AN APPROACH TO UVEITIS

Dr. Soumyava Basu
LV Prasad Eye Institute, Bhubaneswar.

Uveitis forms an exciting interface between diseases affecting the body and the eye. While it is an easy option to push steroids and give symptomatic relief to a patient with uveitis, a systematic diagnosis and tailored management of this condition is more challenging but gives a better final outcome. In this article, we will formulate a step by step approach to the diagnosis of uveitis and look at the different management options.

A CASE REPORT

A 65 year old man who had received cataract surgery in the right eye four months back, came with sudden drop in vision in the eye for 3 days. On examination his vision in the right eye was 20/50p. Slit lamp examination revealed a mild anterior chamber reaction. Fundus examination showed a yellowish white full-thickness retinal lesion, inferior to the fovea, with surrounding edema (Fig. 1a). A satellite lesion was also seen. It was classified as retinitis, instead of choroiditis, as the retinal vessels could not be seen passing over it. A full thickness retinitis can be caused by toxoplasma, virus (HSV, HZV, rarely others) or occasionally by candida infection, in that order.

We looked back at his systemic history. He was under immunosuppressive treatment for rheumatoid arthritis with methotrexate and oral steroids for last eight years. We ordered for complete blood counts to check his immune status and toxoplasma antibody titres. Blood and urine cultures were done. When reviewed after three days, the blood counts were normal and the toxoplasma IgG titres were found to be marginally raised. A yellowish pre-retinal clump was seen overlying the lesion. This was clinically suggestive of a candidal infection. A vitreous biopsy was done over the lesion and intra-vitreal amphotericin B injected based on the presumptive diagnosis. We also started oral fluconazole and asked for a physician reference to taper his oral steroids. Our diagnosis was confirmed when the vitreous sample grew candida on culture. Three weeks after treatment, the lesion had completely healed into a superficial scar (Fig. 1b), and vision improved to 20/30.

We approached the above case in the following manner:

1. **Pattern identification:** The lesion was classified as a full-thickness retinitis, based on its appearance. Later, the appearance of a pre-retinal clump over the lesion pointed towards candida infection.
2. **Rechecking the history and systemic examination:** We found that patient was under immunosuppressive treatment for rheumatoid arthritis. We were thus looking at a full-thickness retinitis in an immuno-compromised patient.
3. **Ancillary testing – direct and surrogate evidence:** Most tests done for uveitis are only indirect indicators (surrogate evidence) of a possible cause. In this case, raised toxoplasma IgG titres only indicated past infection with the organism. However, we suspected candida infection clinically and confirmed it with direct evidence from the vitreous biopsy.
4. **Treatment – causative agent and anti-inflammatory:** We first treated the causative agent with intra-vitreal amphotericin B, and oral fluconazole. As the patient was already using steroids, no anti-inflammatory treatment was needed.

STEPS TO UVEITIS PATTERN IDENTIFICATION

1. **Is it actually uveitis?** Sub-retinal fibrin in central serous chorioretinopathy is commonly mistaken for choroiditis. Look for a central clearing within the white patch (Fig. 2).
2. **What is the primary location of uveitis?** Mild to moderate anterior uveitis can be seen in many cases of intermediate and posterior uveitis. But the diagnosis will depend on the primary location.
3. **If anterior uveitis, is it granulomatous or non-granulomatous?** All cases of granulomatous and recurrent cases of non-granulomatous anterior uveitis(particularly unilateral), need to be investigated.
4. **In cases of posterior uveitis, what is the pattern of retino-choroidal involvement?** It is prudent to remember that almost all causes of uveitis can have atypical presentations.

PATTERNS OF RETINO-CHOROIDAL INVOLVEMENT

1. **Focal lesion:** The presence of retinal vessel passing over the lesion, points to choroiditis. Otherwise, it is retinitis or retinochoroiditis. As mentioned above, retinitis is commonly seen in toxoplasmosis (Fig 3), viral and rarely fungal infections in that order. Choroiditis is usually multifocal, though a focal lesion can be seen in tuberculosis or sarcoidosis. An overlying vitritis is usually present.
2. **Multi-focal lesions:** Can be seen in tuberculosis, sarcoidosis or one of the 'white dot syndromes'. Evaluation of the lesion morphology and laterality helps in identifying 'white dot syndromes'. Associated retinal vasculitis and optic neuritis could be present. Serpingenous choroiditis, which can have a tuberculoid origin, is identified by its active pseudopodal edges (Fig 4).
3. **Flat, geographic lesions:** The only possibilities are acute retinal necrosis(ARN, Fig 5), cytomegalovirus(CMV) retinitis or progressive outer retinal necrosis(PORN). Evaluation of lesion morphology, immune status and serological tests help in identification.
4. **Retinal vasculitis:** Can be associated with retino-choroidal lesions as in tuberculosis, Behcet's disease or sarcoidosis or with systemic diseases like systemic lupus erythematosus(SLE) or multiple sclerosis. When not associated with any of the above, it can be classified as Eale's disease.
5. **Serous retinal detachments:** could be Vogt-Koyanagi-Harada syndrome (bilateral choroidal thickening on B-scan) (Fig 6a & b), posterior scleritis (unilateral, history of pain), sympathetic ophthalmia (trauma or surgery to other eye) or uveal effusion syndrome (lack of inflammation).
6. **Neuro-retinitis:** Many infections like toxoplasmosis, Cat Scratch Disease or viral infections can give rise to this presentation (Fig 7), which assumes the optic disc edema with macular star (ODEMS) appearance during resolution. There is a role of therapeutic trial and serological confirmation.
7. **Intermediate uveitis:** Presents primarily as vitreous inflammatory haze, with snow balls and exudates on the inferior pars plana (snow banking). Cystoid macular edema and optic neuritis can complicate this condition. Though idiopathic in most cases, one should rule out tuberculosis, sarcoidosis, multiple sclerosis and as recently identified toxoplasmosis.

ROLE OF COMMON INVESTIGATIONS

1. Complete blood counts and erythrocyte sedimentation rate: To check immune and inflammatory status.
2. Mantoux Test (5TU): Induration > 10 mm after 72 hours should be considered significant in endemic areas like India, when associated with clinical signs of ocular tuberculosis.
3. Chest X-Ray: Healed or active foci of tuberculosis. Pulmonary lymphadenopathy in sarcoidosis.
4. Enzyme Linked Immunosorbent Assay (ELISA): For antibody response to toxoplasma, HSV, HZV, CMV and HIV, depending on lesion morphology and clinical suspicion.
5. X-Ray Lumbo-sacral spine and HLA-B27: In cases of recurrent, non-granulomatous anterior uveitis(usually unilateral), especially if a severe fibrinous reaction is present.
6. AC Tap/ Vitreous biopsy/ Chorioretinal biopsy: Particularly in suspected cases of infectious uveitis or masquerade syndromes. Can be subjected to smear examination, culture and polymerase chain reaction (PCR) tests.
7. Ultra-sonography (choroidal thickening), ultra-sound biomicroscopy(pars planitis, masquerades), fluorescein angiography(vascular occlusions, diagnosis of lesion activity, CME) and optical coherence tomography(CME)
8. Rheumatoid factor: probably the most over-rated investigation. Has little value in uveitis, as rheumatoid arthritis is associated with scleritis or sclero-uveitis but never purely uveitis.

MANAGEMENT OF UVEITIS

Key issues

- Uveitis/Non-uveitic
- Infectious/Non-infectious
- Active/Inactive
- Natural course
- Vision threatening
- Presence of complications
- Associated systemic disease

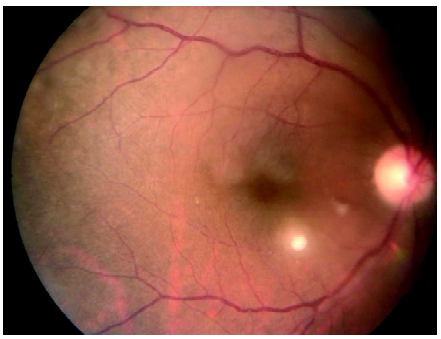

Figure - 1(A)

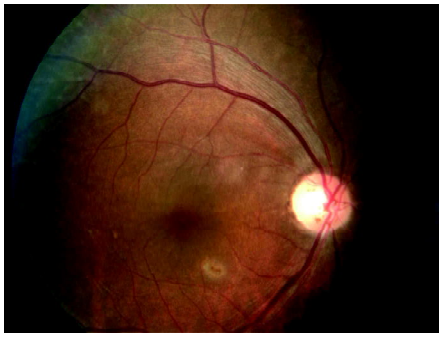

Figure - 1(b)

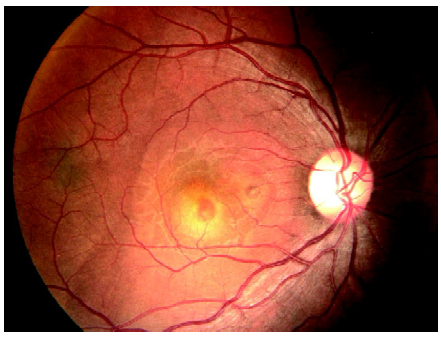

Figure - 2

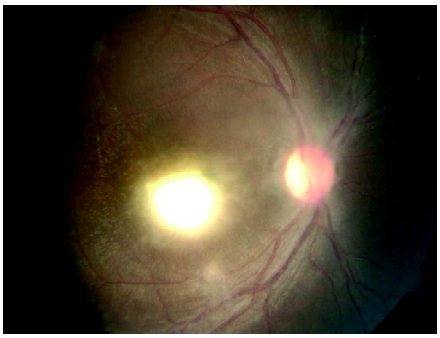

Figure - 3

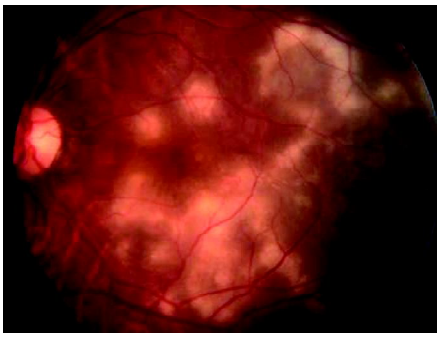

Figure - 4

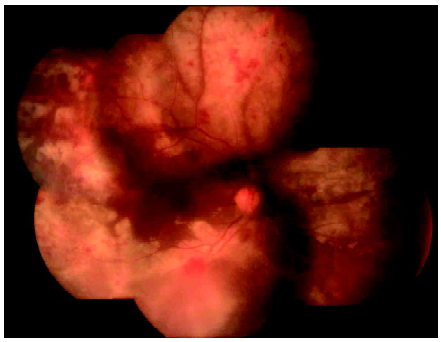

Figure - 5

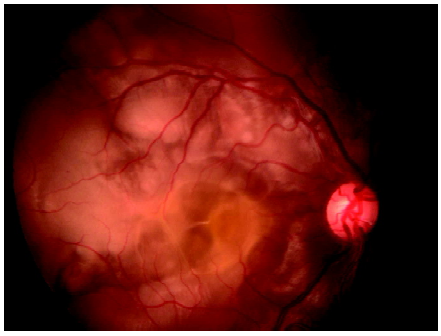

Figure - 6 (A)

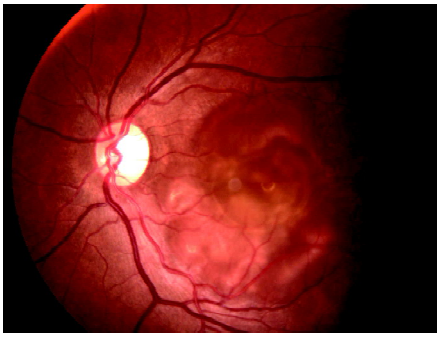

Figure - 6(B)

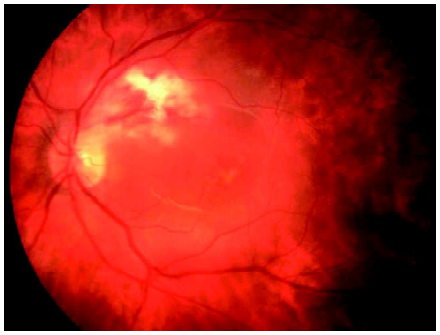

Figure - 7

Anterior uveitis : It is mainly managed with frequent topical steroids (hourly, if severe reaction) and cycloplegics (homatropine is the preferred option). Periocular steroid injections can sometimes be needed.

Intermediate uveitis : Posterior sub-Tenon injection of triamcinolone acetonide(40mg in 1 cc) is the mainstay of treatment. The effect lasts for three weeks. Supplementation with oral steroids is useful in early stages. Other immunosuppressives like Azathioprine(50 mg 2-3 times/ day) are needed in case of long term treatment.

Posterior uveitis: It is essential to rule out an infectious etiology (focal lesion is almost always infectious) and treat it accordingly. Steroids are added after seeing the response to antibiotic treatment. For non-infectious posterior uveitis, oral steroids are the mainstay of treatment. They should be supplemented with antacids and calcium carbonate. Immunosuppressives are added both for steroid sparing and supplementation. Its important to remember that methotrexate or azathioprine take four weeks for the onset of action, and hence should be supported by steroids initially. Periocular or intravitreal steroids are also useful. Vision threatening situations like optic neuritis or foveal lesions may need treatment with intravenous methyl prednisolone.

◆◆◆