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## Orbital Tuberculosis

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**T**uberculosis (TB) is a leading infectious cause of morbidity and mortality worldwide.<sup>1</sup> India has 30% of the total number of infected people in the world and TB is a leading cause of death as an infectious killer in India (WHO report, 1999). However, even in an endemic country like India, TB causing ocular and orbital disease has become increasingly rare.<sup>2</sup> TB may involve soft tissues, lacrimal gland, periosteum or bones of the orbital walls.<sup>2</sup> It usually occurs due to the hematogenous spread

of pulmonary tuberculosis systemically or due to spread from contiguous structures like the lacrimal gland.<sup>2</sup> Orbital and adnexal tuberculosis is exceedingly rare even in areas where pulmonary and extrapulmonary tuberculosis is endemic. Aggarwal et al reviewed literature and reported that fewer than 35 cases of orbital TB are listed in literature.<sup>3</sup> We present here a review of seven patients who developed extraocular soft tissue or bone involvement. All these cases had microbiological, histopathological or

polymerase chain reaction (PCR) derived evidence of *Mycobacterium tuberculosis* infection.

### Materials and Methods

A cohort of seven patients presenting to our institute from 1987 to 2003, with tuberculosis of the orbital bony wall and soft tissues were analyzed retrospectively. We analyzed these cases to describe the demographic profile, clinical profile, histopathological features, microbiological features & clinical course of these patients. We tried to correlate these manifestations with presence of systemic tuberculosis and immunosuppressive conditions like Acquired Immune Deficiency Syndrome (AIDS). This study also evaluated the role of the Polymerase Chain Reaction (PCR) in the diagnosis and the efficacy of surgical excisional biopsy and antitubercular therapy in the treatment. All the cases underwent detailed ophthalmic evaluation including a detailed history, visual assessment, slit-lamp biomicroscopy, applanation tonometry and indirect ophthalmoscopy with scleral depression. Systemic investigations included a complete blood count, erythrocyte sedimentation rate (ESR), Mantoux test, chest x-ray and detailed evaluation by an internist. Coagulation profile was performed in all patients prior to surgery. All patients clinically suspected of immunosuppressive disorders were evaluated for HIV by enzyme linked immuno-sorbent assay (ELISA). Radiological evaluation with computed tomography scan (CT) was carried out in all patients. Excisional biopsy, incisional biopsy and curettage of bony lesions were carried out as per the need. The diagnosis was confirmed microbiologically by demonstrating acid fast bacilli using Ziehl - Neelsen's method of staining or by culturing the bacilli in Lowenstein - Jensen media. Histo-pathological evidence of granulomatous inflammation was considered suggestive of tubercular etiology. PCR to detect IS 986 genome of *M. tuberculosis* was used to aid diagnosis, whenever HPE and microbiological

examination did not provide collaborative evidence of tubercular aetiology. All the cases were treated with a standard four drug systemic anti-tuberculous therapy (ATT) consisting of isoniazid, rifampicin, ethambutol and pyrazinamide for 12 months, as advocated by the World Health Organisation (WHO). In addition, topical treatment with antibiotics, steroids and a cycloplegic were prescribed for associated ocular inflammation, as and when required.

### Results

The age at presentation ranged from 4-60 years in the study group (Mean age = 25.28 years). The ratio of male patients to female patients was 3:4. All the patients had uni-orbital involvement, with left orbit being involved in 5 patients and the right orbit in 2 patients.

Duration of symptoms prior to presentation ranged from 1-10 months (Mean = 4 months). Three patients presented with frontal bone osteomyelitis (42.86%), 3 patients presented with soft tissue orbital involvement (42.86%) and 1 patient had lacrimal gland involvement (14.29%). The complete patient demographic profile is listed in Table 1. The results of investigation and management are listed in Table 2. Specimens in patients 1, 3, 4 and 6 were positive for acid-fast bacilli (57.14%) by smear and in these patients subsequent culture proved *M. tuberculosis* origin. All specimens, except in patients 1 and 6 showed characteristic granulomatous inflammation with caseation necrosis (71.43%). PCR was performed in 2 patients (Patient 2 & 7). It was negative in patient 2 and positive for patient 7 (50%). None of the patients had a demonstrable systemic focus of infection. All 7 patients showed clinical improvement with complete resolution of mass and healing of osteolytic bone lesions. The follow-up of the patients ranged from 12-26 months (Mean = 19.2 months). None of the patients had recurrence of symptoms or disease. None of the patients had any history or symptoms

suggestive of immunosuppression and were HIV negative.

### Discussion

The chronic inflammatory lesions involving the orbit are usually of unknown aetiology. Clinically these lesions may be mistaken for neoplasms and may simulate a pseudotumor. Most of these inflammatory reactions are non-granulomatous. Truly granulomatous lesions rarely involve the orbit and tubercular involvement is particularly rare.<sup>4</sup> Various organisms like *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Acinetobacter* spp. and *Streptococcus* spp. have been included in the differential

diagnosis of orbital abscesses. However, in these bacterial causes of orbital abscesses, the presentation of the patient is more fulminant, the symptoms are of shorter duration and the patient is usually systemically toxic. Nevertheless, suspicion of these organisms must be entertained as the treatment is different from that of a tubercular aetiology.<sup>5</sup> The involvement of the extraocular structures by *M. tuberculosis* has been described as developing in a slow and chronic fashion with minimal signs and symptoms. The lesions may be accompanied by pain, lacrimation and in involvement of the orbit, gradually increasing proptosis, frequently simulating a pseudotumor of the orbit.<sup>3</sup> In our

**Table 1: Results–Demographic**

S.No	Age (Years)	Duration of symptoms (Months)	Eye	Presenting BCVA	Presenting symptom	Clinical Diagnosis
1	32	10	OD	20/20	Upper eyelid fistula	Osteomyelitis
2	15	6	OS	20/20	Upper eyelid fistula	Osteomyelitis
3	10	5	OS	20/20	Proptosis	Soft tissue involvement
4	4	2	OD	Pt Uncooperative	Proptosis	Soft tissue involvement
5	6	2	OS	20/20	Fluctuant forehead swelling	Osteomyelitis
6	50	1	OS	20/20	Upper eyelid mass	Dacryoadenitis
7	60	2	OS	20/20	Enophthalmos, Mass lower eyelid	Soft tissue involvement

**Table 2. Results – Investigation & Management**

Sl. No.	Smear/ Culture	PCR	HPE	Diagnosis	Rx	Response to Rx	Recurrence	Follow-up (mths)
1	AFB + Done	Not	No Granulomas	I & C	ATT	Resolved	Nil	12
2	AFB +	-ve	No Granulomas	I & C	ATT	Resolved	Nil	15
3	AFB +	Not Done	Granulomatous Inflammation	Incisional biopsy	ATT	Resolved	Nil	18
4	AFB - Done	Not Inflammation	Granulomatous	Excisional biopsy	ATT	Resolved	Nil	17
5	AFB -	Not Done	Granulomatous Inflammation	Aspiration	ATT	Resolved	Nil	26
6	AFB + Done	Not	No Granulomas of lacrimal	Excision Bx gland	ATT	Resolved	Nil	22
7	AFB -	+ ve	Granulomatous Inflammation	Incisional	ATT	Resolved	Nil	24

series the mean age of presentation was around 25 years of age with greater female preponderance. All patients had unilateral involvement, with the left orbit being involved in 5 patients. The systemic history of the patient including history of past tubercular exposure, history suggestive of pulmonary tuberculosis and nutritional status should be completely evaluated in patients with lesions suggestive of tubercular aetiology. Usually, erosion of a parenchymal pulmonary tuberculous focus into a blood or a lymph vessel may lead to extra-pulmonary dissemination of *M. tuberculosis*<sup>1</sup> and involvement of the extraocular structures. However in our series, no systemic focus of tubercular infection could be demonstrated in any patient. Differential diagnoses of these masses include other endemic infectious pathologies, foreign body granulomas and orbital malignancies. In cases of childhood orbital tuberculosis, presenting with proptosis, initial diagnosis can include an orbital malignancy. In patients 4 and 5, due to the rapid increase in the size of the mass within a fortnight, possibility

of a rhabdomyosarcoma was evaluated. However, treatment with antitubercular drugs resulted in resolution of the condition. The diagnostic difficulty also stems from the fact that clinicians the world over, have limited exposure to these lesions in the modern era. In cases of orbital tuberculosis, adequate ATT should be instituted as soon as possible. In our study group, all the patients were examined by an internist and prescribed drugs by him. Therapy was instituted with a 4 drug regimen as per the WHO guidelines.<sup>3</sup> Failure to respond to conventional drugs in these patients may be due to Multi Drug Resistant (MDR) strains of *M. tuberculosis*. Second line ATT may be instituted in these patients, as per the internist. We conclude that orbital tuberculosis is an extremely rare disease, the diagnosis of which requires a high index of clinical suspicion. Diagnosis and management of these lesions depends on the close co-ordination of the ophthalmologist, microbiologist, pathologist, radiologist and internist. Treatment of these lesions is highly successful, without any sequelae provided prompt ATT is instituted.

**Discussant Comments from DR. ASHOK GARG, Hisar:** This paper has reviewed 7 patients who developed extraocular soft tissue/orbital involvement of tuberculosis. This presentation is quite excellent & clinically important in relation to India where Tuberculosis infection rate is very high. Extrapulmonary Tuberculosis is on the rise specially in developing countries. Ocular involvement may occur in one of several ways. It occurs from hematogenous dissemination from a distant site. Greater vascularity may be a contributing factor. The uvea (iris, ciliary body & choroid) is a good example of spread of tuberculosis through the hematogenous spread. Other modes of transmission like primary exogenous infection (eyelid and conjunctiva), Direct extension from surrounding tissue, contamination with patient's own sputum, due to hypersensitivity reaction to the tubercle protein (Phlyctenular disease and Eale's disease) should also be kept in mind. Since the advent of HIV infection and AIDS epidemic, the incidence and prevalence of tuberculosis has increased throughout the world. As a result of this percentage of extrapulmonary TB specially the cases of ocular tuberculosis has increased manifold. Ocular involvement should be kept in the mind of every physician and ophthalmologist while examining the tubercular patient, which otherwise can be damaging to the visual acuity of the patient. They should work in close liaison for optimal results.

### References

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