

DOI: 10.36648/2472-1093.6.1.49

# Ocular Tuberculosis: Clinical Profile, Management and Outcome at Tertiary Hospital in South India

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## Abstract

**Aim:** Aim is to study the various clinical manifestations in the cases of Ocular TB, management and outcome of these patients.

**Study design:** Retrospective study.

**Duration of study:** Two years duration from June 2017 to June 2019.

**Source of study:** Sarojini Devi Eye Hospital, Hyderabad, Telangana State, India.

**Materials and methods:** All patients presented to Vitreo Retina department with various complaints were studied. Data collected from medical records.

Patients underwent detailed ocular and systemic examination, BCVA, Slit lamp examination, fundus examination, fundus fluorescence angiography, B scans, OCT. In systemic examination uveitic work up done like CBP, ESR, Montoux test, Chest X ray; HIV, VDRL and Rheumatological work up. Based upon clinical presentation patients were treated with ATT (Anti tuberculosis treatment) and steroids. Systemic steroids (oral and intra venous), peri bulbar steroids and intravitreal steroids were used based on severity, unilateral or bilateral involvement.

**Results:** Patients who presented early showed good response to the treatment, few patients who lost follow up after initial examination developed secondary glaucoma, painful blind eye and few eyes became physical due to irregular management.

**Conclusion:** Ocular TB is one of the causes of blindness in uveitis cases, delayed presentation can cause complications and blindness, early diagnosis and proper management is required.

**Keywords:** Ocular tuberculosis (OTB); Choroidal tubercles (CT); Choroiditis; Tuberculous optic neuropathy; Intermediate uveitis (IU); Retinal vasculitis (RV); Steroids

## Introduction

Ocular tuberculosis is one of the causes of uveitis; incidence is 10.5% in uveitis cases. Ocular TB can cause by haematogenous spread or due to immune mediated reaction that is type IV Hypersensitive reaction to latent tuberculosis elsewhere in the body. It can occur as isolated condition or along with other organs like lung, intestines and bones. India is the country with highest prevalence nearly 2.5 million cases reported in the year 2015. Usually extra pulmonary disease is commonly seen in immunocompromised individuals.

Tuberculosis is the disease caused by Myco bacterium tuberculosis (MTB). According to WHO one third of the world population are infected by tuberculosis, 10% of individuals are symptomatic and 90% of the people will have latent TB. Posterior uveitis is the most common presentation of Ocular TB. India is endemic country for TB; prevalence is 9.8% in north India. In Asian countries, India has highest prevalence rate.

MTB is obligate aerobic bacteria seen in highly oxygenated tissue. Pulmonary tuberculosis is the common clinical presentation seen in 80% of the cases, whereas extra pulmonary tuberculosis seen in 20% of the cases. Various structures are involved in eye, but uvea is the common tissue involved due to high vascular supply [1].

OTB in HIV patients will present in aggressive pattern, risk of drug interactions can occur if ATT and ART started simultaneously, according to literature ATT should be started immediately after diagnosis and ART after two months in patients where the immune status is good. Immune status can be predicted by CD4 count [2].

## Aim

Purpose of our study is to study the various clinical manifestations of OTB in our institute, management with ATT plus steroids, tapering of doses and outcome of the disease after 6 to 9 months of management.

## Materials and Methods

All data collected from medical records from June 2016 to June 2018, were studied retrospectively in Vitreo Retina Department, Sarojini Devi Eye Hospital, Hyderabad, Telangana State, India. All patients underwent detailed ocular and systemic examination, necessary Laboratory investigations done, and managed with ATT for 6 to 9 months duration. Most of our patients presented with vision drop, few patients were presented with severe pain and redness. Common complaint in our patients was impairment of vision. Both male and female gender was almost in equal ratio, but slightly male predominance was noted. Age range was between 10 to 40 years old. Common age presentation was between 20 to 30 years, young adults. Bilateral eye involvement was more common than unilateral.

Almost all cases were isolated, extra pulmonary TB cases. Patients with multi drug resistant TB referred from chest hospital for posterior segment examination were normal without any Ocular TB manifestations.

## Results

Patients with OTB in one eye with involvement of macula and other eye healed choroiditis scars were presented early, patients who were treated immediately had good visual prognosis.

Most of the patients started improving within few weeks after the treatment except HIV patients. In HIV cases outcome was not favorable due to aggressive presentation, delayed presentation and poor immune status. BCVA in cases of posterior pole involvement was good with posterior sub tenon steroid injections.

Various routes and different doses of steroids were used for treatment based on the lesion site, size, severity, unilateral or bilateral involvement, associated systemic co morbidities and pre-existing infections.

Commonly used dose was one to two mg per kg body weight in cases of systemic routes, peri bulbar 1 cc/40 mg and 0.1 cc/4 mg intra vitreal route. Intra vitreal injections were given in cases of cystoids macular edema due to posterior uveitis.

Patients with active disease in macula, immune compromised patients like HIV and uncontrolled diabetic patients were treated with posterior sub tenon kenacort/Aurocort injections, 1 cc/40 mg, repeated every two weeks till the activity ceases. One female patient received only one posterior sub tenon steroid injection for macular choroiditis, she developed steroid induced glaucoma three months after injection, anti-glaucoma medication started, there was no response, and gonioscopy showed closed angles, patient underwent trabeculectomy. Immediately after trabeculectomy patient developed hypotony, after 2 week's patient lost follow up. Steroid induced glaucoma noted only in one patient. One patient who received frequent peri bulbar injections superiorly for intermediate uveitis developed acquired ptoxis, probably

faulty technique of injection. All post graduates should be trained well to give peri bulbar injections to avoid the complications.

Prognosis was poor in cases like massive sub retinal abscess with surrounding exudative retinal detachment, in patients with co infections like HIV and in patients with systemic disorders like uncontrolled diabetes mellitus.

## Discussion

OTB is complex issue to diagnose and manage. Anterior segment and posterior segment can occur as pan uveitis. Posterior segment involvement is commonly presented as vitritis. Granulomatous uveitis is seen in OTB.

36 patients presented to our department with various complaints. Common complaint was blurred vision in most of the patients, pain, redness and watering noted in patients presented with pan uveitis. Few patients were referred from TB centre for screening. Age range was between 8 to 35 years (Table 1).

**Table 1** List of patients presented with various clinical condition.

Clinical Conditions	No. of Cases	Percentage
Retinal Vasculitis	10	27.70%
Intermediate Uveitis	6	16.60%
Multifocal Choroiditis	6	16.60%
Choroidal tubercles	3	8.30%
Unexplained Cystoid Macular edema	2	5.50%
Tuberculous Optic Neuropathy	2	5.50%
Tuberculous Granuloma in macula	2	5.50%
Massive sub retinal abscess	1	2.70%
Extra Macular Neuro sensory retinal detachment	1	2.70%
Macular Neuro sensory detachment	1	2.70%
Posterior Scleritis	1	2.70%
Cilio retinal artery occlusion	1	2.70%

Tuberculin skin tests (TST), chest X-ray were advised in all patients, few patients were asked for high resolution chest CT scan. Regarding PCR there is no proper evidence in published literature.

TST is a simple, low cost test to assess immunological evidence of MTB infection, whether latent or active. Positive predictive value is low in active TB patients and immune compromised patients, falsely negative results are seen in 30% of active TB patients. Test is read after 48 to 72 hrs, 10 mm to 12 mm in duration and erythema is considered as borderline, and more than 15 mm of induration and erythema is considered as positive reading.

Chest X-ray is advised to see any evidence of old tuberculous lesions.

All patients were managed based on TST reading, if more than 15 mm of erythema and induration noted patients were advised to start ATT first and then systemic steroids were started 2 weeks after ATT.

Steroids were given in various forms and different doses, most of patients received one mg or one and half mg per kg body weight. In few cases where there was severe bilateral involvement, intra venous methyl prednisolone 1 gram per day for 3 days followed by high doses of oral steroids was given. Steroids were tapered once the lesions started resolving. All these patients were maintained on ATT and tapered doses of steroids for few weeks. ATT was continued for 6 to 9 months duration.

Various routes of steroids used were Posterior sub tenon and intra vitreal, doses were 1 cc /40 mg for peri bulbar injections and 0.1 cc/4 mg for intra vitreal injections.

Reoccurrence was not seen in patients who were treated with ATT for 9 months, few patients who stopped ATT after 3 to 4 months, showed reoccurrence after 2 to 3 years, again ATT was started and continued for 3 months, drug toxicity is one of the major complications noted due to irregular management, drug resistance is also one of the factor which is responsible for reoccurrence.

Two patients had co existing HIV infection, they were on ART also. One patient was 55 years old diabetic who developed choroidal tubercles in both eyes, known case of pulmonary tuberculosis, posterior sub tenon steroids 1 cc/40 mg were given, after 6 to 8 weeks the lesions were resolved completely in one eye but other eye two lesions were in resolving stage, one 8 years old girl presented with history of treatment for tuberculous meningitis, her fundus revealed multiple choroidal tubercles in all quadrants, advised to use systemic steroids 1 mg/kg body weight for 3 months with tapered doses and ATT for 9 months, after 6 to 8 weeks all lesions were faint and almost resolved, patient followed for every six months, she is fine without any ocular manifestations. Choroidal tubercle is one of the pathognomonic features of miliary tuberculosis. Repeated fundus examination will help in detection of miliary tuberculosis, which need to be treated as early as possible. Though tuberculosis is common in India, miliary tuberculosis is rarely seen, only 2% of miliary tuberculosis is noted of all TB cases [3].

Choroidal tubercles will predict the severity of infection and also indicates the poor prognostic factor.

Retinal vasculitis is a sight-threatening inflammatory condition; occurring in approximately one in every eight eyes with uveitis. Pathogenesis in these cases is infiltration of inflammatory cells of vessels. Retinal vascular obstruction can cause release of vascular endothelial growth factor (VEGF), which increases vascular permeability and results in macular edema and induced neovascularization [4].

Patients with retinal vasculitis presented as frosted branch angitis, non-resolving vitreous haemorrhage, perivascular exudates, some patients presented with sequelae like tractional retinal detachment and combined retinal detachment in one eye and vitreous haemorrhage in other eye, all these patients underwent Florescence angiography, OCT. Control of inflammation with corticosteroids is mainstay of treatment. Patients were managed with pan retinal photo coagulation, anti VEGF injections and pars plana vitrectomy based on clinical presentation. Some patients had intra operative complications like severe intra operative bleed in spite of anti VEGF injection 2 days prior surgery. Most of the patients with active vasculitis were started on steroids before surgery, 2 weeks after steroids surgery was planned. Early vitrectomy in these patients showed favorable outcome.

One young female presented with massive sub retinal abscess, exudative retinal detachment, advised laboratory workup, patient lost follow up, reported back after one month with severe redness, pain and vision was no perception of light, she developed neovascular glaucoma, enucleation done, artificial prosthesis placed. Time of presentation is very important to control infection and reduces the blindness. Delayed presentation not only causes blindness, globe preservation also becomes impossible due to painful blind eye. Massive sub retinal abscess can present as early manifestation of disseminated tuberculosis in immune competent patients [5].

Persistence of the granuloma despite antituberculous therapy may indicate enhanced vascularity of the lesion and respond favorably to intra vitreal bevacizumab, an antivascular endothelial growth factor agent [5]. One female patient of Tuberculous granuloma received intra vitreal Ranibizumab for the retinal haemorrhage surrounding granuloma in the posterior pole. Her BCVA improved to 6/36 from CF ½ mts after anti VEGF injection.

One young male labour presented first with neurosensory detachment nasal to disc, started with steroids and ATT, after 2 weeks presented with macular serous detachment due to paradoxical worsening, which usually occurs after starting ATT, treatment should be continued, this usually occurs if the patient stops the systemic steroids abruptly, in this situation again start the oral steroids with excess dose to control the paradoxical reaction.

- It is usually immunological reaction to tubercular antigen released during ATT [6].
- Management: By escalating steroid therapy.
- In ocular inflammation under dose of oral steroids and immediate tapering of steroids will not help in resolving the inflammation.
- This phenomenon is paradoxical reaction, occurs during treatment of tuberculosis in which existing disease worsens or new lesions appear.
- Clinicians should be aware of this condition and prompt recognition and treatment will resolve the inflammation.

Two male patients presented with unexplained cystoids macular edema, were treated with topical and peribulbar

steroids, reoccurrence was common, TST done, showed positive Montoux with 22 mm induration and erythema, treated with ATT, after 6 months cystoids macular edema resolved.

Macular edema was the only ocular finding in these two patients, one patient had CME in both eyes, second patient had only in one eye. Both the patients were 40 year old.

Multi focal and serpigenous choroiditis was one of the common presentations reported in ocular tuberculosis.

### Intraocular tuberculosis in the HIV patient

Tuberculosis is one of the most common opportunistic infection in HIV patients, in our study two patients presented with ocular tuberculosis; in these patients management is quite different, two diseases –one patient, requires some special care to target both HIV and tuberculosis.

In north India, infective uveitis is more common than south India, incidence of infective uveitis is 30%, and out of these two third patients have ocular tuberculosis, remaining one third have other infections [7]. Most of the uveitic cases presented to our department were non-infectious, less than one third of the cases showed positive Mantoux test.

Tuberculous optic neuropathy noted in two patients, young female patient presented with pale optic disc in one eye and other eye was normal, patient was on medication, confusion was whether it is due to tuberculosis or ethambutal toxicity, patient advised to stop ethambutal and we observed other eye.

In tuberculosis, optic neuropathy is commonly manifested as papillitis (51.6%), neuroretinitis (14.5%) and optic nerve tubercle (11.3%) [8].

One young male presented with sudden loss of vision, fundus revealed pale retina in macular area, cilio retinal artery occlusion was diagnosed, systemic workup was normal, serum homocysteine levels were within normal limits, mantoux was positive with 20 mm induration, rare case presented as presenting manifestation in presumed ocular tuberculosis. Infective and inflammatory retinal artery occlusions usually occur due to infiltration of vessel walls with inflammatory cells which may cause thickening, disruption of blood flow and arterial thrombosis. Patient started ATT, lost follow up.

If associated with active focus of retinitis or chorio retinitis, risk of artery compression and disruption of blood flow occurs near active focus.

Middle age female presented with posterior scleritis, uveitic workup showed positive Mantoux test, managed with steroids and ATT, recovered well.

Two female patients were reported with reoccurrence of active choroiditis lesions, these patients used ATT for 9

months, disease was not active for one year, again patient reported after 18 months with similar complaints, may be drug resistant ocular tuberculosis, started on two drug regimen for 3 months duration after discussing with physician.

In our study neither tuberculous endophthalmitis nor panophthalmitis were diagnosed, we are considering only Mantoux test for diagnosis, other test like serological, PCR and advanced techniques not followed, probably we are missing the diagnosis.

### Conclusion

*Mycobacterium tuberculosis* is a bacillus which can affect any part of the eye; we included only patients with the posterior segment manifestations in our study. Air borne communicable disease. One in three in case of HIV patients will die due to tuberculosis. Extra pulmonary tuberculosis is due to haemotogenous spread. Early detection will prevent the blindness. Four drug regimens is used to treat for the duration of 6 to 9 months, risk of resistance is common. Patients are advised to use drugs regularly. Drug toxicity is common. Most of the patients had good outcome except few patients became blind due to delayed presentation. Though it is a curable disease, regular follow up is necessary to avoid blindness.

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