



TO EVALUATE THE THERAPEUTIC EFFECT OF ANTI TUBERCULAR THERAPY IN PATIENTS WITH PRESUMED OCULAR TUBERCULOSIS IN A TERTIARY CARE HOSPITAL

Ophthalmology

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ABSTRACT

Aim – The objective of this study was to determine the effect of anti tubercular therapy (ATT) in patients with presumed ocular tuberculosis and determine the prognostic factors of visual outcome **Methods** – The study was prospectively performed in 100 patients who were diagnosed with presumed ocular tuberculosis and underwent a complete ophthalmological examination, relevant multimodal imaging, laboratory and radiological investigation. All patients after chest physician opinion were started on ATT for a minimum of 6 months and corticosteroids. They were followed at 1 month, 3 month, 6 month and at the end of treatment for determining the visual outcome. **Results** - In this study of 128 eyes of 100 patients diagnosed with presumed ocular tuberculosis, 24 patients had pulmonary tuberculosis, 4 patients had extrapulmonary tuberculosis and rest 72 patients were subclinical. The common age group presenting with presumed ocular tuberculosis were found to be between 25-34 years with a mean age of 32.84 years and 61% were male. Posterior uveitis (52%) was the most common presentation. Among posterior uveitis, multifocal choroiditis and choroidal tuberculoma are together present in 65.38%. On comparing the means of best corrected visual acuity (BCVA) at presentation and after treatment showed statistically significant improvement ($p < 0.001$). **Conclusion** - Presumed ocular tuberculosis can be associated with significant ocular morbidity. Early recognition, treatment and regular follow up of this complex disease may help to reduce visual morbidity and ocular complication.

KEYWORDS

Presumed ocular tuberculosis, ATT Abbreviations – Anti tubercular treatment (ATT) Best corrected visual acuity (BCVA) Tuberculosis (TB) High resolution computed tomography (HRCT) Bacilli Calmette-Guerin (BCG)

INTRODUCTION

Tuberculosis (TB) is of a growing concern because of its high prevalence in endemic nations. It is estimated that 23% of the world's population are infected with latent TB [15]. Of these patients with TB, 16-58% are found to have extrapulmonary involvement, which includes intraocular presentation [13]

Intraocular TB most commonly presents as uveitis due to high regional oxygen tension within the ciliary body and choroid although clinical findings can vary significantly. Getting biopsy specimens from intraocular tissues for making a confirmatory histopathologic diagnosis is difficult. In addition, due to difficulty in obtaining microbiologic evidence, the diagnosis of tuberculous uveitis is usually presumptive

The Diagnostic Criteria For Presumed Tuberculous Uveitis Were:

- (1) Ocular findings consistent with possible intraocular TB with no other cause suggested by history of symptoms or ancillary testing.
- (2) Strongly positive tuberculin skin test results (15 mm or more area of induration/necrosis).
- (3) Response to anti-tuberculous therapy with the absence of recurrences [9]

The absence of pulmonary TB does not rule out the possibility of ocular TB, as about 60 % of patients with extrapulmonary TB have no evidence of pulmonary TB [1]

When analyzing the result of a tuberculin skin test, the size of the reaction, contact history, and patient characteristics such as age and immune status should be kept in mind. The specificity of the tuberculin skin test increases with larger skin reactions and with a history of exposure to an active case of TB. "It was demonstrated that an induration >14 mm is unlikely to be due to prior vaccination with bacilli Calmette-Guerin (BCG)".

In recent years, measurement of interferon gamma by QuantiFERON-TB has become a new technique to diagnose TB infection. QuantiFERON-TB is an indirect test for Mycobacterium tuberculosis infection and has higher specificity than tuberculin skin test. But in

diagnosis of ocular TB, the two methods may provide limited benefit as a diagnostic tool compared with tuberculin skin test because of the minimal improvement in diagnostic yield over tuberculin skin test and their prohibitive cost for routine use in most settings.

Radiology such as chest X-ray can suggest active or remote TB, which in turn can support a diagnosis of ocular TB. High resolution computed tomography (HRCT) Chest is a costly investigation but is superior to chest x ray.

It is now generally accepted that these patients should receive four drug anti TB treatment (Isoniazid, Rifampicin, Ethambutol and Pyrazinamide) for a minimum of 6 months [14]. An area of remaining uncertainty with regard to treatment is the pattern of topical or oral steroid use and that depends on the diagnosis.

METHODS:

It is a prospective study, conducted over a span of 1 year from December 2021 to December 2022 in Regional Institute of Ophthalmology (M. D. Eye hospital) Prayagraj, which is a tertiary care center and one of the largest eye hospitals in Prayagraj, after taking permission from ethical committee of M.L.N. Medical College Prayagraj.

The study enrolled the patients (1) who is diagnosed TB with ocular involvement (2) who is currently on ATT (3) with refractory tuberculosis (4) completed ATT course. Exclusion criteria were (1) patients with significant cognitive impairment (2) Other systemic diseases like Sarcoidosis, Syphilis, Leprosy, VKH, Varicella Zoster, Herpes that shows similar ocular involvement like Tuberculosis (3) patients with TB associated with HIV

100 patients diagnosed with presumed ocular tuberculosis underwent a complete ophthalmological examination that includes Slit lamp biomicroscopy, direct and indirect ophthalmoscopy, optical coherence tomography, fundus fluorescein angiography / fundus autofluorescence, b scan and investigations such as complete blood count, mantoux test, chest xray, HRCT chest, Interferon gamma test).

All patients were given anti tuberculosis therapy and corticosteroids after chest physician opinion . Choice of route of corticosteroids was made depending on the diagnosis .They were followed at 1 month , 3 month , 6 month and at the end of treatment for determining the visual outcome.

Student's T test (paired) was used to investigate the significance in difference between pre and post intervention indices in continuous variables and p value < 0.05 was taken as statistically significant .

RESULTS:

In this study of 100 patients diagnosed with presumed ocular tuberculosis , 24 patients had pulmonary tuberculosis , in which 1 patient had MDR TB. 4 patients had extrapulmonary tuberculosis, in which 1 patient had koch's abdomen , 1 had cervical lymphadenitis and 2 had Pott's spine and rest 72 patients were subclinical. All patients , after chest physician opinion were started on anti tuberculosis therapy and corticosteroids. Choice of route of corticosteroids was made depending on the diagnosis..Pan retinal photocoagulation was performed in patients of retinal vasculitis presented with vitreous hemorrhage .

In this study of 128 eyes of 100 patients , the common age group presenting with presumed ocular tuberculosis were found to be between 25-34 years with a mean age of 32.84 years and 61% were male . 28 % of patients had a bilateral involvement .

Defective vision was present in 90% of the patients and is the commonest presenting symptom. The causes for defective vision are lesion over the macula , vitritis, serous detachment at macula, macular edema and anterior segment reaction. Floaters were present in 49% and redness, pain and photophobia in 51%. 10% patients did not notice any decrease in vision and these patients had recurrent episcleritis . 64% patients had a history of recurrence of the disease prior to anti-tuberculous therapy .

Posterior uveitis (52%) was the most common presentation followed by anterior uveitis (26%) . Among posterior uveitis , multifocal choroiditis and choroidal tuberculoma are together present in 65.38% . [Figure 1-3]



Figure 1 - Dignosed as Bilateral retinal vasculitis with tubercular abscess with macular star LE

(Mantoux Test – 24mm & ESR – 40 mm/hr)

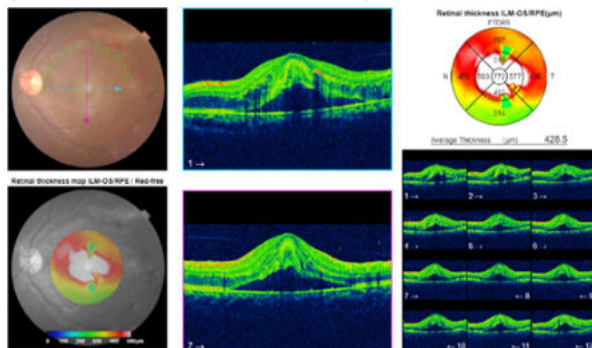


Figure 2 – OCT of the figure 1 at presentation

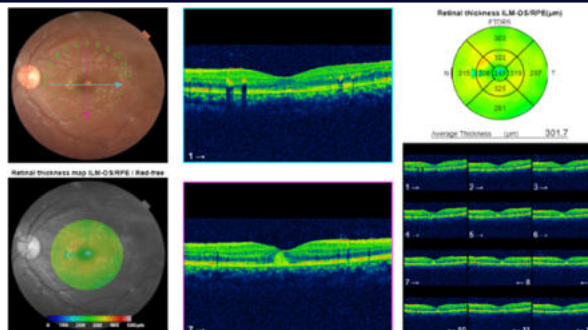


Figure 2 – Vision improves to 6/24P from 2/60 after treatment with ATT and Oral Corticosteroid.

60 (60%) patients had BCVA between 6/18-6/60 of which 39 patients had posterior uveitis and 18 patients had anterior uveitis .18 (18%) patients had BCVA at presentation of <6/60 in which 9 patients had posterior uveitis . 12 (12%) patients had BCVA 6/9-12 and 10(10%) patients had no defective vision. [Table 1]

Table 1 - Correlation of vision at presentation with diagnosis

Diagnosis		Vision(BCVA)				Total
		6/6	6/9-6/12	6/18-6/60	<6/60	
Anterior Uveitis	No. Of Patients	0	8	18	0	26
	Percentage	0	25%	75%	0	100
Intermediate Uveitis	No. Of Patients	0	0	3	2	5
	Percentage	0	0	60%	40%	100
Posterior Uveitis	No. Of Patients	0	4	39	9	52
	Percentage	0	8.7%	71.7%	19.6%	100%
Panuveitis	No. Of Patients	0	0	0	7	7
	Percentage	0	0	0	100%	100%
Recurrent Episcleritis	No. Of Patients	10	0	0	0	10
	Percentage	100%	0	0	0	100%
Total	No. Of Patients	10	12	60	18	100
	Percentage	10%	12%	60%	18%	100%

The mean BCVA (log MAR) at baseline was 0.67 which was changed to 0.41 at 1 month and the change was statistically significant. At 3rd month the mean BCVA (logMAR) further changed to 0.28 and this change was statistically significant. At 6th month or at the end of treatment the mean BCVA (logMAR) further changed to 0.23 and this change was also statistically significant. [Table 2]

Table 2: Visual acuity at presentation, 1 month , 3 months & 6 months/ at the end of treatment

PERIOD	No. Of Eyes	BCVA(logMAR)			p- value
		Mean	SD	SE of Mean	
Baseline	128	0.67	0.46	0.04	
1st month	128	0.41	0.47	0.04	<0.00001
3rd month	128	0.28	0.48	0.04	<0.00001
6th month/at the end of treatment	128	0.23	0.48	0.04	<0.00001

DISCUSSION:

"Tuberculous uveitis is the most common cause of infectious uveitis in immunocompetent patients". Difficulty in diagnostic techniques to arrive at a 'definite' diagnosis because of limited samples of ocular fluids and highly controversial biopsy, the true prevalence of ocular tuberculosis is often masked.

This study done at a highly endemic country features the importance of recognizing the various presentation of ocular tuberculosis among the population and to make a clinically 'presumed' ocular tuberculosis diagnosis taking the cues from the patient and the physician's experience.

In this study , a presumption of ocular tuberculosis was made on the basis of strongly positive tuberculin skin test results, with no other cause suggested by history, symptoms, or accessory testing, and a strong clinical response after initiation of anti-tuberculous therapy combined with systemic corticosteroids either oral or topical depending upon the diagnosis.

When analyzing the result of a tuberculin skin test, one should

consider the size of the reaction, contact history, and patient characteristics such as age and immune status. The specificity of the tuberculin skin test increases with larger skin reactions and with a history of exposure to an active case of TB. Purified protein derivative skin testing was strongly positive in 96 patients. 4 patients who were Mantoux negative were Interferon gamma positive. Radiology such as chest X-ray can suggest active or remote TB, which in turn can support a diagnosis of ocular TB. HRCT Chest being a costly investigation, advised to selected patients.

In this study of 100 patients diagnosed with presumed ocular tuberculosis, 24 patients had pulmonary tuberculosis, in which 1 patient had MDR TB. 4 patients had extrapulmonary tuberculosis, in which 1 patient had Koch's abdomen, 1 had cervical lymphadenitis and 2 had Pott's spine and rest 72 patients were subclinical in contrast with Leon Paolo R Lara et al.[11] conducted a study regarding prevalence of presumed ocular tuberculosis in pulmonary tuberculosis patients only.

In this study, 128 eyes of 100 patients were taken and the common age group presenting with presumed ocular tuberculosis were found to be between 25-34 years with a mean age of 32.84 years which is near about similar to the study conducted by Bansal R et. al., 2008 [5] which showed the mean age to be 34.79 ± 10.74 years.

In this study, presumed ocular tuberculosis was more common among males (61%) whereas in Ang M et. al. 2012 [10] showed an inclination towards the female population and Sanghavi et al 2011[7] study also showed a slight female (59%) preponderance in non-endemic areas.

In this study, 40% of patients had involvement of the left eye and 28% of patients had a bilateral involvement.

In this study, defective vision was present in 90% of the patients and is the commonest presenting symptom. The causes for defective vision are lesion over the macula, vitritis, serous detachment at macula, macular edema and anterior segment reaction. Floaters were present in 49% and redness, pain and photophobia in 51%. 10% patients did not notice any decrease in vision and these patients had recurrent episcleritis.

In this study, 64% patients had a history of recurrence of the disease prior to anti-tuberculous therapy and a study by D. Varma et. al., [4] showed chronic and recurrent tubercular uveitis responding well to ATT.

In this study posterior uveitis (52%) was the most common presentation in Presumed ocular tuberculosis followed by anterior uveitis (24%) which is similar to Gupta et. al.[2] study. However studies by Al Mezaane HS et al (2008)[6] and Gineys R et al (2011)[8] showed panuveitis was the most common presentation followed by posterior uveitis. This has been attributed to the choroid being vulnerable to hematogenous seeding by the bacilli due to its extensive blood supply.

Among posterior uveitis, multifocal choroiditis and choroidal tuberculoma are together present in 65.38%.

In this study, 28 (28%) patients had bilateral involvement of which 10 (21.7%) patients had posterior uveitis and 8 (25%) patients had anterior uveitis. Among the 10 posterior uveitis, 3 patients had multifocal choroiditis, 3 patients had choroidal tuberculoma, 2 patients had choroidal tubercle, 1 patient of serpiginous-like choroiditis and 1 patient presented with retinal vasculitis with vitreous hemorrhage.

Tuberculomas, however, may be confused with other pathologies, such as ocular tumors, metastatic tumor, choroidal hemangioma, or foreign body granuloma. Demirci et al [3] reported five cases of ocular TB that were referred with the suspicion of ocular malignancy.

In this study, 60 (60%) patients had BCVA between 6/18-6/60 of which 33 patients had posterior uveitis and 24 patients had anterior uveitis. 18 (18%) patients had BCVA at presentation of $<6/60$ in which 9 patients had posterior uveitis. 12 (12%) patients had BCVA 6/9-12 and 10 (10%) patients had no defective vision.

The mean BCVA (log MAR) at baseline was 0.67 which was changed

to 0.41 at 1 month and the change was statistically significant. At 3rd month the mean BCVA (logMAR) further changed to 0.28 and this change was statistically significant. At 6th month or at the end of treatment the mean BCVA (logMAR) further changed to 0.23 and this change was also statistically significant.

It is imperative that patients with suspected disease are promptly referred to specialist center for early diagnosis. This was exemplified by Patel et al., [12] who emphasized that the reasons for poor outcomes were delayed diagnosis and delay in initiation of therapy leading to recurrent/chronic inflammation and worse visual impairment.

The study is limited by a lack of investigation such as indocyanine green angiography and HRCT chest is not performed in all patients because it is a costlier one. Future studies could look at the clinical / radiological spectrum of tuberculosis cases associated with presumed ocular tuberculosis. Since active tuberculosis can easily be genotyped, genotypic profiling of these cases can also be done.

CONCLUSION :

Presumed ocular tuberculosis can be associated with significant ocular morbidity. Early recognition, treatment and regular follow up of this complex disease may help to reduce visual morbidity and ocular complication.

Posterior uveitis was the most common presentation in this study followed by anterior uveitis. In posterior segment, multifocal choroiditis was the commonest presentation followed by choroidal tuberculoma.

Patients responded to treatment with anti-tuberculosis therapy and corticosteroids and there were no recurrences in the follow-up period and is associated with a significant improvement in visual acuity.

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