive investigations, further investigations, referrals and treatment before finally being recognized as healthy⁷. Increasing the awareness on need of evidence based medicine and increasing the access of information will improve the limitations of the healthcare system in our specialty⁸.

In addition, standard laboratories are not uniformly available all over the country. Semi urban and rural centers lack such facilities and suffer from poor quality management. With lack of quality management in substandard laboratories, the challenge ranges from a simple question such as ‘was the test correctly done?’ to ‘was the right test carried out on the right specimen and was the right result delivered to the right patient at the right time?’ It is not uncommon for the uveitis specialist to face the challenge of handling the laboratory result which might not be from a standardized laboratory.

Treatment

Uveitis is a potentially blinding disease in children and adults. Accurate treatment of severe inflammation preserves vision as well as prevents systemic morbidity and mortality. With no or limited national health insurance schemes and a large private sector, individuals face high economic consequences of ill health^{9,10}. The most visible impact of health economics on uveitis is on spending for investigation and treatment which are unaffordable for most of the patients from developing country. Often times patients can neither afford for cyclosporine nor for newer biological agents. This is one of the major challenges for the uveitis specialist to handle chronic uveitis which do not respond to routine treatment.

Compliance

When the uveitis is associated with systemic disease, comprehensive systemic and ocular treatment forms the basis of success of uveitis management. Patients’ knowledge, awareness and participation are important factors in treatment compliance. Patients do not always understand and may forget prescription instructions, a study done in India shows poor communication by ophthalmologists resulting in 30% of the sample population of the study using an incorrect drop regime¹¹. Nearly 5% of smear-positive Pulmonary

TB patients diagnosed in the study period were confirmed as not having initiated treatment and they were grouped as 'initial defaulters'¹². People who are prescribed self-administered medications often take less than half the prescribed doses. Compliance improves when patients understand the purpose of the prescription; an enhanced health literacy can improve the prevailing situation. Right now health research in India is not adequate and we do not have sufficient evidence based literature to help the clinician. Western literature may not be directly applicable here, we, tropical countries have to learn our lessons through our own experience.

References:

1. Harper SL, Chorich LJ, Foster CS. Diagnosis of uveitis. In: Foster CS, Vitale AT, eds. *Diagnosis and Treatment of Uveitis*. Philadelphia, WB Saunders Co; 2002:79-103.
2. Rathinam SR, Namperumalsamy P. Global variation and pattern changes in epidemiology of uveitis. *Indian J Ophthalmol*. 2007; 55:173-83.
3. Rathinam SR, Cunningham TC. Infectious causes of uveitis in the developing world. *Int Ophthalmol Clin*. 2000; 40 : 137-152
4. United Nations Development Programme (UNDP). New York: Human Development Report, 2005
5. Bagchi S. Telemedicine in Rural India. *PLoS Medicine* [Serial Online] 2006;3:e82. Available at doi:10.1371/journal.pmed.0030082
6. Mohammadi M, Talebkhan Y, Khalili G, et al. Advantage of using a home-made ELISA kit for detection of *Helicobacter pylori* infection over commercially imported kits. *Indian J Med Microbiol* 2008;26:127-31.
7. Rang M. The Ulysses syndrome. *Can Med Assoc J* 1972;106: 122-123.
8. Chryssafidou E, Arvanitis TN, Khan KS, et al. South Asian health: what is to be done? Skills of evidence based medicine need to be taught. *BMJ* 2004;328 (7443):839.
9. Sadana R, D'Souza C, Hyder AA, et al. Importance of health research in South Asia. *BMJ* 2004;328 (7443):826-830.
10. Varatharajan D. Special issue on South Asia: health economics is neglected in this region. *BMJ* 2004;328 (7434):288.
11. Buller AJ, Connell B, Spencer AF. Compliance: clear communication's critical. *Br J Ophthalmol* 2005; 89:1370.
12. Sai BB, Satyanarayana AV, Venkateshwaralu G, et al. Initial default among diagnosed sputum smear-positive pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2008;12:1055-1058.

Clinical Work up in Uveitis

To know the Unknown

N Venu, S Bala Murugan, S RRathinam

Uveitis work up starts with an elaborate history-taking. Empathetic history taking will increase patient's rapport and confidence and usually offer clues and insights into the type of uveal disease with which one is suffering. It is estimated that over 70% of diagnosis can be made on the basis of detailed medical history and meticulous clinical work up alone. Family history may suggest a correct diagnosis when dealing with tuberculosis or congenital disorders. Systemic history evaluation helps to offer possible systemic association with ocular involvement. Evaluation of the patient's social history may alert the physician to the possibility of endemic diseases, venereal disease, or Acquired Immuno Deficiency Syndrome. It is often the clinical acumen of the ophthalmologist that points out the diagnosis, that is further confirmed or ruled out by a tailored laboratory approach ¹. Ophthalmologist's attention is needed on several variables, which are given below.

History Taking¹⁻⁶

1. Demography - to collect details on- Age, Gender, Race, Geographic location of residence, socio-economic conditions and occupation
2. Ocular history - to collect details on onset, severity, laterality, duration, and course
3. Systemic history- to collect details on all systemic problems and other associated diseases
4. Treatment history - to collect drug details on dosage, response, treatment, complications and compliance of the patient
5. Miscellaneous details on –injury, surgery, migration and specific history on exposure to risk factors¹⁻⁶

1. Age

Several conditions have a predilection for certain age groups. Juvenile arthropathies and parasitic uveitis are the most common entities in patients

younger than 16 years of age⁷. In general uveitis secondary to infections is common in extremes of age and immunological diseases are common in middle age⁸. Some of the examples are:

1. Children: Juvenile Rheumatoid Arthritis, Toxocariasis
2. Young adults: Bechets, Human Leukocyte Associated antigen B27– associated uveitis, Fuch’s uveitis.
3. Old age: Vogt Koyanagi Harada syndrome, Herpes Zoster Ophthalmicus, Tuberculosis and Leprosy. (Table 1)

Table 1 History in uveitis

Demography	Age Gender Race Residence Occupation
Ocular history	Laterality Primary symptom Duration Onset Severity Course Associated findings
Systemic history	All systemic problems Associated other diseases
Treatment history	Details on dosage Response Treatment complications Compliance of the patient
Miscellaneous	Injury Surgery Migration Exposure to risk factors

2. Gender

Several conditions have a predilection for either men or women⁹:

1. Males - Ankylosing spondylitis, Reiters, Bechet’s, Sympathetic ophthalmia.
2. Females- Rheumatoid arthritis, Juvenile Rheumatoid Arthritis.

3. Race

Demographic characteristics, such as race and ancestry, can be predispositions to the development of specific conditions

1. Ankylosing spondylitis, Reiters – Caucasians¹.
2. Sarcoid- Blacks
3. Vogt Koyanagi Harada's syndrome, Behcet's syndrome –Orientals^{1, 8}.

4. Domestic Animals

Patients who own dogs or cats, or are handlers of these animals may be exposed to the intestinal parasites. *Toxoplasma gondii* and *Toxocara canii* occur after ingestion of contaminated food sources or contact with soil. Plumbers and sewer workers are at an increased risk of leptospirosis, which is transmitted by a spirochete in sewage water and urine of rats.

- i. Cat- Toxocariasis, Toxoplasmosis.
- ii. Cattle- Leptospirosis, cysticercosis, Toxoplasmosis
- iii. Pigs- cysticercosis, Leptospirosis¹⁰

5. Systemic Conditions

Endogenous endophthalmitis is more common in diabetics, renal failure, immuno suppressed patients. In the presence of an adjacent source of infection, contiguous involvement is also possible in above groups of patients (for example, the sinuses).

Extraocular Examination

The physical signs of extra ocular disease can add evidence to support the diagnostic considerations entertained as a result of the history and ocular examination findings. Frequently, the findings may have escaped recognition by the patient or may have been recognized but deemed insignificant. Thus, it is important for the ophthalmologist caring for the uveitis patient to routinely evaluate patients for evidence of extra ocular disease¹¹.

The Table 2 gives some examples of systemic clinical signs one may see in specific uveitis cases.

After careful history-taking and examination of the patient, the ophthalmologist might suspect certain conditions that help the

ophthalmologist to order appropriate tests to prove or disprove those clinical suspicions.

Table 2 Systemic signs

Poliosis	Vogt Koyanagi Harada's syndrome ¹² , Sympathetic ophthalmia
Loss of hair	Systemic lupus erythematosus, Vogt Koyanagi Harada's syndrome, and Syphilis.
Hypo-pigmentation of the skin	Leprosy, Sympathetic ophthalmia, and Vogt Koyanagi Harada's syndrome
Rash	Vasculitic disease, Systemic Lupus Erythematosus, Adamantias Behcet's Disease, Syphilis
Erythema nodosum-Tender violaceous subcutaneous nodules in lower extremities	Inflammatory bowel disease, sarcoidosis, Tuberculosis and Behcet's disease.
Scaling of the skin	Systemic Lupus Erythematosus, Psoriatic arthritis, Syphilis, and Reiter's syndrome
Discoid lesions	Systemic Lupus Erythmatosus, Sarcoidosis, leprosy and Tuberculosis.
Nail abnormalities	Psoriatic arthritis, Reiter's syndrome, and Vasculitis
Oral and genital lesions	Behcet disease ^{13, 14} , Reiter's and Syphilis
Oral ulcers alone	Systemic Lupus Erythematosus and Inflammatory Bowel Disease,
Urethral discharge	Reiter's syndrome, Syphilis, Herpes simplex, and Gonococcal urethritis
Epididymitis	Behcet's disease, Tuberculosis
Prostatitis	Reiter's syndrome, Ankylosing spondylitis, and Gonococcal disease
Nephritis	Vasculitis (Wegener's granulomatosis SLE, Behcet) sarcoidosis, tuberculosis
Arthralgias and arthritis	Seronegative spondyloarthropathies, juvenile rheumatoid arthritis, Behcet's, sarcoidosis, Systemic Lupus Erythematosus, Relapsing polychondritis Leprosy reactions
Cartilage loss	Relapsing polychondritis, syphilis, and gonococcal disease, Leprosy, Wegener's granulomatosis

Table 2 Contd...

Nasopharyngeal manifestations including sinusitis	Wegener's granulomatosis, Sarcoidosis, Whipple's disease, and Mucormycosis.
Bladder (cystitis)	Whipple's disease and Reiter's disease.
Lymph nodes	Tuberculosis, Sarcoidosis, lymphoma
Neuropathy	Leprosy, Herpes zoster, Sarcoidosis, Multiple sclerosis, Syphilis and Sarcoidosis
Hearing loss	Vogt Koyanagi Harada's syndrome, Sarcoidosis.
Respiratory symptoms	Tuberculosis, Sarcoidosis, Wegener's granulomatosis (sinusitis)
Bowel disease	Whipples disease, Crohn's disease, Ulcerative colitis
Fever	Collagen vascular disease, Tuberculosis Leptospirosis

Ocular Symptoms

With respect to ocular symptoms, pain, redness and photophobia are the important symptoms when ever anterior uvea is involved while floaters with or without decrease in vision is important for intermediate and posterior uveitis. Pain on ocular movement is seen in posterior scleritis or in orbital inflammatory diseases. Sudden bilateral loss of vision would indicate either Vogt Koyanagi Harada's syndrome or Sympathetic ophthalmia²⁻⁵.

Ocular Examination

A comprehensive eye examination is a requirement for all patients with uveitis, beginning with an assessment of the patient's best-corrected visual acuity. A good day's light examination and external examination with torch light is essential in every patient. Often clues on infectious diseases like Hansen's disease or Herpes can be obtained on adnexal examination. (Table 3)

Conjunctiva, Episclera, and Sclera and Pupillary examination

Examination of the anterior surface of the eye should first be performed in ambient illumination for subtle color differences. Inflammation of the conjunctiva and episclera appear bright red in daylight and it is more in fornix. In cases of uveitis, the congestion of the perilimbal area is more than

the palpebral and fornical conjunctiva. Scleritis will present with dilation of deep vascular plexus which is better seen with red free illumination and patient will have tenderness on palpation. Examination of pupil is a part of ocular examination & can give us a clue regarding some of the etiological conditions and structural alterations as a result of inflammation¹ (Table 3).

Table 3 Ocular signs

Anatomical location Condition

Forehead & adnexa	
Vesicles	Herpes Zoster Ophthalmicus
Poliosis	VKH
Nodules	Sarcoid, Leprosy
Madarosis	Leprosy
Conjunctiva	
Granulomas	Forigen body granulomas Sarcoid
Cornea	
Dendritic keratitis, superficial punctuate keratitis	Viral uveitis
Sclero kerato uveitis	Syphilis , tuberculosis, Hansen’s and viral
Exposure and neurotropic keratitis	Leprosy
Band keratopathy	Juvenile rheumatoid arthritis, Sarcoidosis
Iris/pupil	
Miotic and irregular pupils	Posterior synechiae(but the response of the pupil to light and near is symmetric)
Relative Affarent Pupillary Defect	Asymmetric disc involvement as a result of disc edema due to uveitis or optic atrophy as a result of chronic uveitis
Sectoral iris atrophy	Herpetic uveitis (irregular constriction of pupil)
Argyl Robinson pupil	Neurosyphilis.
Gonioscopic evaluation	
Peripheral Anterior Synechiae	Sarcoid , Tuberculosis
Iris nodules	Sarcoid, Tuberculosis
Hyphema	Herpetic
Foreign body	Trumatic uveitis

On slit lamp examination, uveitis can be classified either as granulomatous or non granulomatous, few differences are given in Table 4.

Table 4 Nongranulomatous Vs Granulomatous Uveitis

	Nongranulomatous	Granulomatous
Onset	Acute	Insidious
Evolution	Spontaneous regression(mostly)	Chronic
Keratic precipitates	Confluent, fine white coloured small (lymphocyte, plasma cells pigments)	Non confluent, large mutton fat Keratic precipitates (epithelioid cells, hystiocytes)
Iris	Occasionally Koeppe's nodules	Frequent Koeppe's and Busacca's nodules
Flare	Intense	Mild
Synechia	Easy to break with mydriatics in early stage.	Dense broad based, difficult to break
Vitreous exudates	Fine punctate opacities in vitreous	Heavy vitreous exudates

Rarely KPs may be uniformly distributed.

The causes of diffusely distributed keratic precipitates are:

- [1] Fuch's uveitis
- [2] Possner-schlossman syndrome
- [3] Sarcoid uveitis
- [4] Lens induced uveitis

Anterior Chamber Reaction :

The presence of cells and protein in the anterior chamber is a marker for iris and ciliary body inflammation in the iris and ciliary body. The field size recommended is a 1 mm by 1 mm slit beam. For the grading of anterior chamber cells, the presence or absence of a hypopyon is recorded separately.

The SUN* Working Group Grading Scheme¹⁵ for Anterior Chamber Cells :

Grade	Cells in Field†
0	<1
0.5+	1–5
1+	6–15
2+	16–25
3+	26–50
4+	>50

Flare gives evidence of only previous inflammation or breakdown of blood aqueous barrier.

Flare	Description
0	Complete absence
1 +	Faint flare (barely detectable)
2 +	Moderate flare (iris and lens details clear)
3 +	Marked flare (iris and lens details hazy)
4 +	Intense flare (fixed coagulated aqueous humor with considerable fibrin)

Iris

An important finding on the examination of iris includes the presence of posterior synechiae which can be extensive to produce seclusio pupillae, that increases the patient’s risk of iris bombe and angle-closure glaucoma.

Iris atrophy is a diagnostic feature of herpetic uveitis. Varicella zoster virus generally produces sector iris atrophy due to a vascular occlusive vasculitis, where as herpes simplex virus usually produces patchy iris atrophy. Other causes of atrophy includes anterior segment ischemia, Hansen’s disease, syphilis and previous attacks of angle-closure glaucoma.

Granulomas may be prominent in the iris stroma or the choroid. Iris nodules are most commonly seen at the pupillary margin, described as Koeppe’s nodules and those on the surface of iris are referred to as Busacca’s nodules^{1,2}.

Normal radial iris vessels can be seen dilated, producing iris hyperemia as in rubeosis irides. Hetero-chromia of iris can be either hypochromic (abnormal eye is lighter than fellow eye) as seen in Fuch's heterochromic iridocyclitis or hyperchromic (abnormal eye is darker than fellow eye) as seen in melanosis of iris.

Anterior Chamber Angle

Gonioscopic evaluation can reveal peripheral anterior synechiae sufficient to account for elevated intraocular pressure. Additionally, one may find angle keratic precipitates, a small hypopyon which was invisible on slit lamp examination, and inflammatory debris, suggesting an additional mechanism of intraocular pressure elevation from occlusion of filtering trabecular meshwork. Abnormal iris vessels, neovasclarization or fine branching vessels. (as seen in Fuch's heterochromic iridocyclitis) are easily identified by gonioscopy, and their presence can direct subsequent therapy. In cases in which traumatic uveitis is suspected, angle recession and presence of foreign body may be seen.

Lens

Important lenticular findings include cataract, lenticular deposits (composed of inflammatory debris or pigment, or both), and necrosed lens epithelial cells with degenerated cortex (glaukomflecken). The most common type of cataract in uveitis patients is the posterior subcapsular opacity. Anterior lens changes may also occur, often in association with lens capsule thickening at a site of iris adhesion. Anterior lens opacities following extreme elevations in intraocular pressure (glaukome flecken) provide insight into a history of acute uveitis glaucoma.

Intraocular Pressure [IOP]

The IOP in patients with uveitis is most commonly decreased owing to impaired production of aqueous by the non pigmented ciliary body epithelium.

The factors that can affect IOP include the accumulation of inflammatory material and debris in the trabecular meshwork, inflammation of the trabecular meshwork (trabeculitis), obstruction of venous return, and steroid therapy.

The causes of elevated IOP include:

- [1] Posner-Schlossman's syndrome
- [2] Herpetic uveitis
- [3] Toxoplasmosis
- [4] Fuchs' heterochromic iridocyclitis
- [5] Sarcoidosis
- [6] Iridocyclitis with secondary angle closure glaucoma^{1,2}

In the patient with uveitis, anterior chamber reaction should be assessed before the instillation of fluorescein to prevent obscuration of anterior chamber details due to the production of a greenish hue after fluorescein penetration into the anterior chamber.

Indirect Ophthalmoscopy

When initiating indirect ophthalmoscopy it is important to direct the illumination beam into the patient's eye without the concomitant use of the condensing lens. The red reflex is then evaluated in the primary position as well as in the eight cardinal directions. This technique gradually allows the patient's retina to become light-adapted, without the strong concentrated light delivered by the condensing lens, thereby increasing patient's comfort and cooperation with the examination. More important is the valuable information that the examiner may immediately obtain if the quality and nature of the red reflex changes. For example, if there is an area of active chorioretinitis in one quadrant the red reflex is replaced by a yellowish reflex. If a choroidal hemorrhage or tumor is present in a given area the red reflex is dark in that area only. In addition this review of the red reflex may disclose highly elevated masses as well as intravitreal changes such as foreign bodies, membranes and parasites.

Vitreous

In active vitritis, cells appear white and are evenly distributed between the liquid and formed vitreous. Old cells are small and pigmented, whereas debris tends to be pigmented but larger in size. Active cells can be found in locations that can be helpful diagnostically. A localized pocket of vitritis may suggest underlying focal retinal or retinochoroidal disease. Focal accumulation of inflammatory cells around vessels is seen in active retinal vasculitis.

Inflammatory cells that accumulate in clumps (snow balls) may precipitate on to the peripheral retina, usually inferiorly (for example, in intermediate uveitis, associated with sarcoidosis) Cells may accumulate in the retrovitreal space following contraction of vitreous fibrils and posterior vitreous detachment.

Pars Plana

Examination of the peripheral retina and pars plana for snowbanking usually requires scleral depression or use of a three-mirror Goldmann contact lens. Exudation, fibroglial band formation and revascularization are pathologic processes that occur at the pars plana.

Retina and Choroid

Retinitis presents with a yellow-white appearance and poorly defined edges, often associated with hemorrhage and exudation. Involvement may be focal or multifocal. Retinal vasculitis can involve the arteries (Wegener's granulomatosis, Systemic Lupus Erythmatosus) or veins (Leptospirosis, Sarcoidosis) as inflammatory cells accumulate around the involved vessels. Revascularization of the retina can be a manifestation of ischemic uveitis.

Choroidal inflammation can also be focal or multifocal. It is not frequently associated with vitritis due to intact retinal pigment epithelial cells that prevents inflammatory cell migration. The inflamed choroid may appear thickened and prominent infiltrates and granulomas may be present. Decomposition of the retinal pigment epithelium can alter the permeability of the blood-ocular barrier, resulting in retinal detachment. It should be highlighted that Tuberculosis can cause both focal & multifocal choroiditis and Sarcoidosis can cause both multifocal retinitis & choroiditis.

Optic Disc

Optic disc inflammation can occur with or without other signs of uveitis. Optic disc involvement takes the form of papillitis or disc edema, neovascularization, infiltration, and cupping. Neovascularisation occurs in ischemic states and is characterized by fragile vessels that are easily ruptured. Sarcoidosis and leukemia can infiltrate the disc tissue, producing an appearance similar to papillitis. Optic neuritis can occur in multiple sclerosis.^{4, 5}

Macula

Chronic inflammation can lead to the following pathologies at macula

- [1] Cystoid Macular Edema (CME)
- [2] Macular lamellar holes
- [3] Retina Pigment Epithelial clumping
- [4] Choroidal Neo-Vascular Membrane (CNVM)
- [5] Exudative macular detachment

Once we collect history and complete the systemic examination, we will be able to specifically give a name using set of descriptive terminologies in Uveitis¹ (Table 5)

Table 5 Descriptive terminologies in Uveitis According to,

Age	Severity
* Paediatric	* Mild
* Yound adults	* Moderate
* Geriatric	* Severe
Chronology	Pathology
* Acute	* Non-granulomatous
* Acute recurrent	* Granulomatous
* Chronic	
Anatomical	Pattern
* Anterior	* Focal
* Intermediate	* Multifocal
* Posterior - Retinitis - Choroiditis	* Disseminated
* Pan uveitis	* Diffuse
Laterality	Etiological
* Unilateral	* Infectious
* Unilateral alternating	* Immunologic
* Bilateral	* Traumatic
* Symmetrically bilateral	* Masquerade
* Asymmetrically bilateral	* Idiopathic

Once we have the descriptive name for our uveitis patient, we compare with existing uveitis patterns that we know and this step is known as meshing step. Probable list of etiologies are constructed and this is known as differential diagnosis (DD). After arriving at DD we look for investigations to confirm or rule out the specific diagnosis. The final step is plan on treatment ¹ (Table 6).

Table 6 Systematic work up

Descriptive naming	Example unilateral/bilateral: granulomatous/ non granulomatous: acute/chronic
Meshing	Comparison with the existing diagnosis
General and specific lab testing	To evaluate the patient for treatment; To rule in/rule out diagnosis
Specialist consultation	To confirm the systemic disease and start the treatment
Therapy	General and specific treatment
Follow up	Evaluation for the course of the disease and effectiveness of treatment

It is comprehensive work up that takes the clinician to the list of differential diagnosis and then laboratory work up before he finalizes his prescription.

References :

1. Smith RE, Nozik RA: Uveitis: A clinical approach to diagnosis and management, Baltimore, Williams and Wilkins: 1989; Ed 2.
2. Cunningham ET, Nozik RA. Uveitis: Diagnostic approach and ancillary analysis. In: Duane's Clinical Ophthalmology, Vol 37. Philadelphia: Lippincott-Raven: 1997:1-25
3. Pepose JS, Holland GN, Wilhelmus KR: Ocular Infection and Immunity: St. Louis, Mosby: 1996.
4. Nussenblatt RB, Whitcup SM, Palestine AG : Examination of the patient with uveitis. (Ed) Uveitis. Fundamentals and clinical practice, Mosby publications, 1996:pp 58-68.
5. Rao NA, Forster DJ, Aigsburger JJ: General approach to the uveitis patient. The Uvea. Uveitis & Intraocular neoplasms. Vol.2, New York, London, Gower Medical publishing: 1992
6. Foster CS, Vitale AT. In: Diagnosis and Treatment of Uveitis. Philadelphia: WB Saunders; 2002
7. Cunningham ET. Uveitis in children. Ocular Immunology and Inflammation 2000; 8:251-261
8. SR Rathinam, P Namperumalsamy:Global variation and pattern changes in epidemiology of uveitis. Indian Journal of Ophthalmology 2007; 55:173-183.
9. Chang JH, McCluskey PJ, Wakefield D. Acute anterior uveitis and HLA-B27. Survey of Ophthalmology. 2005;50:364-88
10. Rathinam SR, Leptospirosis. Current Opinion of Ophthalmology 2002; 13:318-386.

11. Harper SL, Chorich LJ, Foster CS. Diagnosis of uveitis. In: Foster CS, Vitale AT, eds. *Diagnosis and Treatment of Uveitis*. Philadelphia, WB Saunders Co; 2002:79-103.
12. Rajendram R, Evans M, Rao NA. Vogt-Koyanagi-Harada disease. *International Ophthalmology Clinics*. 2005;45:115-34.
13. Evereklioglu C. Current concepts in the etiology and treatment of Behcet disease. *Survey Ophthalmology* 2005;50:297-350
14. Janati K, El Omari K, Benchiki H, Hamdani M, Lakhdar H. [Ocular manifestation of Behcet disease (study of 50 patients consulting in dermatology department) *Rev Med Interne* 2005;26:771-6.
15. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol*. 2005;140:509-16.

Investigations in Uveitis

S R Rathinam

The term uveitis represents inflammation of one or all parts of the uveal tract. It may be the first presentation of a wide variety of underlying ocular and systemic diseases including noninfectious, infectious and neoplastic causes. Diagnosis of potentially sight threatening intraocular inflammation can be very difficult as the clinical features are often less specific, and there are often no associated systemic signs. Single uveitic entity may present in a variety of different ways, and may mimic another known cause. There are several investigations in uveitis to differentiate various causes; however investigatory work up in uveitis is usually a puzzling task¹.

Baseline mega work up of ordering all the investigations do not contribute to a cause or help in management, and it only proves to be expensive⁶⁻⁹. The investigations in uveitis are planned in a systematic tailored approach to each patient¹. Tests are ordered only if there is a strong clinical suspicion of a specific disease. Further one cannot expect to find a 'definitive' aetiology in the vast majority of patients in their first visit. In some patients with recurrent or chronic uveitis, repeating investigations during follow up may increase the yield of positive results.

Pre investigatory work up

- Thorough history taking (ocular and general)
 - Complete ocular examination
 - General physical examination
 - Specialist medical referral (for further evaluation)
-
-

Thorough history and examination findings are pre requisite for the laboratory investigations. All uveitis patients need to be asked about known systemic diseases, past or present, with specific questions aimed to identify major systemic problems. It is essential that a detailed history is taken and direct

questioning includes asking about back / joint problems, skin diseases, respiratory diseases, neurological diseases, gastrointestinal disease, mouth and genital ulcers and sexually transmitted disease. Those patients in whom an underlying systemic disease is suspected should be referred to a physician as they may require more detailed/invasive investigations. History is followed by a thorough ocular examination²⁻⁴. Presence of conjunctival or iris nodules or iris atrophy may point to a specific diagnosis¹. Following history and examination, a differential diagnostic list is compiled, taking into consideration the clinical features and the causes of uveitis seen in the patient's age and gender. It is important for the ophthalmologist to make a clinical differential diagnosis in order to plan the investigation needed¹.

The investigations in uveitis may be discussed under following questions:

- Who will need the investigations?
- Why do we do?
- When do we do?
- Where will we get the specimen?
- What do we do?
- How do we interpret?

Who will need the investigations?

The investigatory work up is needed only for the patients in whom the investigation,

- Will provide a 'definitive' aetiology
- Will confirm or reject a possible diagnosis
- Will identify any underlying systemic disease process or association
- Will help in the management of the patient
- Will study a possible iatrogenic complication
- Will study the sequela of the disease
- Will play as a prognostic indicator

Uveitis may form part of a systemic disease process, however, in most uveitis patients, the routine serological and radiological investigations are usually not helpful⁶. For example, there are no serological markers of disease activity in most of the uveitis including VKH syndrome, sympathetic

ophthalmia, Fuch hetrochromic uveitis, HLA B 27 related diseases, or Behcets syndrome. In such situations routine serological investigations may not be beneficial. Further in patients who have the definitive diagnosis on clinical examination for example, traumatic uveitis, the investigations meant for etiology are not needed. In patients with old resolved uveitis where additional treatment is not needed, for example, a healed retinochroiditis, the investigations are not required.⁸

Why do we do?

Although the investigations are mainly meant for, confirmation of the diagnosis, it is important to remember that the patients need different set of investigations for assessing their fitness for the treatment. Some patients come in late stage or being followed for a long time, they need the tests that will measure the Sequela / Iatrogenic complication

Investigations and their purpose

1. Confirmation of diagnosis-eg- work up for etiology-Toxoplasmosis, ELISA
2. Fitness for treatment –Liver function test-before starting Methotrexate
3. Sequela measurement- FFA for CNVM
4. Iatrogenic complication- Blood sugar after chronic steroid treatment

When do we do?

Investigations are done after methodical record of symptoms, signs and progress of the disease. Diagnostic testing in the absence of complete knowledge of the patient will often lead to incorrect test result interpretation and may affect the diagnosis^{1, 2, 8}. Simple anterior uveitis need not be investigated mainly because it may be a very early stage of any uveitis and characterization of uveitis is needed before we plan for any investigation⁶. However, investigation is warranted in all cases of intermediate, posterior, diffuse, or bilateral inflammation and when the uveitis is granulomatous, recurrent, bilateral, chronic or associated with systemic symptoms or signs, or a history of unexplained systemic inflammation such as erythema nodosum. In some patients with recurrent or chronic uveitis, repeating investigations during follow up may increase the yield of positive results.

Where will we get the specimen?

The diagnostic clue is obtained either from the systemic work up or from the ocular work up. Systemic work up in ocular inflammation has limited value in confirmation of the diagnosis. A negative work up cannot rule out the diagnosis; however a positive result may increase the clinical suspicion in relevant cases.

The systemic work up includes

1. Body fluid analysis
2. Tissue analysis
3. Imaging techniques

The body fluid analysis includes tests such as ANA for Collagen vascular disease¹⁰ and biochemical analysis of blood (angiotensin converting enzyme in Sarcoid)⁸. The best example of tissue analysis is the biopsy of the lymph node for Tuberculosis⁵. Imaging technique include radiological studies (eg: Xray chest PA view for Tuberculosis) and CT Scan and MRI (Eg: CNS cysticercosis in cases of intravitreal cysticercosis)

Similar to the systemic work up, one can order for the specific ocular work up.³

The ocular work up includes,

1. Ocular fluid analysis eg: Aqueous humour and vitreous studies^{7, 11, 12}
2. Ocular tissue analysis eg: Iris/chorioretinal biopsy⁷
3. Ocular imaging techniques eg: FFA, ICG, USG^{7, 13}

The study of aqueous obtained by tapping the anterior chamber has the promise of an invaluable aid in diagnosis. Analysis of ocular fluids or the tissues for microbiological/ molecular techniques and antibody detection studies are more relevant than the systemic evaluation. Vitreous biopsy may be helpful because T cells and macrophages are more common in the immune mediated disorders than in lymphoma, where B cells predominate. However collecting the fluid or tissues is often difficult in inflamed eyes.

What do we do?

In the clinical setting, the minimum number of investigations that will give

the maximum information regarding the management of the patient is recommended.

General Investigations

Complete Blood count- CBC

ESR/ C Reactive Protein

Syphilis Serology- TPHA, VDRL

Blood sugar & Urine analysis (Diabetes Mellitus)

Kidney and Liver function tests in case where patient may need immunosuppressive drug or anti tubercular drugs.

Although Complete blood count is done in every patient it is not to yield any specific diagnosis but eosinophilia may point out a parasitic infection and sarcoid, raised white count in bacterial infections, relative lymphocytosis in viral infections or tuberculosis. Aplastic anemia and thrombocytopenia have to be ruled out in patients on immunosuppressive treatment.

Specific Investigations

I. Infectious Uveitis

A. Bacterial Diseases

1. Tuberculosis

Chest X Ray,

Mantoux test,

Acid-fast stain of ocular fluid,

Culture in LJ media & Bactec culture ocular fluid,

Nucleic acid amplification,

Morning sputum & urine stain & cultures for *M. tuberculosis*,

Mantoux test help in diagnosis of Tuberculosis in almost 50% of the cases of systemic TB¹⁴.

Interpretation of tuberculin skin testing can be difficult. There is no specific amount of induration that confirms TB, nor does a negative test exclude TB.

*Routine BCG vaccination at birth, using a reduced dose of 0.05 ml, is unlikely to interfere subsequently with the diagnostic value of the Mantoux test. However, revaccination at 10 years may affect the response¹⁵. Newer tests are being developed based on gamma interferon production by T cells sensitized to specific antigens, which are specific to *M. tuberculosis* and therefore not influenced by BCG or most nontuberculous bacteria. These tests, including Quantiferon TB Gold and enzyme-linked immunospot (ELISPOT) test, may prove useful in the future.*

2. Leprosy

Slit smear test or other tissue biopsy.

3. Syphilis

Treponemal and nontreponemal serology,
VDRL, and FTA-ABS (fluorescent treponemal antibody absorption test),

4. Leptospirosis

Microagglutination test
ELISA for *Leptospira* antigens,

5. Lyme disease

Borrelia burgdorferi by ELISA and Western blot

6. Postsurgical / traumatic / endogenous endophthalmitis

Gram's stain and culture of throat, nasal, blood, urine culture and culture of any catheter if present.

Gram's stain and cultures of aqueous and vitreous.

Echocardiogram for right-to-left shunt/vegetations

Ultrasound abdomen for liver abscess

*When chronic postoperative endophthalmitis is considered, the microbiology labs can be informed of need for special stains and cultures to rule out *P. acnes*, *Staph. epidermidis*, *Candida* species and others in differential diagnosis.*

B. Parasitic Diseases

1. Toxoplasmosis

- ELISA for Toxoplasmosis Serum anti-*Toxoplasma* IgG and IgM,

- Toxoplasmosis: IgM is important in neonates, while it is rising IgG in adults
- Skull X Ray for calcification, if congenital Toxoplasmosis,
- HIV if bilateral Toxoplasmosis,
- CT/MRI if HIV positive and symptomatic Toxoplasmosis

2. Cysticercosis

- B-scan ultrasound (USG), ultrasound Bio Microscope (UBM) of eye to distinguish from choroidal melanoma.
- Computerised tomography (CT) and MRI (Magnetic Resonance Imaging) of body tissues of brain, muscle,

3. Toxocariasis

- ELISA for Serum anti-*Toxocara canis* IgG and IgM

4. Pneumocystis choroiditis

- CD4 count,
- Induced sputum for staining, bronchoalveolar lavage

C. Viral diseases

1. HIV (Human Immunodeficiency Virus)

- Western blot
- ELISA
- Tridot

2. Herpes simplex virus; Herpes varicella-zoster virus;

- Aqueous and vitreous fluid for PCR (polymerase chain reaction),
- Goldmann-Witmer quotient ARN Serum titers to HSV-I, HSV-II, HZV, CMV

II. Non Infectious Uveitis

1. Juvenile idiopathic arthritis (JIA)

- ESR
- ANA,

- X Ray

2. HLA-B27 related anterior uveitis,

- HLA-B27 typing
- X-ray sacroiliac joints (2 yearly Sacroiliac joint X rays in males if initial X ra normal)

3. Sarcoidosis

- Angiotensin-converting enzyme;
- Lysozyme,
- Serum or urine calcium,
- Anergy to common antigens,
- Chest radiography,
- Gallium scan,
- Biopsy for noncaseating granulomas,
- Pulmonary Function Test,
- Bronchoalveolar lavage

ACE- Relatively nonspecific, elevated levels may occur normally in children,

Lysozyme- Specificity is lower than ACE, may be useful for monitoring disease activity. It is generally acceptable to diagnose presumed ocular sarcoidosis in the absence of biopsy evidence by obtaining three positive tests of either an elevated serum angiotensin-converting enzyme (ACE), elevated serum lysozyme, skin test anergy, or hilar lymph node enlargement ⁸

Collagen vascular diseases

Systemic lupus erythematosus (SLE)

- CBC (complete blood count)
- ANA (antinuclear antibody)
- dsDNA, ssDNA (double- and single-stranded deoxyribonucleic acid)
- Anti-SM

- Anti-RNP, C3, C4 (complement components)

ANA- false-positive test results are common in elderly population.

Progressive systemic sclerosis

- Patient may be anemic
- Urinalysis for red blood cells
- Pulmonary function tests - restrictive lung disease
- Chest X-Ray - fibrotic changes
- Elevated sedimentation rate and hypergammaglobulinemia
- ANA may be positive
- Rheumatoid factor may be elevated
- ACE levels, LE cell test, and cold agglutinins may be altered
- Scleroderma anti-body (SCL-70) is positive in up to 30 percent of the patients
- Anticentromere antibody is positive in 50 percent of the patients

Relapsing polychondritis

- Biopsy showing granulomatous chondritis

Wegener's granulomatosis

- Chest radiography,
- Sinus x-ray film,
- cANCA (antinuclear cytoplasmic antibodies),
- Urinalysis,
- Tissue biopsy

Polyarteritis nodosa (PAN) group

- Serum eosinophils,
- P ANCA,
- Angiography

Temporal arteritis

- ESR,

- C reactive protein
- Arterial biopsy

Behcet's syndrome

- Fundus Fluorescein Angiography (FFA)
- HLA-B51 and B52,
- Pathergy on skin testing
- FFA

Vogt-Koyanagi-Harada syndrome

- USG, (ultrasonogram)
- FFA

Sympathetic ophthalmia

- USG, (ultrasonogram)
- FFA
- Enucleation of the blind eye and histopathology

Fuchs' heterochromic iridocyclitis

- Currently no specific test

Retinal vasculitis

- ESR,
- VDRL/FTA-ABS,
- Sarcoidosis tests,
- Vitreous biopsy for lymphoma,
- Viral work up,
- Toxoplasma and Tuberculosis work up
- Leptospirosis work up

Intraocular lymphoma

- Vitreous biopsy for cytology, immuno histochemist(CD-20 cells)
- MRI,

- lumbar puncture,
- CSF cytology

White Dots Syndrome

- FFA , ICG

Non-Hodgkins lymphoma

- Vitreous biopsy
- Choroidal biopsy

Amyloidosis

- Vitreous biopsy

How do we interpret?

Interpretation of results is very important, particularly with regards to false negatives and false positives. The latter are not uncommon with regards to syphilis serology and the Mantoux test^{8,14-16}. If the test has poor test sensitivity and specificity, neither the positivity confirm the diagnosis nor the negativity rules out the disease.

Conclusion

Although helpful, patient's history and examination alone may not be sufficient to make a definitive diagnosis in some cases. Inflammatory eye disorders have wide, overlapping clinical characteristics that are difficult to distinguish different causes. New diagnostic advancements over the past few decades have improved the timely diagnosis of these often devastating illnesses that range from infectious, auto-immune, and neoplastic etiologies. Aim of this article is to summarize the most useful investigatory methods employed in the inflammatory diseases.

References

1. Cunningham ET, Nozik RA. Uveitis: diagnostic approach and ancillary analysis. In: Duane's Clinical Ophthalmology, vol 37. Philadelphia: Lippincott-Raven, 1997:1–25
2. Pepose JS, Holland GN, Wilhelmus KR: Ocular Infection and Immunity. St. Louis, Mosby, 1996.
3. Nussenblatt R, Whitcup SM, Palestine A. In: Nussenblatt R, ed. Diagnostic testing: uveitis fundamentals and clinical practice, 2nd ed. St. Louis, MO: CV Mosby; 1996;6: 79–90
4. Rao NA, Forster DJ, Aigsburger JJ: General approach to the uveitis patient. The Uvea. Uveitis & Intraocular neoplasms. Vol.2, New York, London, Gower Medical publishing, 1992

5. Foster CS, Vitale AT. In: *Diagnosis and Treatment of Uveitis*. Philadelphia: WB Saunders; 2002.
6. Forooghian F, Gupta R, Wong DT, Derzko-Dzulynsky L. Anterior uveitis investigation by Canadian ophthalmologists: insights from the Canadian National Uveitis Survey. *Can J Ophthalmol*. 2006;41(5):576-83.
7. Singh, Rishi P; Young, Lucy H "Diagnostic Tests for Posterior Segment Inflammation" *INT OPHTHALMOL CLIN: Ocular Inflammation* 46;2006:195-208
8. Wade, N. Kevin *Diagnostic Testing in Patients With Ocular Inflammation*. *Articles International Ophthalmology Clinics*. 40:37-54; 2000.
9. Priem H, Verbraeken H, de Laey JJ. Diagnostic problems in chronic vitreous inflammation. *Graefes Arch Clin Exp Ophthalmol*. 993;231:453-456.
10. Tan EM, Feltkamp TE, Smolen JS, et al. Range of antinuclear antibodies in "healthy" individuals. *Arthritis Rheum* 1997;40(9):1601-1611
11. Kijlstra A, Luyendijk L, Baarsma GS, et al. Aqueous human analysis as a diagnostic tool in toxoplasma uveitis. *Int Ophthalmol* 1989;13(6):383-386
12. Knox CM, Chandler D, Short GA, Margolis TP. Polymerase chain reaction-based assays of vitreous samples for the diagnosis of viral retinitis. Use in diagnostic dilemmas. *Ophthalmology* 1998;105(1):37-44
13. Finamor, Luciana Peixoto; Muccioli, Cristina and Belfort Jr., Rubens "Imaging Techniques in the Diagnosis and Management of Uveitis" *INT OPHTHALMOL CLIN: Uveitis and Related Ocular Inflammations: a global perspective from the international uveitis study group*: 45;2005:31-40
14. Chaudhuri N, Shaw BP Value of Mantoux Test in diagnosis of tuberculosis in chronic illness.. *Indian J Public Health*. 37;37-41:1993
15. Karaliedde S, Katugaha LP, Urugoda CG Tuberculin response of Sri Lankan children after BCG vaccination at birth. *Tubercle*.68:33-8; 1987
16. Larsen SA, Steiner BM, Rudolph AH. Laboratory diagnosis and interpretation of tests for syphilis. *Clin Microbiol Rev* 1995;8 (1):1-21

Treatment Modalities

Science & Art of healing uveitis

Manohar Babu, Yohish Kamath

Introduction and general principles

Uveitis, denotes inflammation of the iris, ciliary body, choroid and can also involve contiguous structures like the cornea, vitreous, retina, and sclera as well- in short, the entire eye. The problems caused by this condition are prevalent worldwide- and if not treated adequately can cause visual impairment and blindness due to permanent structural damage. It accounts for 10% of blindness in the even in developed countries¹.

There are many causes of uveitis:

- Infectious- seen more commonly in developing countries, and
- Immunological- seen more in the developed regions².

Diagnosis can be elusive, hunt for an underlying cause can be time and money consuming in some cases. Care of the patient is long, can be tedious for the patient, their family, and the treating consultant as well.

Intraocular inflammation or uveitis has been treated since the 18th century AD. Presence of hypopyon has been described by Scarpa in 1805 and he treated this patient by bleeding her abundantly from her arm and foot, by applying leeches near both angles of her eyes and by purging. Also by applying small bags of gauze filled with emollient herbs boiled with milk the inflammation she was entirely relieved of symptoms by the eleventh day³. In 1830, tincture of belladonna was used to dilate the eye, and later opiates were used to relieve pain. It was not till 1952 that it was discovered that corticosteroids helped to care for patients with inflammatory disease.

Every effort is to be made to diagnose the underlying cause of uveitis.

One needs to go beyond the basic workup of a patient if

- Inflammation is *granulomatous*
- Positive history on questioning

- Posterior Uveitis or retinal vasculitis
- If the patient does not improve on steroid treatment or patient has more than 3 episodes of Uveitis.

The basic therapeutic principles are:

- (1) To treat infectious causes of uveitis specifically (eg. ocular tuberculosis, syphilis),
- (2) Non infectious uveitis are treated with corticosteroids (not indefinitely but to taper and stop) in any appropriate form to control or abolish inflammation,
- (3) To use immunomodulatory agents if patient has steroid induced complications, Uveitis unresponsive to steroids, and associated with ocular or systemic condition for which steroid therapy alone is associated with a poor long term outcome (e.g. Behçet's disease)¹.

The treatment of non-infectious Uveitis is discussed in the last part of this section.

A. Treatment of Anterior Uveitis

It may not be possible to always find an underlying cause for the uveitis. The treatment of anterior uveitis can be easy when the patient comes early during the inflammatory episode. To eliminate flare and cells in the anterior chamber, one can use strong topical corticosteroids like Dexamethasone 0.1% or the moderate Prednisolone Acetate 1% or the milder Fluoromethalone 0.1% eye drops in a tapering fashion. One has to be sure to have graded and have recorded the severity of the anterior chamber reaction according to the SUN (preferably) classification, and begin to taper the topical steroid only when the inflammation subsides (e.g. from 3+ cells to 2+ cells, from 3+ flare to 1+ flare etc.). In the absence of posterior synechiae, cycloplegics are to be used to relieve photophobia due to ciliary muscle spasm.

Thus typically in a patient presenting with mild to moderate anterior Uveitis, the author would use topical corticosteroid 6 times a day for a week and on review if the grade of inflammation is lessened, would further taper four times a day for a week, two times a day for a week and once a day for a week and stop. A short acting cycloplegic would be preferred, (keeps pupil mobile and permits rapid recovery when discontinued) like Homatropine

1% to Cyclopentolate 0.5-1%, three times a day for a week and then once daily for a week and stop.

Seronegative spondyarthropathies are the commonest cause of anterior Uveitis, of course, next only to idiopathic anterior Uveitis, and can be difficult to treat when presenting with a classic “plastic iridocyclitis”. Every effort is to be made to break the synechiae (which can form due to the transient and translucent Koeppel’s nodules or due to fibrin in the anterior chamber) within a few hours of onset by using strong mydriatics/ cycloplegics. When treating such patients the anti-inflammatory therapy consists of half hourly or even more frequent administration of the more potent Dexamethasone 0.1% drops along with the mydriatic, Phenylephrine 0.5-1% along with a cycloplegic, Atropine 1% or the less potent Homatropine 1% drops three to four times, review the patient 2 to 3 hours later to make sure the synechiae are broken in at least a quadrant (very important in those with an occluded pupil- to prevent iris bombe), and send them home on half hourly or one hourly corticosteroid drops along with three to four times of Atropine or Homatropine use. We should review the patient a day or two later to make sure the synechiae are still broken, to make sure that the patient is compliant, the amount of flare and cells are dropping, and give further instructions on the tapering schedule.

Contrary to popular belief that, use of Atropine 1% can cause a dilated and fixed pupil with annular posterior synechiae, the frequent use of concomitant topical corticosteroids will ensure that does not happen by lessening the amount of flare and cells in the anterior chamber in those crucial 2 days.

Apart from the seronegative spondyarthropathies, Behçet’s disease can present with a hypopyon, an infectious endophthalmitis can present with anterior chamber inflammation- both these conditions can present with an acute onset anterior Uveitis with or without hypopyon. Sarcoidosis, syphilis, low grade endophthalmitis – e.g. *P. acnes* can also present with a mild to moderate anterior Uveitis⁴. We should also note that immune recovery Uveitis, ocular tuberculosis, toxoplasmosis, acute retinal necrosis can also present as anterior Uveitis. These entities will need treatment for the anterior segment involvement in the same lines mentioned above, in addition to addressing their posterior segment disease.

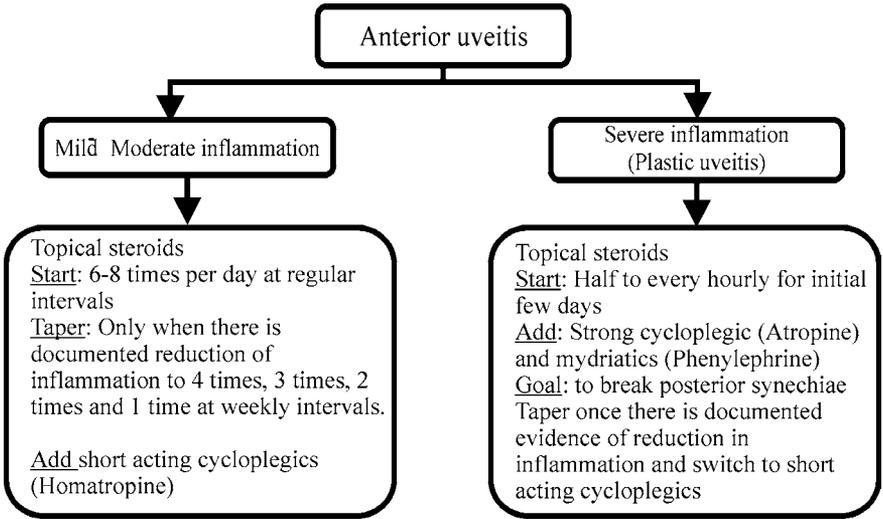


Table 1 Topical corticosteroids used in anterior uveitis

Drug	%
Dexamethasone	0.1
Prednisolone acetate	1.0
Prednisolone phosphate	1.0
Fluoromethalone	0.1
Loteprednol	0.2, 0.5
Rimexalone	1

Table 2 Commonly used topical mydriatics/cycloplegics

Drug	%	Mydriasis		Cycloplegia	
		Maximal-Hours	Recovery	Maximal-Hours	Recovery-Days
Atropine	1.0	30-40	7-10 days	1-3	7-12
Homatropine	1.0	40-60	1-3 days	0.5-1	1-3
Cyclopentolate	0.5-1	30-60	1 days	0.5-1	1
Tropicamide	0.5-1	20-40	3-6 hours	1/2	<1/4
Phenylephrine	0.5-1	20-60	3-6 hours	None	None

Common side effects of mydriatics/cycloplegics:

Atropine	- Toxicity, conjunctivitis, elevated IOP, Angle closure glaucoma, photophobia, blurred vision
Homatropine	- 1/10 as potent & 1/50 of the toxicity of Atropine
Tropicamide	- Hypersensitivity reactions, blurred vision, elevated IOP, ACG
Phenylephrine	- Pain, lacrimation, keratitis, allergic dermatitis-conjunctivitis. ACG, lid retraction, pigment release from iris, rebound miosis, tachycardia- in 10%, hypertension, angina, arrhythmias, MI, cardiac failure/arrest, SAH

B. Treatment of Intermediate Uveitis (IU)

After ruling out infectious causes of IU, the following (modified Kaplan's⁵) algorithm is suggested-

Step 1. *Periocular steroids* administered by local injection of depot corticosteroids, may be repeated every 4 weeks until 3-4 injections have been administered. Generally the inflammation responds and the CME improves. (Intravitreal triamcinolone (IVTA) may be an alternative to periocular injections in refractory cases.)

Step 2. If local therapy is not effective or bilateral severe disease is seen at presentation *oral corticosteroids* are indicated.

Step 3. *Systemic immunomodulatory therapy* is indicated in the treatment of bilateral disease, and can be considered if corticosteroids fail, are not tolerated or contraindicated

Step 4. If corticosteroids fail, or if corticosteroids and immunomodulatory therapy are contraindicated, and if pars plana snowbanks are present, peripheral ablation with *cryotherapy or indirect laser photocoagulation* to the peripheral retina can be done.

Step 5. If all the treatment modalities fail to control inflammation, pars plana *vitrectomy* with induction of posterior hyaloidal separation and peripheral laser photocoagulation to pars plana snowbank may be performed, along with immunomodulatory therapy.

C. Treatment of Posterior Uveitis with Vitritis

When you see focal chorioretinitis - think of tuberculosis, syphilis toxoplasmosis, toxocariasis and cytomegalovirus retinitis (CMVR) as possible differential diagnosis⁴.

Table 3 Treatment of Toxoplasmosis⁴

1. Triple therapy		
• Pyrimethamine	• Loading dose 50-100mg, 25-50mg daily	Add Folinic acid 5mg to prevent leucopenia/thrombocytopenia due to inhibition of folic acid metabolism
• Sulphadiazine	• Loading dose 2-4g, 1gm 4 times dailt	In new born with congenital disease-sulpha and pyrimethamie for 1 year
• Corticosteroid	• 0.5-1mg/kg/day	
2.Clindamycin- oral		
	300mg 4 times a day	Can be used alone or in combination (Pseudo membranous colitis is a reported adverse reaction
3.Trimethoprim/ sulpha metho-xazole (DS) - oral		
	(160mg/800mg) Twice daily	
4. Azithromycin		
5.Spiramycin (in newly acquired infection in pregnancy) - oral		
	250mg daily 400mg three times daily	Sulpha safe in first 2 trimesters
6. Atovaquone- oral		
	750mg four times daily	Along with sulpha, pyrimethamine and clindamycin- can be used in HIV/AIDS

If the chorioretinitis is multifocal consider sarcoidosis, tuberculosis, acute retinal necrosis syndrome (ARN), progressive outer retinal necrosis (PORN) fungal infections (Candida, Aspergillus), intraocular lymphoma (masquerade syndrome), multifocal choroiditis with panuveitis (need to rule out tuberculosis, sarcoidosis and syphilis). Toxoplasmosis and CMVR can be multifocal as well.

Table 4 Treatment of CMV retinitis⁴

1.Ganciclovir- intravenous/oral	Intravenous- Induction- 5mg/kg twice daily for 2 weeks then once daily- maintenance. Oral 1g three times daily as maintenance Can be given intravitreal-2mg in 0.1ml- once a week as maintenance	Side effect- reversible myelosuppression
2.Oral valganciclovir	Induction- 900mg twice daily for 21 days, then once daily maintenance	
3.Foscarnet- intravenous	Induction- 90mg/kg every 12 hours for 2 weeks then once daily maintenance	Can be given intravitreal 2.4mg in 0.1ml twice a week for 2-3 weeks
4.Ganciclovir implant		Delivers drug 6-8 months
5.Cidifovir-intravenous	Induction 5mg/kg once a week for 2 weeks then same dose once every 2 weeks maintenance	Can be given intravitreal 15- 20µg every 6 weeks

Definitive diagnosis of intraocular TB is based on demonstration of acid-fast bacilli on direct smear or growth of *Mycobacterium tuberculosis* from ocular fluids or tissue specimens. In the absence of the above, however, most of the cases of intraocular TB remain presumptive based only on corroborative evidence such as positive tuberculin skin test, healed lesions on chest x-ray, or associated systemic TB⁶. Oral and typical steroid may be needed in some cases in addition to ATT.

Table 5 Treatment of tubercular uveitis (Antitubercular treatment ATT)

Isoniazid- oral	5mg/kg/day once daily for 9 months
Rifampicin- oral	Body weight < 50kg- 450mg once daily for 9 months Body weight > 50kg- 600mg once daily for 9 months
Ethambutol- oral	15mg/kg/day once daily for 2 months
Pyrazinamide- oral	25-30mg/kg/day once daily for 2 months

When the chorioretinal involvement is diffuse- Vogt Koyanagi Harada syndrome (VKH), sympathetic ophthalmia and an infectious endophthalmitis are the possible differential diagnosis.

Table 6 Treatment of Acute Retinal Necrosis⁴

Acyclovir- intravenous/ oral	10mg/kg/day in 3 doses IV for 10-14 days
Acyclovir- oral	800mg five times daily for 3 months in VZV infection/ one half dose for HSV infection
Valacyclovir- oral	1g three times daily for 3 months in VZV infection/ one half dose for HSV infection
Prednisolone- systemic	1mg/kg/day and tapered subsequently
Ganciclovir/ Foscarnet	Intravitreal (same dose as in CMVR) twice weekly

When there is grade IV vitreous haze, rule out toxoplasmosis and ARN.

D. Treatment of Posterior Uveitis without vitritis⁴

Posterior uveitis without vitritis may sometime include neoplastic causes or masquerade syndromes (Primary Central Nervous System Lymphoma, Neoplastic Masquerade syndromes secondary to Systemic Lymphoma/ Leukemia/ uveal lymphoid proliferation, Uveal melanoma, Retinoblastoma, Juvenile xanthogranuloma, metastatic tumours, diffuse bilateral uveal melanocytic proliferation).

Table 7 Treatment of Masquerade Syndromes⁴

Primary Central Nervous System Lymphoma	Methotrexate-weekly/ biweekly 400µg intravitreal	Methotrxate-high dose intravenous/ intrathecal, radiation, IV cytarabine, surgery to remove CNS tumor
Neoplastic Masquerade syndromes secondary Uveal lymphoid proliferation	Systemic / periocular steroids	External beam irradiation
Juvenile xanthogranuloma	Systemic/ periocular/ topical steroids	Local resection/radiation/ immunomodulatory therapy

E. Treatment of Vasculitis

If retinal vasculitis is present, check out for arterial or venous involvement or both. Arteritis is a feature of systemic lupus erythematosus, polyarteritis nodosa, viral infections, syphilis, IRVAN (Idiopathic Retinal Vasculitis Angitis Neuroretinitis). Phlebitis is a feature of sarcoidosis, Behçet's disease, Eale's disease. Both arteries and veins are affected in toxoplasmosis, Crohn's disease, Frosted branch angiitis, Relapsing polychondritis, Wegener's granulomatosis. The same principles stated above apply that is to treat infections if present, to consider corticosteroids / immunomodulatory therapy in other types of vasculitis.

Table 8 Treatment of Syphilis⁴

Patients with syphilitic uveitis are to be considered as having CNS disease, hence neurologic dosing is recommended.

	Primary treatment	Alternative regimen
<ul style="list-style-type: none"> • Congenital syphilis Crystalline penicillin G - intravenous 	100, 000-150, 000 MU*/ kg/12 hourly for first 7 days of life, then every 8 hourly- total 10 days	Procaine penicillin G- 50, 000 MU/kg/dose IM as a single dose for 10 days
<ul style="list-style-type: none"> • Primary, secondary, or early latent syphilis Benzathine penicillin G - intramuscular 	2.4 MU single dose	Doxycycline 100mg bid oral for 2 weeks Tetracycline 500mg qid oral for 2 weeks
<ul style="list-style-type: none"> • Late latent or latent syphilis of uncertain duration, tertiary syphilis in the absence of neurosyphilis Benzathine penicillin G - intramuscular 	2.4 MU weekly for 3 doses	Doxycycline 100mg bid oral for 4 weeks Tetracycline 500mg qid oral for 4 weeks
<ul style="list-style-type: none"> • Neurosyphilis Aqueous Penicillin G - intravenous 	18-24 MU per day Given as 3-4 MU every 4 hours for 10-14 days	Procaine penicillin 2.4 MU intramuscular daily for 10-14 days and Prebenecid 500mg oral qid for 10-14 days

*MU- Million units

F. Treatment of Non- Infectious Uveitis

Once we have ruled out infective causes of uveitis, we should consider use of corticosteroids. The therapeutic plan should be to limit the total use of corticosteroids because of their potential side effects. They are indicated in treatment of active inflammation of the eye, prevention or treatment of complications like CME and to reduce the inflammatory infiltration of the retina, choroid or optic nerve.

Table 9 Use of corticosteroids in Uveitis

• Topical Steroids	Initially hourly – in severe Uveitis 8-6 th hourly – in mild forms Maintenance- depending upon the severity tapered over a month	- Monitoring- to look for cataract and raised IOP
• Periocular steroid injection Triamcinolone acetate- posterior sub-tenon	- 0.5 ml (20mg) - Once in a month- Two to 10 injections	-do-
• Oral steroids Prednisolone-oral	1mg/kg/day	- G-J ulcer, P.B.P, increased blood sugar, Osteoporosis, Ovascular necrotic of fumur head
• Intravenous steriod Methy-lprednisolone- intravenous	500-1000mg once a day for 3 days	- To look for Anaphylactic reaction while starting the intravenous treatment

Recent advances in steroid therapy

Deflazacort is a third generation glucocorticoid which has potent anti inflammatory activity, comparable to, or slightly more than that of prednisolone, but with fewer adverse effects viz. secondary osteoporosis and growth impairment in children.[7] It is being successfully used in treatment of chronic inflammatory arthritis, especially in children, due to it's low side effect profile. However, the ideal immunosuppressive dose is still being debated upon. [8]

Intraocular implants with sustained release formulations of steroid such as fluocinolone acetonide are effective in chronic non infectious posterior

uveitis, but are associated with significant risk of adverse effects including cataract and vision threatening secondary glaucoma, which need to be closely monitored and managed.[9]

Immunomodulatory and immunosuppressive therapy

The use of immunomodulatory or immunosuppressive therapy has greatly benefitted patients with sight threatening uveitis and those who are resistant / intolerant to corticosteroids. These agents are thought to work by killing the rapidly dividing clones of lymphocytes which are responsible for inflammation.

These drugs are used as steroid sparing agents (in view of the known complications of long term use of corticosteroids), and is to be considered for patients who require chronic corticosteroid therapy (> 3 months) at doses > 5-10mg/ day. Its early use is advocated in Behçet's disease/ Sympathetic ophthalmia, VKH syndrome/ necrotizing sclerouveitis.

The following are indications for its use:

- a. Vision threatening intraocular inflammation
- b. Reversibility of the disease process
- c. Inadequate/failure of response to corticosteroids
- d. Contraindication to corticosteroids- side effects/chronic corticosteroid dependence

Before initiating therapy, we should ensure:

- a. Absence of infection
- b. Absence of hepatic/hematological complications
- c. Meticulous follow up, including physician follow-up
- d. Informed consent

G. Use of NSAIDS in Uveitis¹

Nonsteroidal anti-inflammatory agents work by inhibiting cyclooxygenase and by reducing prostaglandin synthesis. Their use is indicated in

- a. Treatment of postoperative inflammation and CME
- b. Chronic iridocyclitis of Juvenile Idiopathic Arthritis

- c. Allows maintaining patient on a lower dose of topical corticosteroid when used as an adjunct.

The following drugs are approved for use (FDA) in treatment of ocular conditions

- a. Flurbiprofen 0.03%, for inhibition of intraoperative miosis during cataract surgery
- b. Diclofenac 0.1%, for inflammation after cataract surgery
- c. Ketorolac 0.5% for treatment of allergic conjunctivitis

Conclusion

The therapeutic algorithm is :

- Treat infections if present,
- Treat noninfectious uveitis with corticosteroid therapy (limit total steroid used) and,
- Immunomodulatory therapy whenever indicated

References

1. Foster CS, Vitale AT, eds. Diagnosis and treatment of uveitis, Philadelphia: W.B.Saunders and Company; 2002;p 27.
2. SR Rathinam, P Namperumalsamy. Global variation and pattern changes in epidemiology of uveitis. Indian Journal of Ophthalmology 2007; 55:173-183.
3. Scarpa A. In: Cadell T, Davies W, eds: Practical observations on the principle diseases of the eyes. London, Strand, 1806, General principles and p 292-321.
4. Ehlers JP, Shah CP.eds. Basic and clinical science course. American Academy of Ophthalmology 2008-2009; Intraocular inflammation and Uveitis, Section 9.
5. Kaplan HJ. Intermediate uveitis (pars planitis, chronic cyclitis): a four-step approach to treatment. In: Saari KM, ed. Uveitis Update. Amsterdam: Experta Medica; 1984:169–72.
6. Reema Bansal, Vishali Gupta, Amod Gupta et al. Role of Anti-Tubercular Therapy in Uveitis with Latent/ Manifest Tuberculosis: American Journal of Ophthalmology 2008; 146:772–779.
7. Markham A, Bryson HM. Deflazacort. A review of its pharmacological properties and therapeutic efficacy : Drugs 1995 Aug;50(2) : 317-33
8. Gonzalez-Castaneda RE et al. Deflazacort induced stronger immunosuppression than expected. Clin Rheumatol. 2007 Jun;26(6):935-40
9. Bollinger KE, Smith SD. Prevalence and management of elevated intraocular pressure after placement of an intravitreal sustained release steroid implant: Current Opinion Ophthalmology 2009 March;20(2):99-103

Unusual cases in Uveitis & rare causes for common signs

Things are not what they seem.....

Yohish Kamath, S Bala Murugan, T R Sathya,
S R Rathinam

Orbital cellulitis in elderly male

A 73 year old farmer, presented with complaints of swelling, defective vision, pain and redness in his right eye since 10 days.

He claimed to have lost vision in his left eye a month earlier, which had minimal pain and redness. He firmly denied the presence of any pre existing systemic illness and claimed to be actively working in the fields till a few months earlier. The only major surgical intervention he had undergone was cataract extraction with intraocular lens implantation at a camp 6 months ago in his right, and 2 months ago for his left eye. Following the surgery he had been applying topical dexamethasone eye drops for 6 months, 4 times a day in both eyes. Though his postoperative vision in the right eye had lasted him almost 6 months, his left eye had lost vision after a month of surgery.

On examination, his vision was hand movements in his right and perception of light with inaccurate projection of rays in his left eye.

The lids of his right eye were edematous with almost total restriction of movements. There was severe chemosis and congestion, but the cornea appeared intact with a posterior chamber intraocular lens seen. Anterior chamber seemed to have mild reaction but was not gradable, due to the chemosis obscuring the view. The left eye showed mild ciliary congestion with occasional cells in the anterior chamber with optic capture of the posterior chamber intraocular lens.

A provisional diagnosis of orbital cellulitis with probably an orbital apex syndrome was made and evaluated in detail in the Orbit specialty clinic. He was started on broad spectrum intravenous antibiotics for 5 days along with 3 doses of intravenous dexamethasone. The response to the treatment was good with complete recovery of eye movements as well as visual acuity

improvement to 4/60 in his right eye. He walked out of the OPD on his own, quite relieved.

He was brought again after 2 weeks, appearing more distraught, this time with a vision of only perception of light in both his eyes, with other clinical features as before.

Ultrasound B scan done revealed retinochoroidoscleral complex thickening of 4.13mm in the right eye with choroidal detachments. Left eye showed a closed funnel configuration of retinal detachment. (Fig 1.1, 1.2)

Now, considering his age, a differential diagnosis of a lymphoma or intracranial or orbital space occupying lesion were also thought. CT scans of orbit revealed mushroom shaped swellings within both eyes, with retinal detachment, but other areas were normal. There was no evidence of any space occupying lesion in the visualized portion of the brain.

(Fig 1.3) Chest x-ray, abdominal ultrasound was within normal limits. Complete hemogram and peripheral smear were normal apart from an ESR of 60mm at end of an hour by Westegren method.

While awaiting the reports, he was started on injection dexamethasone 0.5cc bd i.m.

Two days later, as a possibility of a biopsy was being considered, a repeat USG B Scan revealed a considerable decrease in the RCS complex thickness in both eyes and an “opening of the funnel” in the left eye. His vision and ocular movements were gradually recovering. Now anterior segment showed 2+ cells in the anterior chamber of both eyes.

In the Uvea clinic, as he was questioned in detail, he revealed points which he considered irrelevant earlier, including a mild headache associated with a ringing sound which he heard for a few days after the second eye surgery. These symptoms had subsided after 2 weeks and were overshadowed by the more concerning problem of visual loss.

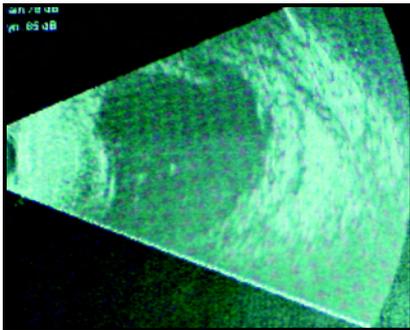
Thus, meshing together the history of ocular trauma in the form of IOL surgery, a prodromal symptom of headache and tinnitus, followed by bilateral exudative retinal detachment and a panuveitis, a diagnosis of Sympathetic ophthalmia was made.

His systemic steroids were stepped up to the full recommended dose equivalent to 1mg /kg of prednisolone. As the response was below

expectations, periocular Triamcinolone acetate and oral Cyclophosphamide were started. One month later his vision in right eye had improved to 4/60 again, and he perceived hand movements in his left eye. At the 3 month follow up, his vision was 4/60 in both eyes and he was delighted to be walking out of the OPD once again on his own.(Fig 1.4)He last visited us after 18 months of his first presentation, and he was comfortably able to carry out his activities of daily living on his own, with well controlled inflammation with cyclophosphamide, and a best corrected vision of 4/60 in right and surprisingly, 6/60, N12 in left eye.

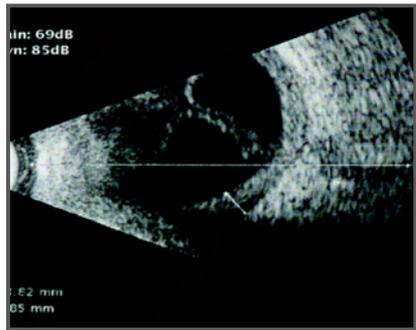
The case described above was an example of a suspected orbital neoplasia which turned out to be an atypical presentation of sympathetic ophthalmia.Though sympathetic ophthalmia has been reported after intraocular lens implantation^{1, 2}, its primary presentation as orbital apex syndrome with restriction of ocular movements was unusual, and is thus being presented here.

Figures: Fig 1.1



RE

Fig 1.2



LE



Fig 1.3

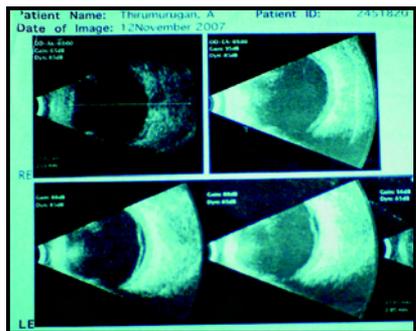


Fig 1.4

Legends :

Fig 1.1: Ultrasound B-scan image showing thickening of the retino sclero choroidal (R.C.S.) complex in right eye.

Fig 1.2: Ultrasound B-scan image showing an almost closed funnel retinal detachment in the left eye.

Fig 1.3: CT scan of the orbits showing “mushroom” shaped swellings in both eyes with retinal detachment in left eye, but without any orbital space occupying lesion

Fig 1.4: Ultrasound B-scan image showing the resolution of the RCS complex thickening in both eyes and opening up of the closed funnel retinal detachment in left eye

Reference :

1. Lakhanpal V, Dogra MR, Jacobson MS. Sympathetic ophthalmia associated with anterior chamber intraocular lens implantation. *Ann Ophthalmol.* 1991 Apr;23:139-43
 2. El-Asrar AM, Al-Obeidan SA. Sympathetic ophthalmia after complicated cataract surgery and intraocular lens implantation. *Eur J Ophthalmol.* 2001;11:193-6.
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Granulomatous Uveitis in a young boy

Fifteen years old boy presented with complaints of redness and profound visual loss in his left eye since a month.

His symptoms had been acute in onset and were worsening despite topical and oral medications he had received elsewhere.

The symptoms were not preceded by any form of ocular or systemic trauma, or febrile illness. He had not received any intravenous fluids or medications. He had no symptoms suggestive of skin or joint disease. His chest, neurological and abdominal examinations were within normal limits. He had no palpable lymphadenopathy.

He had been earlier diagnosed elsewhere to have mitral and aortic valve disease, which was attributed to probable rheumatic etiology, but left ventricular systolic function was normal.

In the end, he made a passing mention of mild hearing deficit since one and half months in his right ear.

On examination

His best vision was 6/6 in right and 1/60 in his left eye. Intraocular pressures were 17mmHg in right and 29mmHg in left eyes.

Slit lamp biomicroscopic evaluation of his right eye was within normal limits. His left eye had marked ciliary congestion with corneal edema with pigmented but fresh granulomatous keratic precipitates (as shown in adjoining Fig.)

along with 3+ cells and flare in anterior chamber. The iris was studded with Busacca nodules, and the lens was clear.

The posterior segment of the right eye was within normal limits. As the view of the fundus in his left eye was not clear, a USG B scan was done which was suggestive of vitritis. (Fig 2.1) An anterior chamber fluid tap was done for nested polymerase chain reaction (PCR) which was revealed presence of Varicella zoster virus, and was negative for Mycobacterium tuberculosis.

The complete hemogram including peripheral smear, liver function and renal function tests were normal. Mantoux test was negative. A diagnosis of viral anterior uveitis with possible acute retinal necrosis was made and under Physicians supervision, he was administered intravenous acyclovir in the standard dose. Low dose oral steroids were later added. Topical steroids, cycloplegics and antiglaucoma medications were being continued. He responded well to the treatment, with his vision improving after 15 days to 6/9 in affected left eye.

An ENT evaluation done was within normal limits except for a deviated nasal septum to the left and the hearing loss for which, an audiometric evaluation was advised. However by the end of one month, his anterior uveitis reappeared. On evaluation now through a relatively clearer cornea, a faint bulge in the temporal iris was noted. Ultrasound biomicroscopy done revealed the presence of a 5.40 x 2.59 mm irregularly reflective mass in the temporal ciliary body. (Fig 2.2)

CT scan of the Brain was ordered which was within normal limits, and the paranasal sinus area showed a deviated nasal septum to the left with a fullness of the right lateral pharyngeal recess. A MRI with contrast enhancement focusing on the orbits revealed a T1W iso intense lesion which in T2W was having a low signal and heterogeneous enhancement in the temporal ciliary body region of left eye, more in favor of an inflammatory lesion rather than a melanoma.

Hence, in view of granulomatous picture of the uveitis, a trial course of antituberculosis therapy (ATT) was advised. He next presented to us after 2 months and had not taken ATT as was advised.

On examination, his anterior uveitis was persistent, and a repeat UBM revealed increase in size of the mass to 7.31 mm x 4.04 mm. (Fig 2.3) At this

stage, all his earlier records were scrutinized again closely, and in view of the fullness of the right lateral pharyngeal recess on CT and his symptom of hearing loss, a review of the ENT evaluation was sought.

A diagnostic nasal endoscopy and repeat MRI this time revealed a nasopharyngeal mass which was occupying the lateral pharyngeal recess on the right side, blocking the Eustachian tube. The MRI also revealed multiple cervical lymph node enlargement.

The left half of the nasopharynx was normal. The lesion in the ciliary body showed an increase in size compared to the earlier scan.

The histopathological study and immunohistochemistry of a biopsy from the nasopharyngeal mass, along with a clinical evaluation by the oncologist, revealed a Non Hodgkins Lymphoma. The patient subsequently is receiving chemotherapy, and his nasopharyngeal lesion has regressed. The ciliary body mass has decreased in size, but persists. His best corrected vision in his left eye during last follow up was 6/12.

Thus the diagnosis was a Masquerade syndrome, wherein a malignancy masqueraded as an intractable uveitis. The common causes of ciliary body mass lesions include granulomas due to infective causes such as tuberculosis and syphilis¹, as well as neoplasms such as melanomas² and secondaries from other sites³. Non hodgkin lymphomas presenting as a ciliary body mass with associated uveitis is an unusual presentation and is thus presented here.

Fig 2.1

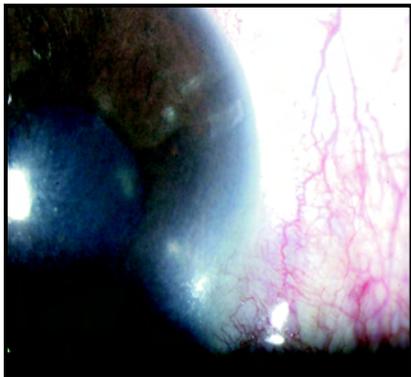
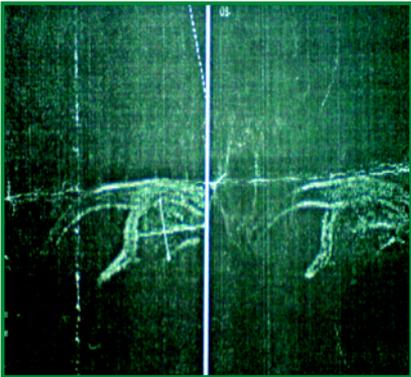


Fig 2.2



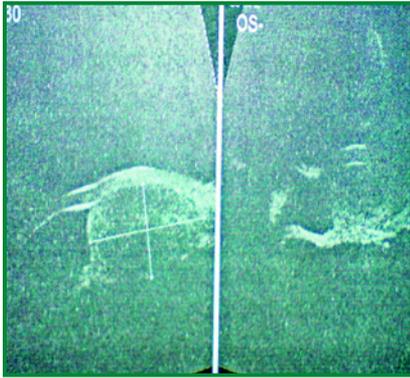


Fig 2.3

Legends :

Fig 2.1: Slit lamp biomicroscope photograph of left eye showing granulomatous keratic precipitate near temporal limbus of left eye

Fig 2.2: Ultrasound biomicroscopy (U.B.M.) of temporal iris of left eye showing the mass involving the root of the iris and ciliary body

Fig 2.3: UBM of the mass after an unintended treatment free interval due to poor follow up, showing an increase in size of the mass

References :

1. Campochiaro PA, Gonzalez-Fernandez F, Newman SA, et al. Ciliary body adenoma in a 10 year old girl who had a rhabdomyosarcoma. Arch Ophthalmol. 1992 ;110: 681-3.
2. Nguyen QD, Foster CS. Ciliary body melanoma masquerading as chronic uveitis. Ocul Immunol Inflamm. 1998 ; 6:253-6.
3. McCarron MJ, Albert DM. Iridocyclitis and an iris mass associated with secondary syphilis. Ophthalmology. 1984 ;91:1264-8.

Bilateral granulomatous uveitis in young lady

A thirty year old lady presented to us with complaints of blurred vision in both eyes of four days duration. On clinical examination she had bilateral granulomatous keratic precipitates along with anterior chamber cells of grade 4+, flare of grade 2+, intense circum-corneal congestion with posterior synechiae in her eyes.[Fig:1a, 1b]. Her posterior segment in either eye remained free of any uveitic activity except for the temporal palor of both optic discs. Her colour vision was defective by Ishihara's method and Humphrey's visual fields evaluation revealed features suggestive of generalised reduction in the sensitivity pattern. Hence the diagnosis of bilateral granulomatous anterior uveitis was established. The baseline evaluation for granulomatous uveitis including Mantoux test were within normal limits.

When reviewing her past medical records it was apparent that she was treated for right eye optic neuritis due to multiple sclerosis with parenteral steroids¹, followed by oral steroids seven years back. Her Magnetic Resonance Imaging of the brain showed features suggestive of multiple sclerosis.[Fig:2, 3, 4]. Subsequently she recovered her vision completely²,

only to relapse again 3 years later which was bilateral and so she was retreated with parenteral and oral steroids. On stopping the tapering doses of oral steroids, she developed bilateral avascular necrosis of femur.

Hence she was treated with topical and periocular steroids along with prophylactic antiglaucoma medication in the form of 0.5% Timolol for her borderline intraocular pressure. At follow up, the granulomatous uveitis was in a partially resolving state [Fig:5a, 5b].

She was treated with topical steroids and periocular steroids. When last reviewed by us later at two months, she had keratic precipitates that remained active in addition to a delayed conduction in the anterior visual pathway as shown by her visual evoked response test. Hence topical steroids was alone given owing to the fact that oral and periocular steroids were contraindicated

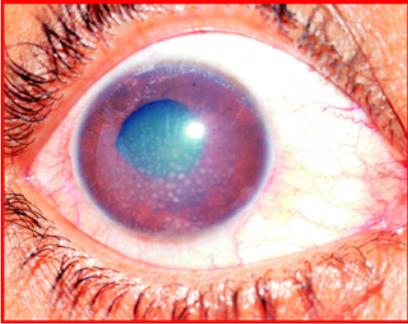


Fig 1a



Fig 1b

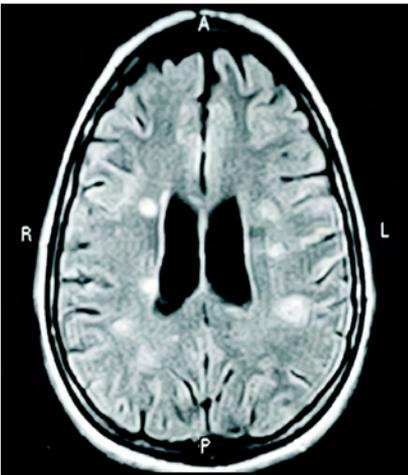


Fig 2

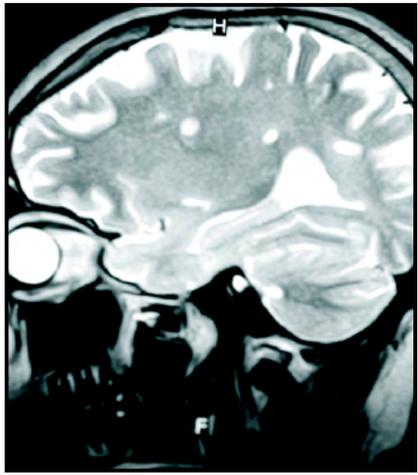


Fig 3



Fig 4

in lieu of avascular necrosis of her femur bone and steroid response respectively.

The reported incidence of uveitis³ among patients with multiple sclerosis is widely varied ranging from 0.4% to 26.9%. In young patients optic nerves are frequently involved but anterior uveitis is a rare presentation⁴ that manifests as a granulomatous iridocyclitis⁵. This case report highlights the problems in treating uveitis of patients with multiple sclerosis when they develop serious systemic adverse effects due to earlier treatment.



Fig 5a



Fig 5b

Legends :

Fig: 1a, 1b Multiple granulomatous keratic precipitates seen on the endothelium

Fig: 2 Magnetic Resonance Imaging of brain shows multiple hyper intense signals in the peri-ventricular areas

Fig: 3 Magnetic Resonance Imaging of brain shows multiple ovoid shaped Hyper intense signals in the peri-ventricular white matter.

Fig: 4 Magnetic Resonance Imaging of spine shows multiple ovoid shaped periventricular plaques

Fig: 5a, 5b At follow up the granulomatous keratic precipitates were in the resolving state

References :

1. Bek RW, TrabeJD. What we have learned from the optic neuritis treatment trial : Ophthalmology: 1995: 102:1504-1508
2. The optic neuritis study group : Visual function 5 years after optic neuritis. Experience of the optic neuritis treatment trial:Archives of Ophthalmology: 1997:115:1545-1552

3. Bueger B.C, Leopold TH :The incidence of uveitis in multiple sclerosis: American Journal of Ophthalmology: 1966:62:540-545
 4. Bachman D. M, Rosenthal A.R, Beckingsale A.B.: Granulomatous uveitis in neurological disease: British Journal of Ophthalmology: 1985:69:192-196
 5. Linn J I, Tessler HH, Goodwin JA; Anterior granulomatous uveitis in patients with multiple sclerosis: Ophthalmology:1991:98:142-145
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Hypopyon uveitis in a seven year old child

Seven years old girl presented to us with complaints of pain in the right eye following injury to her right eye by her own finger a week back. On examination her left eye was normal but right eye showed lid oedema, congestion associated with nongranulomatous keratic precipitates. There was a levelled hypopyon of 2mm with dense anterior chamber reaction and posterior synechiae. The lens remained clear with a dull yellow reflex. [Fig 1]

With the possible differential diagnosis of hypopyon uveitis in a seven year old girl as endogenous endophthalmitis, retinoblastoma we ordered for a B-scan in her right eye. Surprisingly it showed us that the vitreous cavity was filled with exudates and membranes. There was a cyst with a scolex¹ seen nasal to disc. The retino-choroidal-scleral thickness was 2.6mm at macula. No obvious retinal or choroidal detachment was initially seen. [Fig:2]

The above features were consistent with a diagnosis of “ruptured cysticercosis along with an intact cyst”. Hence lensectomy with vitrectomy along with cyst removal through pars plana approach in the right eye under extremely guarded prognosis was contemplated. During vitrectomy after meticulous vitreous shaving, the cyst was identified and removed through the scleral port. The histopathological evaluation showed remnant particles suggestive of cysticercosis.

Post operatively the child was started on topical steroids, cycloplegics and tablet Albendazole at the dosage of 400 milligrams twice a day for a week along with tapering doses of oral steroids based on her body weight. When the child was complaining of recurrent headache we ordered a MRI scan which showed features suggestive of cysticercosis [Fig:3] in the brain also. So, the above plan of treatment was continued along with low doses of oral steroids.

Periodic review after a fortnight showed hyphema with vitreous haemorrhage in her right eye. She was continued on the tapering regimen of topical and oral steroids. We are waiting for subsequent follow up of the patient.

Posterior segment involvement is the most common² manifestation of ocular cysticercosis for which pars plana - vitrectomy³ is the established treatment modality. The cyst in vitreous cavity can be removed through the sclerostomy port or aspirated through the hand piece of vitrector with good post operative prognosis⁴. But presence of subretinal cyst associated with retinal detachment and fibrosis carries poor visual prognosis. The fibrous or glial type of vitreous strands rather than the suckers or rostellae of cysticerci can act as a source of attachment of larvae⁵. In addition the toxin released by the ruptured cysticerci acts as a trigger for inciting severe inflammatory reaction⁶ and can lead to loss of vision and extensive intra ocular damage.



Fig 1

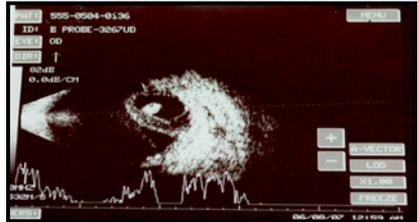


Fig 2

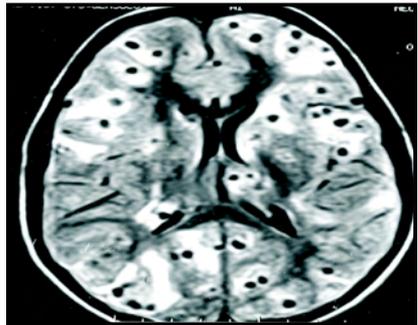


Fig 3

Legends :

Fig: 1 The right eye of the patient shows leveled hypopyon with intense circum corneal congestion

Fig: 2 The B-scan shows vitreous exudates, cyst with prominent scolex along with retino-choroidal – scleral [RCS] thickening.

Fig: 3 Magnetic Resonance Imaging of the brain showing multiple cysts suggestive of cysticercosis

References :

1. Steinmetz RL, Masket.S, Sidikass. Y: The successful removal of sub retinal cysticercus by pars plana vitrectomy: Retina: 1989: 9:276
2. Topilow H W, Yimoyinee D T, Freeman HM et al: Bilateral multifocal intraocular Cysticercus: Ophthalmology :1981:88: 1166-72
3. Kruger- Leite E, Jakh A E, Quiroz H, e al: Intraocular Cysticercosis: American Journal of Ophthalmology: 1985:99:252-7

4. Gupta. A; Gupta R, Panda SS etal: Successful surgical removal of encapsulated subretina cysticercus: RETINA: 1999;8:18:563
 5. Segal.P, Mrzygod S, Dudarewix JS: Subretinal cysticercosis in the macular region: American Journal of Ophthalmology: 1964;57: 653-64
 6. Zinn KM, Guiony S , Friedmann A H: Remova of intravitreous cysticerci from the surface of the optic nerve head - A pars plana approach: Archives of Ophthalmology 1980: 98 :714
 7. Kruger-eite E, Jakh A E, Quito H et a: Intraocular Cysticercosis: American Journal of Ophthalmology: 1985: 99:252.
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Meibomian gland carcinoma and Sympathetic ophthalmia

A 45 year old gentleman presented to us with pain and diminution of vision in his left eye since one week. (Fig 1.1) He had an irregular swelling of the right upper lid, which began as a small nodule near the margin 10 months ago. It had now involved almost the entire lateral half of the lid and resulted in a significant drooping of the upper lid. Since the last three months he had been gradually losing vision in his right eye too, but delayed his visit to an ophthalmologist, as it had been a slow and relatively painless experience.

On examination, he had no perception of light in his right eye, and a best corrected vision of 6/60 in his left eye. The upper lid mass of the right eye was irregular in shape, hard in consistency and appeared to have penetrated deeper structures including the outer coats of the globe.

The left eye showed ciliary congestion with fine keratic precipitates and 2+cells and flare in the anterior chamber. The lens had early nuclear opalescence. The vitreous had occasional cells. Posterior segment examination revealed a hyperemic optic disc, with multiple sub retinal yellow nodular elevations in the periphery, suggestive of Dalen Fuchs nodules. (Fig 1.2.a & b)

A diagnosis of right upper lid Meibomian gland carcinoma with sympathetic ophthalmia was made. Hematological investigations including hemoglobin, blood counts, blood sugar and renal function parameters were normal. CT scan of the orbits revealed a heterogeneously enhancing mass in the superotemporal quadrant of right orbit, measuring 3.6 x 3.6 x 1.75 cm. The mass had infiltrated the upper lid, the preseptal compartment, the lacrimal gland, the anterior part of the lateral rectus muscle and had also involved the outer coat of the globe. The left orbit was within normal limits. (Fig 1.3). The patient underwent total exenteration of the right eye along with medical management of the left eye. (Fig 1.4)

Histopathological examination of the mass revealed presence of polygonal tumor cells with vacuolated cytoplasm and hyperchromatic nuclei arranged in a lobular fashion suggestive of meibomian gland carcinoma. (Fig 1.5) Histopathological examination of the globe revealed diffuse granulomatous inflammation of the uveal tract with preservation of the choriocapillaries. The sclera was thickened posteriorly with granulomatous inflammatory foci primarily involving scleral canals. Exudative retinal detachment with eosinophilic exudates in subretinal space was also noted. All the findings were corroborative to the clinical diagnosis of sympathetic ophthalmia. (Fig 1.6)

The patient received posterior subtenon injection of 0.5cc of triamciolone acetonide to his left eye. He was started on Oral prednisolone at 1mg/kg body weight, which was slowly tapered, and also on oral Methotrexate at 15mg once a week, along with folic acid supplements. Tab Cyclophosphamide 100mg per day was added to the above regime for adequate immuno suppression. (Fig 1.7) He tolerated the above regime well, and on review after 6 months, his ocular inflammation was well controlled with a best corrected vision of 6/12 in his seeing eye. Sympathetic ophthalmia is a bilateral granulomatous inflammation of the uvea that has been usually described to follow penetrating trauma or intraocular surgery. However, the release of previously sequestered ocular autoantigens from the immune privileged intraocular milieu to the conjunctival lymphatics by any form of breach in the outer coats of the eye may incite sympathetic ophthalmia¹, as is exemplified in our case.



Fig 1.1

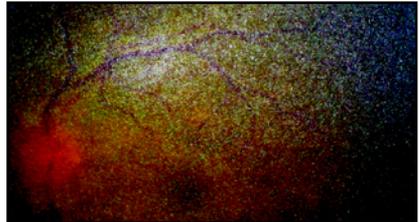


Fig 1.2.a



Fig 1.2.b

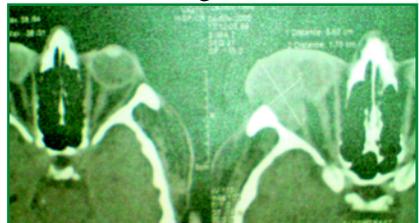


Fig 1.3

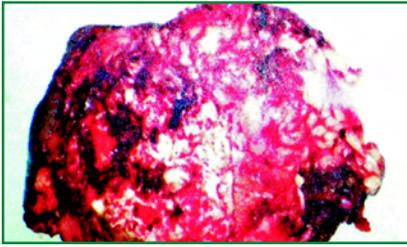


Fig 1.4

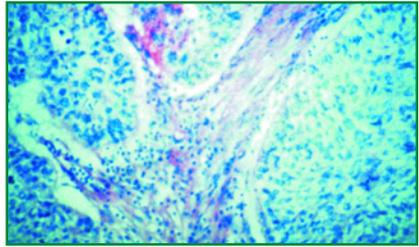


Fig 1.5

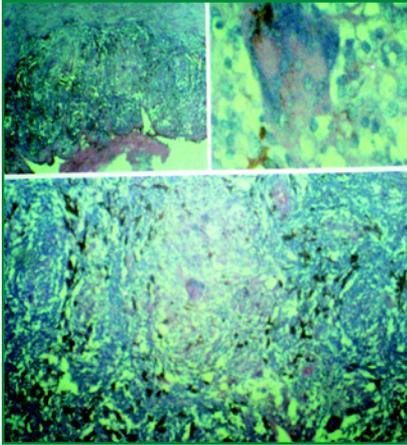


Fig 1.6



Fig 1.7

Legends :

- Fig 1.1: Clinical photograph showing the upper lid mass and ptosis in right eye.
- Fig 1.2.a: Fundus photograph showing hyperemic optic disc in left eye
- Fig 1.2.b: Fundus photograph showing Dalen Fuchs nodules
- Fig 1.3: CT scan showing the invasion of the upper lid mass lesion into the outer coats of the right globe
- Fig 1.4: Gross specimen of lesion including the globe after right orbit exenteration
- Fig 1.5: Histopathology of the lesion suggestive of meibomian gland carcinoma
- Fig 1.6: Histopathology of the uveal tract showing granulomatous inflammation
- Fig 1.7: Clinical photograph of the patient during review after 6 months.

References :

1. Rao NA, Robin J, Hartman D, *et al.* The role of the penetrating wound in the development of sympathetic ophthalmia: experimental observations. *Arch Ophthalmol* 1983;**101**:102-4.

Bilateral exudative retinal detachment –rare cause

A 60 year old lady presented to us with complaints of headache of one month duration and defective vision for the past 15 days, more in the left eye. She gave a history of marsupialization of a frontal arachnoid cyst 6 years ago.

On examination, she had a best corrected Snellen's vision of 6/9 in the right eye and 6/12 in the left eye. Her intra ocular pressures were within normal limits. Her pupils reacted normally to both direct and consensual light reflex. There were no keratic precipitates; the anterior chamber and anterior vitreous face was also quiet. Colour vision was normal in both the eyes. Fundus evaluation revealed clear media, atrophic retinal pigment epithelium around both discs and blood vessels of normal caliber in both the eyes. Meticulous examination revealed choroidal folds at the right macula whereas in the left eye there was an exudative macular detachment in addition to the hyperemic disc. Her vital signs were normal at presentation. (fig 1a and 1b)

The total and differential leucocyte counts were within normal limits. Erythrocyte sedimentation rate was 20mm at ½ hr and 43mm at one hour. Analysis of serum urea, creatinine and urine albumin were also normal. Her Mantoux test read at 48 hours was 15mm with the test dose of ten tuberculin units. Her Treponema Pallidum Haem Agglutination test (TPHA) was negative. With the possible differential diagnoses of posterior scleritis, Vogt-Koyanagi-Harada syndrome and a neuroretinitis we ordered a B-scan and fundus fluorescein angiogram (FFA). Ultrasonography showed thickening of the retino-choroidal-scleral complex in the right eye and shallow exudative retinal detachment in the left eye. There was no evidence of posterior scleritis.

By FFA we confirmed the choroidal folds observed in the right eye and the leaks at the optic discs were corresponding to the left disc hyperemia. Although the macula of left eye showed early hypo fluorescence followed by a leak in the late stages which was similar to that in VKH, the absence of clinical inflammation and starry sky pattern were against it in considering as a diagnosis. Hence the clinical picture was consistent with the diagnosis of hypertensive choroidopathy. (fig 2a and 2b)

On re-evaluating her history, she was diagnosed with systemic hypertension 6 years ago. Though she was on medication for a few months, she later discontinued the same. She reviewed with her neurologist 20 days ago with complaints of a severe headache. Her records showed that she had a

blood pressure of 200/ 110 mm of mercury pressure at that visit with her contrast CT scan showing evidence of left posterior cerebral artery infarction. Later she developed defective vision due to which she landed to our clinic. Hence, the diagnosis of hypertensive choroidopathy was pertinent.

She was referred to our physician and started on a strict anti-hypertensive regime. At review four weeks later, she was relieved of her headache and the exudative detachment in her left eye was also in a resolving state. Her blood pressure was 120/ 80 and her best corrected visual acuity was 6/6p in the right eye and 6/9 in the left eye. There was complete resolution at six months follow-up with anti-hypertensives as the only modality of treatment given. (fig 3a and 3b)

Although hypertensive choroidopathy is not a rare entity, it may present a diagnostic dilemma. The choroidal vasculature responds to systemic hypertension differently from the retinal circulation, because the latter is autoregulated and the former is controlled by sympathetic nerve tones.¹⁻⁴ As a result, the choroidal vascular changes may be seen in the absence of retinal changes in acute systemic hypertension.⁵ Thus, hypertensive choroidopathy should be considered as a differential entity in the diagnosis of exudative retinal detachment.⁶

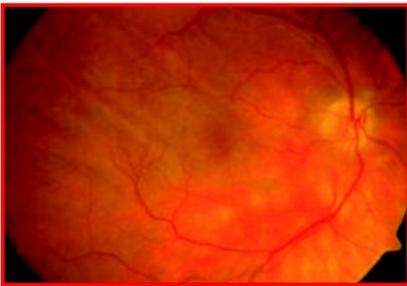


Fig 1a



Fig 1b



Fig 2a

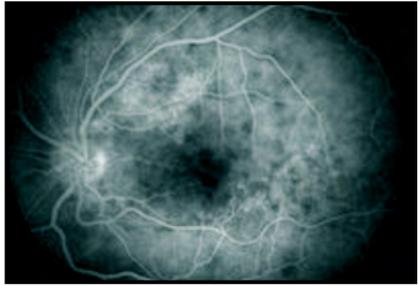


Fig 2b

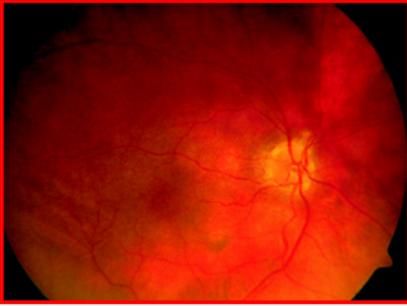


Fig 3a

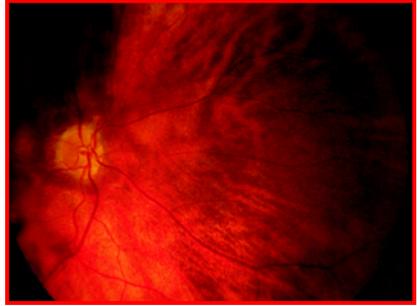


Fig 3b

Legends :

Fig 1a - Fundus of right eye shows atrophic RPE around disc, choroidal folds at macula and normal blood vessels.

Fig 1b - Fundus of left eye shows a hyperemic disc and an exudative detachment at the macula

Fig 2a - Fluorescein angiogram of right eye showing choroidal folds

Fig 2b - Fluorescein angiogram of left eye shows leak at the optic disc and an initial hypofluorescence and a late leak at the macula

Fig 3a and 3b – Complete resolution of the lesions at six months follow-up

References :

1. Kishi S, Tso Mo, Hayreh SS: Fundus lesions in malignant hypertension. A pathologic study of experimental hypertensive choroidopathy : Archives of Ophthalmology: 1985 :Aug 103(8) :1189-97
2. McCaa RE, McCaa CS, Bengis RG, et al: Role of aldosterone in experimental hypertension; Journal of Endocrinology: 1979;81:69-78
3. Hayreh SS: Effects of elevated IOP on blood flow; Archives of Ophthalmology 1983;101:1948-49
4. Ernest JT: The effect of systolic hypertension on rhesus monkey eyes after ocular sympathectomy; American Journal of Ophthalmology :1977;84:341-344
5. De veneria G, Jampol LM The eye in accelerated hypertension II. Localized serous detachments of the Retina in patients :Archives of Ophthalmology :1984 Jan: 102(1); 68-73
6. Schubert MD Ocular manifestations of systemic hypertension Current opinion of Ophthalmology :1998 Dec; 9(6):69-72 :Review

Differential Diagnosis

S R Rathinam

Causes of non-granulomatous and granulomatous Uveitis:

Non granulomatous:

- Sero-negative arthropathy and uveitis
- Traumatic
- Behcets syndrome
- Leptospirosis
- Early Sarcoidosis
- Early Tuberculosis
- Early Syphilis

Granulomatous:

- Tuberculosis
- Sarcoidosis
- Syphilis
- Leprosy
- Herpetic
- VKH
- Sympathetic ophthalmia, Lens induced uveitis, Parasitic, Viral

Non granulomatous unilateral uveitis:

- HLA B27 uveitis
- Traumatic uveitis
- Bechets syndrome
- Fuch hetrochromic uveitis
- Leptospirosis
- Drug induced uveitis

Non granulomatous bilateral uveitis:

- Leptospirosis
- Bechets syndrome
- TINU

Unilateral granulomatous uveitis:

- Viral anterior uveitis
- Lens induced uveitis
- Sarcoid
- Syphilis
- Tuberculosis

Bilateral granulomatous uveitis:

- Vogt koyanagi haradas syndrome
- Sympathetic ophthalmia
- Sarcoid
- Syphilis
- Tuberculosis
- Phaco anaphylaxis

Causes of Anterior uveitis: Ocular diseases		Causes of Anterior uveitis: Systemic diseases	
Non infectious uveitis	Infectious uveitis	Non infectious	Infectious
Traumatic	Herpetic	Seronegative arthropathy *	Tuberculosis
Lens induced	Tubercular	Sarcoidosis	Syphilis
Fuch 's heterochromic uveitis, Iridocyclitis	Parasitic	Masquerade syndrome	Leprosy
Postoperative Post traumatic	Infections	Collagen vascular disease	Leptospirosis

* *HLA B 27 related uveitis, Ankylosing spondylitis, Reiters syndrome, Psoriatic arthropathy, Inflammatory bowel syndrome*

Hypopyon

- HLA B27 uveitis
- Bechets syndrome
- Leptospirosis
- Phacolysis
- Endophthalmitis
- Post operative uveitis
- Leukemia

Hyphema

- Viral uveitis
- Syphilis
- Traumatic uveitis
- Gonococcal
- Leukemia
- Fuch's hetrochromic uveitis

Irregular Anterior chamber depth:

- Iris cyst
- Sub luxated lens
- peripheral anterior synechiae
- Ruptured lens capsule with released cortex in one side
- Ciliary body tumour

Iris atrophy :

- viral uveitis [Herpes zoster & Simplex]
- Traumatic

- Post laser
- Post operative uveitis
- Hansens
- Fuch's
- Anterior segment ischemia
- Essential Iris atrophy
- ICE Syndrome

Posterior uveitis and Pan uveitis

Infections:

Bacterial :

- Tuberculosis
- Syphilis
- Lymes disease
- Leptospirosis
- Brucellosis
- Septic retinitis

Fungal :

- Nocardia Asteroides
- Candidiasis
- Histoplasmosis
- Cryptococcus neoformans
- Aspergillosis

Viral :

- CMV retinitis
- Herpes simplex
- Herpes zoster

Parasitic :

- Toxoplasmosis
- Toxocara canis
- Cysticercosis
- Onchocerca volvulus

Posterior uveitis and Pan uveitis:

Non - Infections:

- Sarcoidosis
- VKH
- Sympathetic Ophthalmia
- Behcets

Vitreous cells & Opacities:

- Inflammatory cells
- Red blood cells
- Degenerated old cells
- Pigments
- Amyloidosis
- Asteroid hyalosis
- Synchysis scintillans
- Malignant cells- Retino blastoma Leukemia lymphoma
- Lens cortical material
- Parasitic cyst
- Foreign body

Macular oedema:

- Pars planitis
- HLA B27 related uveitis
- Post operative uveitis
- Vogt koyanagi haradas syndrome
- Sympathetic ophthalmia
- Traumatic uveitis
- Rarely Behcets syndrome
- Posterior scleritis

Glaucoma in the absence of Peripheral Anterior synechiae & Posterior synechiae:

- Sarcoidosis
- Toxoplasmosis

- Viral uveitis
- Fuch's hetrochromic uveitis
- Phaco anaphylaxis
- Lens protein uveitis

Low Tension in uveitis:

- Bilateral Exudative Retinal Detachment
- Ciliary Detachment
- Retinal Detachment induced uveitis
- Ciliary shock in acute uveitis
- Traumatic & Perforated globe
- Post operative

Optic disc oedema in uveitis:

- Vogt koyanagi haradas syndrome
- Sympathetic ophthalmia
- Leptospirosis
- Pars planitis
- Juxta papillary choroiditis
- Multiple sclerosis
- Neuro retinitis

Retinal vasculitis:

Veins

- Sarcoidosis
- Behcets syndrome
- Eales' disease
- Toxoplasmosis
- Tuberculosis
- Leptospirosis
- Multiple sclerosis

Medium sized Arteries

- Polyarteritis nodosa

Medium and small arteries

- Wegener granulomatosis
- Syphilis

Small arteries

- Systemic Lupus Erythematosus

Capillaries

- Whipples disease
- Syphilis
- Leptospirosis
- Crohns disease
- Polychondritis

Etiological classification of retinal vasculitis:

Bacterial:

- Leptospirosis
- Lymes disease
- Bacterial Endophthalmitis
- Tuberculosis
- Syphilis
- Rickettsia

Viral

- Measles (SSPE)
- CMV
- Herpes Simplex
- Herpes zoster
- Miscellaneous

Fungal

- Candidiasis etc

Parasitic

- Toxoplasmosis
- Toxocarasis
- DUSN

Vasculitis in Immunologic disorders:

- Systemic Lupus Erythematosus
- Polyarteritis Nodosa
- Wegener's Granulomatosis
- Sjogren's syndrome
- Giant Cell Arteritis
- Takayasu's Disease
- Dermatomyositis
- Serum Sickness
- Behcet's syndrome
- Multiple Sclerosis
- Relapsing Polychondritis
- HLA-B27 (Crohn's, AS, Reiter's, Psoriasis, Ulcerative Colitis)

Vasculitis in Idiopathic uveitis

- Birdshot Retinochoroidopathy
- GHPC
- Multifocal choroiditis, pan uveitis syndrome

Joint pain in ocular inflammation :

Non infectious:

- Rheumatoid arthritis
- Seronegative arthropathies
- Collagen vascular disease
- Behcet's syndrome
- Relapsing polychondritis
- Wegener's granulomatosis
- JRA/JIA

Infectious :

- Leptospirosis
- Syphilis
- Lymes disease
- Tuberculosis
- ENL of lepromatous leprosy
(ENL-Erethema Nodosum Leprosum)



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