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OCULAR INVOLVEMENT IN TUBERCULOSIS: THREE UNUSUAL CASE REPORTS

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ABSTRACT **Introduction:** TB remains one of the deadliest infectious diseases globally, taking the lives of an estimated 1.3 million people in 2022, while 10.6 million patients suffer from active disease. Multidrug-resistant TB remains a public health crisis, with only 40% of all affected patients treated. Ocular TB, although less frequent, is still clinically challenging, presenting a potentially serious complication spectrum. **Case Reports:** We present here serial 3 cases that exemplify the diagnostic predicaments and therapeutic challenges of ocular TB, two of which are cases of multidrug-resistant ocular TB, and the third a case of drug-induced optic neuritis resulting from ATT. These underline the need to have a high index of suspicion for any drug resistance in ocular TB and intervene accordingly with close monitoring. **Conclusion:** All these cases highlight the importance of multidisciplinary management in healthcare delivery, where these patients are managed by ophthalmologists, pulmonologists, and infection-disease physicians. Ocular side effects, including optic neuritis due to anti-TB drugs, require very close monitoring with proactive intervention to prevent visual impairment. Future research is necessary to better understand the effect of anti-TB drugs in drug-resistant forms of ocular TB, which would also influence the management.

KEYWORDS : Tuberculosis, Multidrug-resistant, Optic neuritis, Ocular TB

INTRODUCTION

Tuberculosis is one of the leading international health concerns with significant morbidity and mortality. It is estimated that in 2022 there were 10.6 million new contracted cases of TB, with 5.8 million men, 3.5 million women, and 1.3 million children, thus showing its wide prevalence across all nations and all age groups. (1) Multidrug-resistant TB, curable and preventable, remains one of the huge public health crises. Only about 40% of those affected get treatment. Global efforts in fighting TB have saved approximately 75 million lives since the year 2000. Reaching the target set by the 2018 UN high-level meeting requires an annual investment of US$13 billion for TB prevention, diagnosis, treatment, and care. Eradication of the present TB epidemic by 2030 is one of the health targets of the United Nations SDGs. (2,3) The efforts to control TB have been appreciable, with approximately 75 million lives saved since 2000. (4) Despite these efforts, there remains a substantial funding gap. Every year, some $13 billion is needed for TB prevention, diagnosis, treatment, and care if global targets to end TB agreed by world leaders at the 2018 UN high-level meeting on TB are to be achieved. (3)

Tuberculosis is an infectious disease caused by the bacterium Mycobacterium tuberculosis and principally affects the lungs but can extend to other organs, including the eye. (5) As far back as the early 1800s, there has been a firmly established relationship between TB and ocular complications. Interest in ocular tuberculosis has recently increased, perhaps due to heightened awareness, better diagnostic facilities, and challenges in diagnosing and treating the disease. In the face of better diagnostic facilities, molecular diagnosis by polymerase chain reaction and imaging diagnosis by optical coherence tomography are still not easy for establishing a diagnosis of ocular tuberculosis. This is mainly due to varied clinical presentations that frequently masquerade as other ocular conditions, resulting in delays in diagnosis. (6)

Ocular tuberculosis is a rare but serious manifestation of the disease that can cause relevant visual loss in case of delayed diagnosis and treatment. (7) The presentation of ocular TB can vary greatly but most usually includes granulomatous uveitis, choroiditis, scleritis, retinal vasculitis, and optic neuropathy. (8) It can thus affect any part of the eye, starting from the eyelid to the optic nerve, thereby producing protean symptoms which make it very difficult to diagnose. (9) The true prevalence of ocular TB is not easy to determine due to the non-availability of uniform diagnostic criteria and the frequent absence of systemic symptoms among such patients. However, ocular involvement is estimated to occur in up to 1-2% of cases of TB. (10) The absence of systemic symptoms of TB in many cases of ocular TB also obscures the clinical picture. (11) In most cases, diagnosis was based on a combination of clinical and imaging findings with microbiological or histopathological confirmation of Mycobacterium tuberculosis. (12) The treatment of ocular TB consists of prolonged ATT, usually combined with corticosteroids or other immunosuppressive drugs to reduce inflammation. (13,14)

The timely and accurate diagnosis of optic neuritis is of paramount importance, because early intervention may improve visual outcome and limit further damage to the optic nerve. In most cases, the diagnostic evaluation for optic neuritis consists of a detailed clinical evaluation, visual field

testing, and imaging studies, including an MRI. (15)

Present here is a case of optic neuritis and two others with involvement of ocular tuberculosis, explaining the course, evolution, diagnostic tests, and treatment received. Through these cases, we hope to highlight the importance of considering ocular tuberculosis in the differential diagnosis of patients with ocular inflammation. A diagnosis must result from a multidisciplinary effort between the ophthalmologist, the pulmonologist, and the infectious disease specialist for both a correct and timely diagnosis and to achieve an optimal management plan.

Case 1: Multidrug-Resistant Ocular Tuberculosis

A 43-year-old male with a medical history of respiratory difficulties and chronic inflammation of the eyes on both sides. He came since his eyesight had deteriorated. He has already completed two cycles of anti-TB therapy (HRZE) as part of the National TB Elimination Program (NTEP). However, the recurrence of eye infection led specialists to suspect that he may have drug-resistant tuberculosis. The chest scans revealed reticular opacities in both lungs and a miliary pattern with lymph node involvement, indicating disseminated tuberculosis. The biopsy results from the Broncho alveolar lavage (BAL) and transbronchial lung biopsy (TBLB) indicated the presence of granulomatous inflammation, which is indicative of tuberculosis. Further genome sequencing of vitreous fluid confirmed the presence of multidrug resistance in the strain causing ocular tuberculosis. These findings underscore the importance of considering drug resistance in ocular tuberculosis cases and highlight the need for appropriate management strategies, such as second-line anti-tubercular drugs and close monitoring for treatment response.

Case 2: Multidrug-Resistant Ocular Tuberculosis

This was an 18-year-old female patient who, for one month, had a high fever, a decreased appetite a significant weight loss. Her chest imaging revealed a mediastinum and right hilar lymphadenopathy. Her sputum tests for acid-fast bacilli and the Xpert MTB/RIF assay were inconclusive. She was finally diagnosed with Mycobacterium tuberculosis, susceptible to Rifampicin with fibrotic bronchoscopy with transbronchial needle aspiration. He was initially started on sensitive anti-tubercular drugs. However, persistent lymphadenopathy led to further investigations, which revealed signs of probable drug resistance. The patient was prescribed a shortened course of oral Bedaquiline for MDR-TB, after which lymphadenopathy and ocular manifestations resolved. The case highlights problems in the diagnosis and management of drug resistance in tuberculosis and reiterates the need for proper evaluation and treatment with careful follow-up.

Case 3: Drug-Induced Optic Neuritis

This 18-year-old male patient was admitted with tubercular meningitis and developed optic neuritis after one month of anti-tubercular therapy. At admission, the patient presented with neck pain, fever, generalized weakness, and altered sensorium as a part of an acute systemic illness. Imaging by MRI revealed a calcific granuloma in the right cerebral peduncle with enhancing exudates in the basal cisterns, thereby pointing toward an infective process. The diagnosis of tubercular meningitis was confirmed with the analysis of cerebrospinal fluid, and the patient was started on standard ATT. After one month, she developed optic neuritis in the form of bilateral visual impairment, which is a well-recognized complication of ethambutol, one of the drugs of ATT. Ethambutol had to be stopped to prevent further damage to the optic nerve. The case epitomizes monitoring and management of ocular side effects that occur as a complication of treatment for tuberculosis. In short, these cases represent the various modes of clinical presentation and the management issues in ocular tuberculosis, which bring out the concept of a multi-disciplinary approach involving a battery of health professionals for optimum care and outcomes of treatment.

DISCUSSION

In the two cases, we just looked at how hard it can be to spot and treat ocular TB that doesn't respond to common TB drugs. They highlight why it's crucial to think about drug resistance when patients keep getting ocular TB. These cases also stress the need for careful checking, treatment, and keeping a close eye on things.

Many researchers have looked into the problems of dealing with TB that resist drugs, including ocular TB. One study by Sharma et al found that drug-resistant ocular TB happened more often in patients who had been treated for TB before. This type of TB also leads to poor eyesight outcomes. (15)

The first case points to the possibility of multidrug resistance, as the patient kept having recurring uveitis even after two rounds of standard TB treatment (HRZE) for six months each. The biopsy showed inflammation with granulomas despite earlier treatment, which raised red flags about drug resistance. Tests on the vitreous fluid confirmed that the TB strain in the eye was resistant to multiple drugs, showing that the previous treatment didn't work to get rid of this resistant strain.

In the second case, the patient's initial test didn't show any acid-fast bacilli (AFB), but a CB-NAAT test came back positive for M. tuberculosis and showed it was sensitive to Rifampicin. But after finishing the first TB treatment, the patient's vision in the left eye got worse. More CB-NAAT tests then showed unclear results for rifampicin sensitivity, hinting at potential drug resistance. The doctors then switched the patient to Bedaquiline, a second-line drug to treat TB that's resistant to multiple drugs (MDR-TB). After completing this new treatment plan, the lymph nodes in the chest improved, and the granuloma in the eye's choroid healed up.

These cases thus emphasise the need for adequate evaluation and management of drug-resistant ocular tuberculosis. In some situations, the diagnosis of drug resistance was almost impossible as AFB was negative and Rifampicin sensitivity was indeterminate. Additional tests, such as genome sequencing, may be necessary to confirm the drug-resistant strains. Second-line antitubercular drugs like bedaquiline are being used for treatment, which are probably more toxic and need close monitoring for side effects. These cases, in line with the literature, therefore reiterate that a multidisciplinary approach with good collaboration amongst health professionals experienced in the management of drug-resistant tuberculosis is paramount. Such collaboration between ophthalmologists, pulmonologists, infectious disease specialists, and others relevant in the field remains key to diagnosis and proper management. It is important to monitor response to treatment and its modification at an appropriate time based on drug susceptibility testing, which remains the mainstay of management in cases of drug-resistant ocular tuberculosis, to prevent complications. Ethambutol is one of the most commonly used drugs against tuberculosis. It often causes ocular side effects, including optic neuritis, which could eventually lead to visual impairment if not intervened promptly. This can be proved in the case of an 18-year-old male who was admitted to the intensive care unit with diagnoses of tubercular meningitis complicated by acute hydrocephalus, severe raised intracranial pressure, and obstructive hydrocephalus. He developed optic neuritis due to ethambutol toxicity. This exemplifies the need to monitor and manage the ocular side

effects of antitubercular drugs. Several case reports of ethambutol-associated optic neuritis mention vigilance. The clinical findings of ethambutol-induced optic neuritis, which include bilateral loss of vision and abnormalities of the optic disc, suggest that the visual function of patients treated with ethambutol has to be carefully monitored, with special attention given to risk factors such as tubercular meningitis.

It should be recognised and managed promptly to avoid further optic nerve damage and reduce the degree of visual impairment. As it was, immediate withdrawal from ethambutol was done, which concurs with recommendations from previous studies. A regular eye examination should be performed to monitor for early signs of ocular toxicity. Diagnosis is mainly clinical, based on drug usage history, ruling out all other possible causes of optic neuropathy through adequate evaluation.

CONCLUSION

In summary, these cases shed light on the complex landscape of diagnosing and treating multidrug-resistant ocular tuberculosis, underlining the necessity of addressing drug resistance in cases that are recurrent or refractory to standard treatments. Early diagnosis, thorough assessment, and management utilizing second-line anti-tubercular medications, all under the supervision of a multidisciplinary healthcare team, stand as crucial pillars for delivering optimal care to patients facing this challenging condition. Furthermore, there's a clear call for additional research and studies to delve deeper into understanding the epidemiology, diagnostic approaches, and management strategies surrounding drug-resistant ocular tuberculosis. Such endeavours hold promise for refining our approaches and ultimately enhancing patient outcomes in the face of this formidable disease.

The case involving optic neuritis triggered by ethambutol toxicity in a patient with tubercular meningitis underscores the imperative of vigilant monitoring and proactive management of the ocular side effects associated with anti-tubercular medications. Swift recognition and discontinuation of ethambutol play pivotal roles in averting further harm to the optic nerve and mitigating the risk of permanent visual impairment. Routine ophthalmological assessments should be integral components of care plans for individuals receiving ethambutol, facilitating the timely detection of early signs of ocular toxicity. Clinicians must maintain a high level of awareness regarding ethambutol's potential ocular adverse effects, incorporating them into the diagnostic considerations when evaluating patients presenting with symptoms suggestive of optic neuropathy while undergoing treatment with this medication. By remaining vigilant and proactive, healthcare providers can safeguard the ocular health of their patients and optimize treatment outcomes in the context of tuberculosis management.

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