

Ocular Tuberculosis; Different Clinical Presentation

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ABSTRACT

Purpose: To present the diversity of clinical features, diagnostic approach with treatment outcome in four cases of ocular tuberculosis.

Methods: An observational case series of four cases of ocular tuberculosis. Detail history, thorough ocular and systemic examination, Fundus fluorescein angiography, B-scan ultrasonography; Optical Coherence tomography scan, Erythrocyte Sedimentation Rate, Skin test for tubercle protein, histopathological examination of biopsy from lesion were performed according to the cases. Diagnosis was made by clinical history, ocular findings, appropriate ancillary tests and laboratory investigations according to the merit of the diseases. Response to anti tuberculous therapy (ATT) were observed which gave an anchor to the diagnosis.

Results: Among four cases of ocular tuberculosis, three were female last case was male and all of them were at or under the age of fourty. Two patients had extra ocular manifestation; one was tuberculous dacryoadenitis & other was tuberculous dacryocystitis. Two patients had eyeball involvement; one was tuberculous necrotizing scleritis, another one had tubercular vasculitis retinae. Out of four three had unilateral involvement. Three of them respond well to anti TB & anti inflammatory therapies; one respond to anti TB therapy only.

Conclusions: Tuberculosis can affect any structure of eye and adnexae. The diagnosis is difficult because of diversity of presentation and most of the time there is absent of concurrent systemic infection. Early diagnosis and treatment can prevent blindness or severe ocular morbidity. In cases of non healing lesion and atypical inflammatory presentation, we stress the need for a high index of suspicion regarding tuberculosis.

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Introduction

Tuberculosis has re-emerged as a public health problem throughout the world. World wide there are approximately 8 million new cases & 3 million death from tuberculosis each year [1,3]. Developing countries bearing most of the burden of tuberculosis [1,3]. Bangladesh is an endemic area.

Tuberculosis classified pulmonary or extra pulmonary. With in extra pulmonary tuberculosis; ocular involvement is rare. The incidence of ocular tuberculosis (TB) was reported 1.46% in a series of 10524 patient of tuberculosis (TB). Though ocular tuberculosis showed a low prevalence but need attention as for visual losing morbidities [1].

Ocular tuberculosis may be primary or secondary [2]. Ocular features may be due to infection by the organism or by an immunologic reaction of delayed hypersensitivity in absence of organism [2]. The clinical manifestation of ocular tuberculosis is diverse and depend on the immunological bacteriological and epidemiological variable [3].

The common clinical presentation of ocular tuberculosis are Chronic granulomatous anterior uveitis; Choroiditis; interstitial keratitis; Selerokeratitis; Retinal vasculitis [1,3]. Other rare

manifestations are Scleritis; Dacryoadenitis; Dacryocystitis; Blepharitis; Proptosis & Opticneuritis. The multiplicity of clinical findings is responsible for the delay in diagnosis.

The diagnosis of ocular tuberculosis usually be presumptive; based upon indirect evidence like clinical presentation, systemic evaluation and response to anti tuberculous therapy [1,2].

The objectives of our presentation is to show the different clinical pattern of ocular tuberculosis in four cases of with ocular and extraocular manifestations. And to discuss the diagnostic approach with treatment modalities.

Method

An observational case series of six cases of periocular and ocular tuberculosis with and without systemic disease.

Detail history, thorough clinical examination, evaluation of best corrected visual acuity, slit lamp examination, indirect ophthalmoscopy were done in all six cases. Ancillary tests like Fundus fluorescein angiography (FFA), B-scan ultrasonography (USG), Computerized tomography (CT) scan were performed depending on the merit of the cases. Laboratory tests like Erythrocyte Sedimentation Rate (ESR), tuberculin test

(Skin test for tubercle protein) were performed in all cases, but histopathological examination of biopsy from tissue affected was performed according to the cases. Diagnosis was presumed; made by clinical history, ocular findings, appropriate ancillary tests and laboratory investigations according to the merit of the diseases. Response to anti tubercular (TB) therapy were observed which gave an extra support to made the diagnosis.

An internet search (medline search) and review of current literature on ocular tuberculosis were done. The information relevant to our objectives were obtained.

Case I: Tuberculous Dacryoadenitis

Tanzina a 17 years girl presented on 15th September, 2005 at Out Patient Department(OPD); Chittagong Eye Infirmary & Training Complex (CEITC). With complaints of painless, swelling right eye for 20 days. She gave history of pulmonary tuberculosis one year back & took anti tubercular drugs for six months.

Her best corrected visual acuity(BCVA) 6/6 in both eyes. There was a tender, smooth surface mass in upper temporal region of right orbit, gave "S" shaped deformity of right ptotic lid. The palpebral part of lacrimal gland inflamed and enlarged. Left periocular region was normal. Ocular motility was normal in all gaze. Anterior and posterior segment of both eyes were unremarkable. Regional lymph nodes were not palpable.



Figure 1: Tanzenna "S" shaped deformity of ight upper lid



Figure 2: Right Lacrimal gland inflamed and enlarged 15th september,05

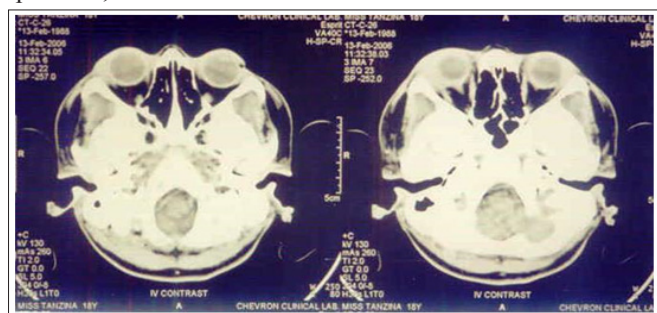


Figure 3: CT scan of orbit showed orbital mass in superolateral orbit

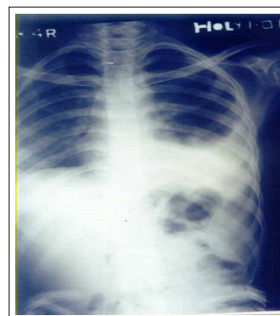


Figure 4: X-ray chest before anti TB therapy showed dense homogeneous opacity in left lower zone obscuring left dome of diaphragm and costo-phrenic angle.



Figure 5: X-ray chest after anti TB therapy showing clear lung



Figure 6: Both lacrimal glands are inflamed on 5th February,06

Her ESR was 65mm at first hour. Tuberculin test was positive. Her X-ray chest (on 24.10.2004) before anti TB therapy showed dense homogeneous opacity in left lower zone obscuring left dome of diaphragm and costo-phrenic angle. After anti TB therapy lung became clear. So with medical history, documents & clinical evidence she was diagnosed as a case of tuberculous Dacryoadenitis. CT scan of orbit showed orbital mass in superolateral orbit.

Immediately after she again suffered from recurrence of pulmonary TB confirmed by X-ray chest and sputum for Acid fast bacilli(AFB). She was treated with Anti-TB therapy.



Figure 7: On 18.06.2006 patient came with improvement

On 05th February, 06 she came with bilateral lacrimal gland swelling, her vision was normal (6/6 in both eyes), anterior and posterior segments of both eyes were unremarkable. With the coverage of anti TB therapy, a short course of systemic prednisolone was given 50mg daily as starting dose, taper the dose over few weeks.

On 18th July, 06 her condition improved. Histopathological examination of lacrimal gland and isolation of Acid fast bacilli from lacrimal secretion were not performed. Diagnosis was mainly based on systemic association.

Case II: Tuberculous Dacryocystitis



Figure 8: Tubercular ulcer involve medial canthus

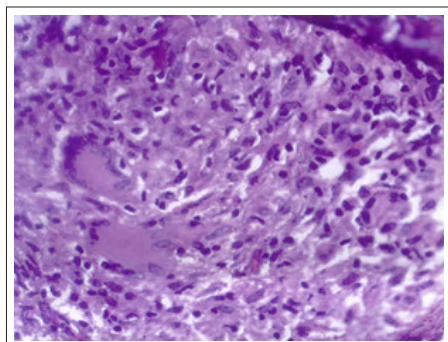


Figure 9: Sections showed multiple small granulomata consisting of epithelioid cells, Langerhans giant cells and lymphocytes surrounded by fibroblasts. No malignancy was seen.

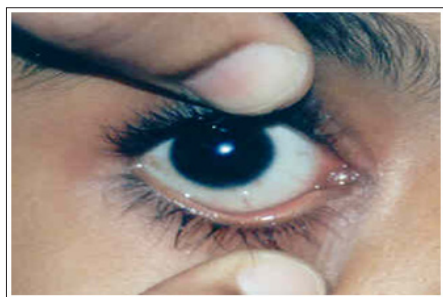


Figure 10: Ulcer healed after treatment

On 30th September, 2003 A girl of 12 years old reported at OPD CEITC with complaints of watering and discharge from right eye for 2 yrs. Sac patency test revealed right nasolacrimal duct obstruction. Examination of nasal cavity was normal. She was advised for right dacryocystorhinostomy. But on 23rd May, 2004 she came with right medial canthal ulcer involving both upper and lower canaliculi.

Histopathological examination of tissue from ulcerated area revealed multiple small granulomata consisting of epithelioid cells, Langerhans' giant cells and lymphocytes surrounded by fibroblasts. Her erythrocyte sedimentation rate was 55mm at first hour. Tuberculin skin test was positive, but x-ray chest remained normal. The case was diagnosed as tuberculous dacryocystitis. She was treated with anti TB therapy. She respond dramatically; ulcerated area healed with mild epiphora due to both upper and lower canaliculi blockage.

Case III: Tuberculous Scleritis



Figure 11: Slit lamp photograph showing multiple scleral necrosis in both eyes with scleral patch graft in right eye

A 40 yrs old lady presented at OPD, CEITC on 19th April 2009 with complaints of pain, redness, photophobia in right eye for seven days. Her BCVA was 6/6 in right eye, 6/24 in left eye. Right Eye- with in normal limit. Anterior segment revealed normal in right eye but left eye lid was oedematous, Conjunctiva congested Localized Corneal stromal infiltration present 9'0 clock. Anterior chamber (A/C) showed mild inflammation. Pupil round, reacting Fundoscopy was normal in both eyes. Patient was diagnosis left marginal keratitis and was treated with topical and systemic ciprofloxacin. But after seven days patient came with severe pain, photophobia and reduced vision left eye. On examination we get BCVA - R/E - 6/6. L/E - 3/60. Anterior Segment revealed normal in right eye. Left eye showed lid oedema, conjunctival congestion, corneal oedema at upper part with stromal infiltration. Sclera showed two sloughing ulceration with huge swelling and congestion near upper limbus. Pupil constricted, less reacting to light, Fundus could not visualized properly in left eye.



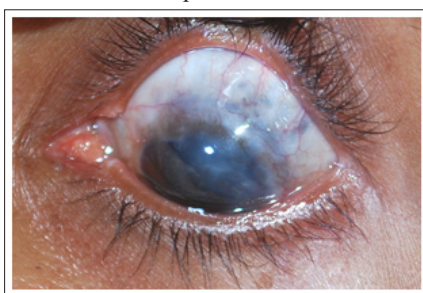
At that time her ESR was 36 mm in first hour. Tuberculin test was strongly positive (30 mm induration at 48 hour) with dermatolisis, x-ray chest was normal, urine analysis was normal,

RA factor negative Serum ANF was negative. She was diagnosed as a case of left tuberculous anterior necrotizing scleritis.

She was treated with topical cycloplegic, steroid antibiotic combination and systemic anti tubercular drugs (Rifampicin 10mg/kg, Isoniazid 5mg/kg, Pyrazinamide 25mg/kg, Ethambutol 20mg/kg), and systemic steroid (Prednisolone 1mg/ kg body weight. Her condition was improved remarkably with anti-TB & anti immune therapy.



On last visit after one month of therapy her BCVA was 6/24 in left eye, intraocular pressure was 14 mm mg in the right eye, 16 mm mg in the left eye. Thin sclera with reduced inflammation in left eyes. Anterior chamber was quiet & fundus normal in both eyes.



Case IV: Tuberculous vasculitis retinae

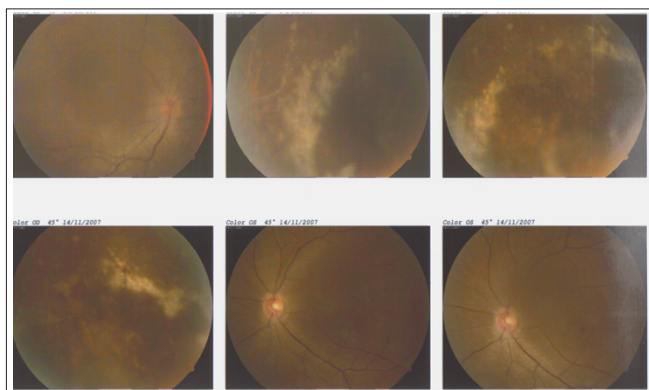


Figure 16: Colour fundus photograph of the right eye showed peripheral retina exudates and vascular sheathing

On 14th November 07, Moinuddin Ahmed, 20 yrs male visited our clinic CEITC with complaints of watering and reduced vision, floaters right eye for 7 days. He gave history of kidney transplantation 8 yrs ago and was on immunosuppressive therapy (cyclosporin). He also gave history of pulmonary tuberculosis with pleural effusion one year back, (diagnosed on basis of positive x-ray chest, USG of chest, 03-08-07) and get anti tuberculous therapy (Tab INH 300 mg –once daily, Pyrazinamide 750mg once daily for 3 month, Ethambutol 40mg once daily 18 months, Ofloxacin 400mg once daily) and Tab Prednisolone 10 mg once daily, by his physician.

His BCVA was 6/9 both eyes with + 0.25 DS lenses. Anterior segment examination revealed trace cell in the right anterior chamber and cell+ in the anterior vitreous. In the left eye a paraxial corneal opacity but anterior chamber and vitreous was quite. Posterior segment examination showed peripheral exudates in right fundus with vascular sheathing & normal left fundus. And he was diagnosed as a case of right tuberculous vasculitis retinae. As he was already on anti-TB and immunosuppressive therapy he was given topical steroid and cycloplegic only.

Discussion

Incidence of ocular tuberculosis is 1-4% [4,5,15]. Patients of 35 to 50 years are predominantly affected where as all of our patients were below 40 years.

Six patients of ocular tuberculosis presented with ocular and periocular inflammation. Three of them gave history of pulmonary tuberculosis (TB). Other three were discovered as tubercular infection after ophthalmic examination. Two patients were suffered from periocular tuberculosis. The first one gave history of pulmonary TB and self interruption in anti TB therapy.

Dacryoadenitis is a rare manifestation of tuberculosis [5]. It may found years after pulmonary or lymph node TB resolved [5]. Our case of Dacryo adenitis presented along with pulmonary TB.

Isolation of Mycobacterium tuberculosis is required for definite diagnosis, but it is difficult to isolates. Histopathological examination shows typical granuloma and this usually leads to the diagnosis, when other features of tuberculosis are present [5]. Our case of Tuberculous Dacryoadenitis was diagnosed on basis of history of pulmonary tuberculosis, clinical findings, high ESR & respond to anti TB therapy.

The second case of periocular insolvents was TB Dacryocystitis. The case first present as a case of chronic Dacryocystitis but few months later she developed a lesion at inner canthus which was diagnosed as tubercular granuloma.

Primary tuberculosis of the lacrimal sac and the nasolacrimal duct is an extremely rare [6]. Diagnosis can be done by isolation of AFB(Acid Fast Bacilli), histopathological examination of affected tissue [6]. Histopathological examination of tissue form the affected site showed typical tuberculous granuloma. Tuberculous dacryocystitis was diagnosed on basis of clinical findings, high ESR, histopathological examination, positive tuberculin test, respond to anti TB therapy.

The cases reported by Tosin F et al and Al-Malki A F et al underwent Dacryocysto rhinostomy surgery and diagnosed after surgery [6,7]. But in our case diagnosis made pre-operatively & we did not perform DCR surgery, rather we manage the case conservatively with anti TB therapy.

The remaining four patients had ocular involvement. One was Tuberculous necrotizing scleritis. She initially presented with focal scleral necrosis with impending perforation and was managed surgically by scleral patch graft. Then on systemic evaluation she was diagnosed as a case of tuberculosis. She showed frankly positive PPD test with dermatolys. She also showed rapid clinical response to the anti TB medication in combination with low dose steroids, supporting the diagnosis of presumed ocular TB

Scleritis is an uncommon ocular inflammation caused by tuberculosis [1]. Anterior scleritis due to immunological reaction

against microbial organism sometimes happen [9]. Focal necrotizing scleritis is the most common form, scleral perforation can occur [1].

Scleritis is reported in patients of systemic tuberculosis [9]. Our patient had primary ocular tuberculosis because she did not give any history or symptoms of systemic TB.

Like pulmonary TB intraocular TB is less likely to be diagnosed via microbiological or histological evaluation [8]. Molecular analysis (polymerase chain reaction PCR) has assisted the detection of TB and is rapidly becoming a method of choice for detection of TB DNA. But it is not easy to obtain an intraocular specimen from an inflamed eye, so indirect evidence was considered to reach the diagnosis [8].

case	Sex	Age (years)	Diagnosis	History of Systemic TB	Tuberculin Test	X-Ray Findings	Adenexa Involvement	Anterior Segment Involvement	Fundus Involvement	Response to anti-TB therapy
I	F	17	Tuberculous Dacryoadenitis	+	+	+	+	-	-	+
II	F	12	Tuberculous Dacryocystitis	-	+	-	+	-	-	+
III	F	20	Tuberculous Scleritis	+	+	-	-	+	-	+
IV	M	20	Tuberculous Vasculitis Retinae	+	+	-	-	+	+	+

modality of approaching diagnosis was also followed by Gupta A et al in their case [9]. In our case ANF and RA factor was –ve suggest that there was no association of connective tissue disorder.

To manage the immune mediated ocular TB is a challenge because to address both the infectious and inflammatory component judicious combination of anti TB and anti- immune regimens has to be titrated to clinical effect, with careful monitoring. In TB scleritis, a titrated trial of immunosuppression combined with anti TB therapy is recommended [8].

As an etiological factor tuberculosis represents 0.6% of uveitis showed in two series of patients, one in Eye & Ear Infirmary, Boston 1982 to 1992 and another in an uveitis clinic in India 1992 to 1999 [1]. So evaluation of granulomatous uveitis mandates ruling out TB.

Our 4th or last case was vasculitis Retinae both eye. Intraocular TB has also been reported as retinal vasculitis [1]. Tuberculous retinal periphlebitis was diagnosed on basis of history of pulmonary tuberculosis, clinical findings, high ESR, positive tuberculin test, respond to anti TB therapy.

The diagnosis of ocular tuberculosis is extremely difficult because ocular tuberculosis tends to be negative in chest, X-ray or tuberculin skin test. Therapeutic isoniazide (INH test) Recently to confirmed diagnosis PCR (Polymerase Chain Reaction) technique has been used to detected in aqueous and vitreous. The main stay of treatment is anti TB therapy. Retinal vasculitis, tubercular scleritis responsive to corticosteroid. Although ocular TB is rare must be considered as one of the ocular morbidity [16-17].

Conclusion

With the re-emerges we should always take TB into account as a possible etiology when dealing with cases of ocular inflammation Ocular tuberculosis is difficult to diagnosis because of diversity of presentation and most of the time there is absent of concurrent systemic infection. Early diagnosis and treatment of ocular tuberculosis can prevent blindness or severe ocular mobility. We

stress the need for a high index of suspicion in cases of non healing lesion and atypical inflammatory presentation. A high index of suspicion helps to diagnosis ocular tuberculosis.

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