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Original Research Article

Role of antituberculous therapy in latent tuberculosis with ocular manifestations

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ABSTRACT

Introduction: Tuberculosis is an airborne infectious illness caused by Mycobacterium tuberculosis, and it is the most common cause of morbidity and mortality worldwide. Extra-pulmonary TB, often known as ocular tuberculosis, can occur alone or in conjunction with pulmonary tuberculosis. Tuberculosis of the eye can be caused by an active infection or a type 4 hypersensitivity reaction.
Aim: To investigate the role of antituberculous therapy in the treatment of suspected intraocular tuberculosis.
Materials and Methods: Based on a clinical diagnosis of Ocular tuberculosis, 46 patients were assessed with a chest X-ray, Mx test, and quantiferon gold assay and treated with ATT.
Results: The results showed that out of 46 patients, 29 were females and 17 were males. There were 34 patients with B/L involvement and 12 with U/L involvement. In addition, 76 percent of individuals tested positive for tuberculin on their skin, indicating latent tuberculosis. Quantiferon gold assay was positive in 19.56 percent of patients. On X-ray chest, 17.3% of patients had a healed old tuberculosis lesion. H/O contact with TB family members was reported in 13.04 percent of patients.
Conclusion: All patients who had ATT therapy had a favourable outcome, with inflammation clearance and non-recurrence.

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1. Introduction

Tuberculosis (TB) continues to be a significant global health burden, manifesting itself through both pulmonary and extra-pulmonary manifestations. For decades, tuberculosis has remained a leading global cause of death, with challenges in eradicating the disease attributed to neglect of vulnerable populations and the HIV pandemic.[1] These trends are expected to increase extra-pulmonary tuberculosis, which is significantly more prevalent in patients with tuberculosis and HIV coinfection.[2] As a result, TB is the leading cause of morbidity and mortality worldwide.[3] Initiated by Mycobacterium tuberculosis, TB remains a significant concern in developing countries, accounting for a significant proportion of uveitis cases. Although this mycobacterium is most commonly found in the lungs, it can infect any organ via hematogenous spread or hypersensitivity reactions.[4]

All countries are affected by migration and travel at varying rates of infection. Latent tuberculosis (LTB) occurs when an individual has been exposed to tuberculosis in the past but did not receive anti-tuberculosis (ATT) and has remained systemically healthy.[5] Treatment is needed if a patient exhibits active tuberculosis infection, such as pulmonary signs and symptoms and an abnormal chest x-ray (CXR) with radiologic indicators of active tuberculosis infection or clinically evident extra-pulmonary involvement. In addition, uveitis accompanied with indications of

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ongoing infection may indicate that TB organisms are directly involved in the ocular cavity.[6]

Ocular tuberculosis (OTB) is a collection of symptoms caused by the acid-fast bacillus Mycobacterium tuberculosis that usually arise without systemic tuberculosis symptoms. The most common manifestations are retinal vasculitis (similar to Eales disease) and serpiginous-like choroiditis, but anterior segment and orbital involvement have also been recorded.[7] Unfortunately, there is a dearth of thorough clinical information and agreed-upon diagnostic protocols, which adds to the enigma surrounding the diagnosis and management of OTB.[8]

These limitations result in delayed and even missed diagnosis, resulting in suboptimal clinical outcomes, and may perpetuate missed opportunities to manage systemic TB infection early, as OTB frequently precedes symptoms of systemic TB.[9] Ocular illness may also result from a delayed hypersensitive immune response in the absence of an infectious pathogen within the eye. According to studies, the number of immunocompromised patients with extra-pulmonary TB has been progressively increasing in recent years.[10]

OTB manifests in a variety of ways, depending on the site and intensity of infection. Without indications of systemic illness or evident involvement of other typically affected organs, presentation is possible. OTB is typically a granulomatous infection but can occasionally show as a non-granulomatous infection.[11] Additionally, participation may be unilateral or bilateral. Although lesions can arise in any section of the uveal tract, the choroid is the most frequently affected.[12] Diagnosis and management of intraocular tuberculosis continue to be difficult due to the large variety of clinical signs. There are no linked systemic symptoms, no recognized diagnostic criteria, and the available diagnostic tests and instruments are limited. Delay in diagnosis and treatment may result in persistent structural damage, which may impair long-term functional vision. Thus, early detection and treatment of intraocular tuberculosis are crucial for better visual prognosis.[13]

OTB accompanied with indications of ongoing infection may indicate that tuberculosis organisms are directly involved in the ocular cavity.[14] In some individuals with severe OTB requiring systemic corticosteroids and steroid-sparing medications, ATT may be used to avoid LTB reactivation rather than to treat acute OTB.[15] When patients with OTB are investigated, it is not uncommon to find no recognizable systemic or ocular disease and the sole positive test is a tuberculin/QFT. In such cases, the issue of whether the uveitis is caused by LTB or not and whether ATT would be useful arises.[16]

The primary objective of this study is to evaluate the role of ATT in patients with latent intraocular TB and treatment outcomes.

2. Materials and Methods

The study included 46 patients diagnosed with latent ocular tuberculosis, presented to RIO-GOH's uvea and retina clinic from 2012 to 2018. Institutional ethical committee clearance was obtained informed consent was obtained from all patients. In addition, all of them underwent a detailed eye examination. Clinical phenotypes included episcleritis in 4 patients, scleritis in 2 patients, bilateral anterior uveitis in 8 patients, bilateral intermediate uveitis in 19 patients, choroidal granuloma in 6 patients, vasculitis in 4 patients, optic nerve head tuberculosis in 1 patient, posterior uveitis in 2 patients.

2.1. *Inclusion criteria*

1. Patients aged 12 to 55 years.
2. Patients with a history of old treated pulmonary tuberculosis.
3. Patients with a history of contact with tuberculosis.

2.2. *Exclusion criteria*

1. Patients with pulmonary tuberculosis.
2. Immuno suppression, including HIV.

2.3. *Procedure*

All patients underwent a complete ophthalmic examination, uncorrected and best-corrected visual acuity, IOP measurement with Goldmann applanation tonometry and a detailed anterior segment examination with a slit lamp. A slit lamp bio microscopy did fundus examination with a +90D lens and indirect ophthalmoscopy. All patients underwent complete blood count, ESR, Mantoux, chest x-ray, quantiferon gold TB testing. Chest physician opinion was obtained for all patients to rule out active pulmonary tuberculosis. All patients underwent ELISA test to rule out HIV status. Our study included 8 patients already treated with ATT and completed the course 8 to 10 years back and 6 patients had a history of contact with tuberculosis patients. All patients were started on category I ATT with INH rifampicin ethambutol and pyrazinamide for 2 months followed by INH and rifampicin for 4 months. Patients were also started on oral prednisolone 1mg/kg of body weight tapered over 6 weeks duration with topical steroids in some cases

3. Results

The total number of patients in the study was 46, out of which 29 were female and 17 were male. The age range was from 12 to 55 years, 34 patients had bilateral involvement while 12 patients had unilateral involvement.

76% of patients showed positive for TST. 17.39% showed old healed tubercular lesions. 13.04% of patients had H/O contact with TB family members, 19.56% showed

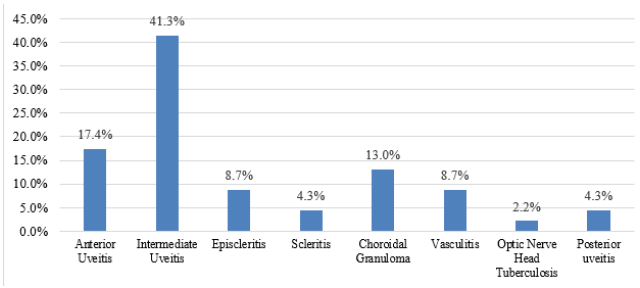


Figure 1: Clinical phenotypes of ocular tuberculosis

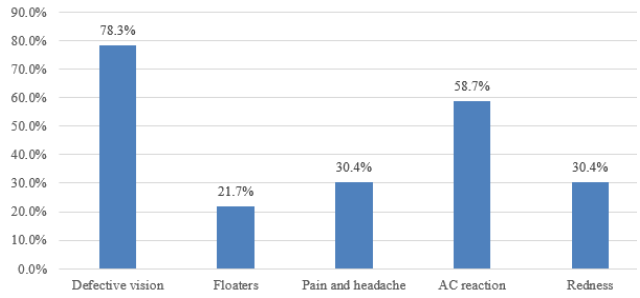


Figure 2: Clinical features of the study population

positive for quantiferon gold assay.

The factors of OTB diagnosis could be attributed to the Mantoux test in a significantly higher number of patients (76%). In addition, some were tested positive in the interferon-gamma release assay test (19.56%), followed by patients who had a previous history of contracting pulmonary TB (8) and those who were in contact with TB patients (6).

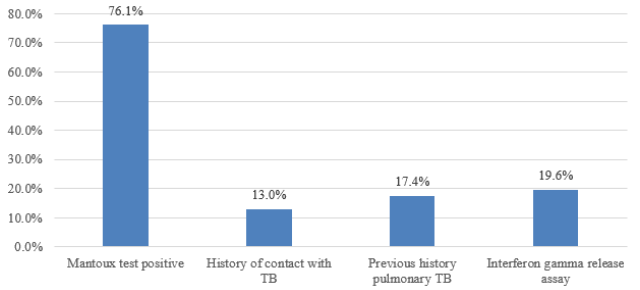


Figure 3: Diagnostic features of the study population

All the patients were started on a standard regimen of INH, Rifampicin, Ethambutol, and Pyrazinamide for a minimum of two months with subsequent administration of two-drug therapy, namely INH and Rifampicin, for a minimum of four months.

Complications encountered were pertained to the development of cataracts, glaucoma, cystoid macular edema and epiretinal membrane. Patients with complicated cataracts were observed in noteworthy numbers (13), followed by those with cystoid macular edema (6), glaucoma (4) and the epiretinal membrane (1).

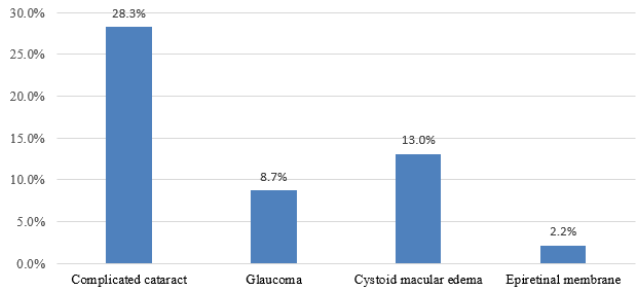


Figure 4: Complications in the study population

Concurrent oral and topical steroid therapy was used. In addition, immunosuppressive for severe inflammation was considered for six cases of intermediate uveitis and two cases of scleritis.

The mean range of follow up was from 3 to 4 years.

There was a favourable and successful outcome in all patients who underwent ATT therapy with resolution and non-recurrence of inflammation. In addition, 80% showed improvement in visual acuity and 90% showed resolution of inflammation.

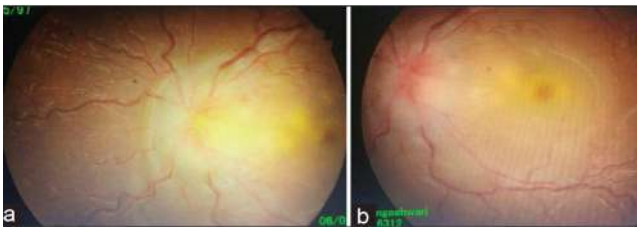


Figure 5: Fundus picture of the left eye shows active papillitis with macular edema

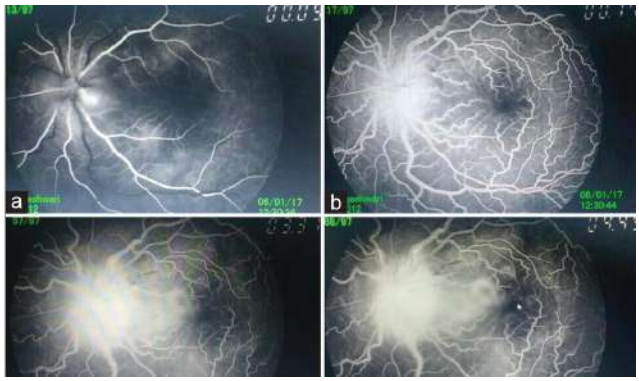


Figure 6: Early and late phase pictures of fundus fluorescein angiography of the left eye

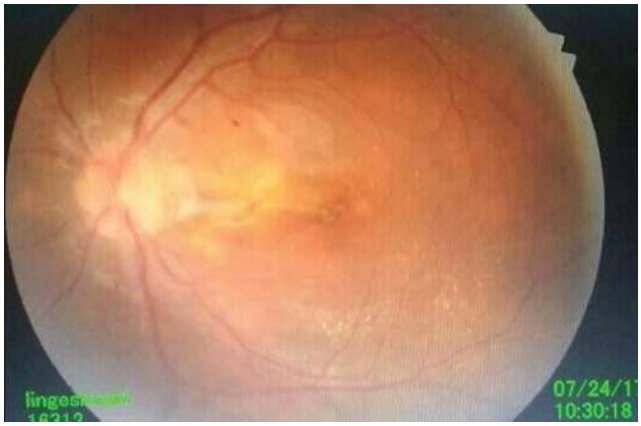


Figure 7: Fundus picture after 2 weeks of treatment

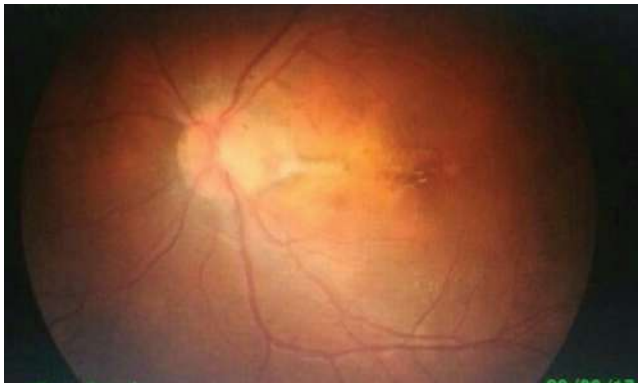


Figure 8: Fundus picture after 2 months of treatment



Figure 9: Scleritis



Figure 10: Episcleritis with positive mantoux

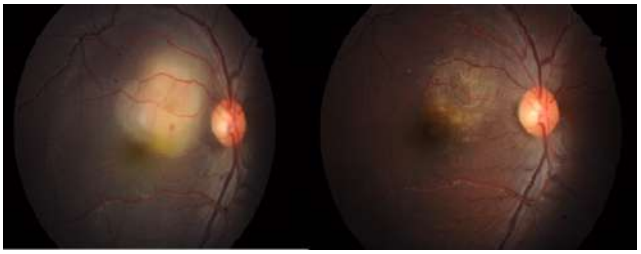


Figure 11: Choroidal granuloma before and after ATT

4. Discussion

According to the WHO, about one-third of the world's population is infected with TB, with about 10% of those afflicted showing symptoms. Apart from the lungs, TB can also affect other organs, including the eye. Although OTB and TB can coexist, a direct link is difficult to establish. Since clinical signs of pulmonary TB rarely accompany OTB, the diagnosis of OTB can be difficult, and virtually all recorded cases had just a tentative diagnosis. OTB is a vision-threatening condition that, if not correctly detected and treated, will result in blindness.[17] The most effective treatment regime for the management of OTB is designated as ATT; however, there is no agreed consensus between ophthalmologists and other physicians about the role of ATT and duration of treatment in cases of isolated intraocular TB.[18]

Hence the study was carried to examine the clinical features of OTB along with outcomes of patients post-ATT. It is critical to have a thorough awareness of a patient's epidemiological history and have a high suspicion index for OTB. The study group involved patients aged 15-55 years with a mean age of 35 years. In a previous study conducted by Shah et al.,[19] the group included patients aged 21-40. In a previous study conducted on determining the causes of OTB, the study population was limited to the age group of 6-60 years, with a mean age of 34.4 years. Like our investigation, OTB predominantly affects the productive age group, as declared by Basu et al.[20] In our investigation, female patients were found to be more recurrent than males. Among the 46 patients analyzed, 63.1% were females and 36.9% were men. In a previous study conducted by Tomkins-Netzer.[21] among the patients, males were predominant. In a study conducted by Shah et al.,[19] male patients were significantly dominant compared to females.

Concerning the anatomy of OTB, all types were recorded in our observation. The most prevalent forms of OTB were intermediate and anterior OTB as well as choroidal

granuloma. In our study, 41.3 percent of patients had intermediate uveitis, 17.3 percent had anterior uveitis, 13 percent had choroidal granuloma, and 8.69 percent of patients had vasculitis. As per the results of Basu et al.[20] the predominant clinical presentation in their study was posterior uveitis, while the multiple recurrences of intermediate uveitis were reported by Gupta et al.[22] In a parallel investigation conducted by Tomkins-Netzer et al.,[21] similar OTB anatomical types were reported to be common in occurrence.

Clinical symptoms, systemic inquiry, and clinical features and investigations were used to rule out other causes of intraocular TB. While observing the factors associated with OTB diagnosis, the defective vision was recorded to be the highest, followed by AC reaction. Pain and headache, and redness contributed equally to OTB while floaters were recorded in a small number of patient populations. Durrani et al.[23] also reported visual loss associated with the occurrence of OTB. They have also correlated visual loss with a predominant occurrence of posterior uveitis.

The patients observed were detected with the presence of infection in both eyes in relatively higher numbers. Our study revealed the presence of bilateral infection in 34 patients and unilateral in 12 patients. In a previous study performed by Chung et al.,[24] among the OTB patients analyzed, 50% of them were detected with bilateral involvement. According to their reports, among the unilateral OTB patients, more infection was related to the right eye than that of the left. In a likely study conducted by Sanghvi et al.,[25] patients with infection in both eyes dominated the study population.

In context to the factors responsible for incurring OTB such as Mantoux test positive, history of contact with TB, Previous history pulmonary TB and interferon-gamma release assay were found to be present. Patients positive for the Mantoux test was found in significantly large numbers, followed by those who had a previous pulmonary TB infection. People who acquired OTB by contact with other TB patients and those who tested positive for interferon-gamma release assay were recorded lower. Shangvi et al.,[25] in their study, have reported that their case study involved patients who contracted OTB through previous communication with TB patients.

Due to the wide range of clinical manifestations and persisting gaps in identification and therapy, OTB management is difficult. The significance of ATT is still debatable, with no international agreement on the timing and duration of ATT and the use of systemic corticosteroids concurrently.[26] In the present study, we utilized a combination of oral and topical steroids. Immune-suppressive agents were added in six cases of intermediate uveitis due to significant inflammation. Eighty percent of patients in our trial responded favourably, and recovery was observed within two weeks to two months. Patients who responded favourably to ATT improved within two weeks to three months of initiating medication. A similar recovery among OTB patients by ATT was reported earlier by Gupta et al., who reported significant recovery rates in less than 2 weeks. Their study also indicated that a prominent recovery rate was evoked in OTB patients with ATT within 2 to 4 weeks. Agrawal et al.[27] described the role of ATT in OTB by including the largest case series of patients with suspected ocular tuberculosis treated with ATT in a low-endemic location. Prolonged treatment duration resulted in a decreased chance of inflammation recurrence, but immunosuppression had a detrimental effect on the final treatment outcome.

About the development of complications cataract, glaucoma, cystoid macular edema, and epiretinal membrane were detected. Patients with a complicated cataract were found in higher numbers, followed by cystoid macular edema. Patients with glaucoma and epiretinal membrane as complications were also recorded in meagre numbers. As per Shah et al.[19] observations, a very small number of patients who already had cataracts were detected with rapid progression post-ATT. No other complications were observed in their study. However, Basu et al.[20] reported that complicated cataract was seen in most patients and other complications such as vitreous haemorrhage besides macular inflammation.

5. Conclusion

Because there is no pathognomic ocular finding for OTB, ophthalmologists have had a tough time identifying disease. The diagnosis is usually made on the basis of circumstantial evidence, as it is in our situation. The factors we examined for instances of refractory uveitis to start on ATT were a history of Koch's contact, positive Mantoux, interferon gamma release testing, and suspicious retinal abnormalities. After ATT, all of the patients responded to the treatment. Investigations such as PCR and Gold TB-quantiferon may be precise. However, they are not cost-effective. As a result, in cases of OTB, indirect evidence of ocular TB can be significant.

6. Conflicts of Interests

No conflicts of interests were disclosed.

7. Source of Funding

None.

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