

## **Brief Review**

# **Intra-ocular Tuberculosis: controversies regarding diagnosis and treatment**

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### **Introduction**

Tuberculosis (Tb) is a chronic bacterial infection caused by Mycobacterium Tuberculosis and is considered as one of the world's leading infectious causes of morbidity and mortality (WHO, 2016). Currently, the interest in TB has been renewed due to HIV pandemic and multidrug-resistant strains (Shakarchi, 2015).

Ocular Tuberculosis is defined as an infection caused by Mycobacterium tuberculosis inside the eye, in the external surface or around the eye (Shakarchi, 2015). Intraocular tuberculosis (IOTB) is the most common form of ocular tuberculosis and that, left untreated, can lead to significant morbidity and visual loss (Basu et al, 2014).

With non-specific signs and systemic associations, the diagnosis and treatment of

IOTB is still controversial with no existing guidelines. The aim of this brief review is to shed light on current practices and controversies regarding diagnosis and management of IOTB.

IOTB occurs mostly due to haematogenous spread of M. Tuberculosis from its primary sites (Shakarchi, 2015; Gupta et al, 2010; Albert et al, 2016). In rarer cases, it can occur due to direct ocular infection or due to hypersensitivity reaction to the distant site infection (Albert et al, 2016).

It can present as anterior, intermediate, posterior, or panuveitis, mostly bilateral but it can occur unilaterally as well (Shakarchi, 2015).

Posterior uveitis is the commonest presentation and it can happen as serpiginous choroiditis (focal or multifocal), choroidal nodules, choroidal granulomas, retinal vasculitis, neuroretinitis, endophthalmitis and panophthalmitis (Shakarchi, 2015). The anterior uveitis is generally granulomatous with mutton fat KPs, iris nodules & broad based PS.

The diagnosis and management of TB Uveitis is challenging because of a wide range of local clinical signs, no associated systemic signs and symptoms and lack of an agreed diagnostic

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criteria (Shakarchi, 2015; Gupta et al, 2010; Gupta et al, 2015). Careful ocular examination plays an important role, particularly when there is no consensus regarding the diagnosis of Tb uveitis (Ang et al, 2017).

Intraocular tuberculosis is still considered as the differential diagnosis even in the absence of pulmonary tuberculosis, as more than half of the patients with extrapulmonary tuberculosis have no evidence of pulmonary disease (Oluleye, 2013).

It is quite challenging to differentiate ocular tuberculosis from other granulomatous diseases, particularly sarcoidosis. Both may have similar clinical findings along with pulmonary changes and high serum ACE levels. The clinical findings/laboratory tests consistent with sarcoidosis according to IWOS (International workshop on ocular sarcoidosis) criteria may be helpful in differentiating sarcoidosis from tuberculosis (Yang et al, 2017).

The stepladder approach is widely followed to diagnose IOTB. That means by looking at the specific clinical signs, excluding other possible causes, followed by chest X-ray or computed tomography scan, PPD or IGRA, and also considering polymerase chain reaction (PCR) of the intraocular sample to confirm the diagnosis in certain cases (Ang et al, 2017).

The clinical signs that can help in diagnosis are mutton fat KPs, broad posterior synechiae, choroidal granuloma, multifocal serpiginous like choroiditis, retinal vasculitis along with either positive AFB smear with radiographic findings in patients with systemic signs or positive Interferon gamma release assay (IGRA) or Tuberculin skin test (TST) in those with no systemic involvement (Basu et al, 2014).

IGRA has better sensitivity and specificity as compared to TST, but there is no current guideline whether it should be used alone or in combination with TST or Chest Xray to screen

and diagnose ocular tuberculosis (Ang et al, 2017).

Recently, polymerase chain reaction (PCR) of aqueous humor has been used successfully with promising results for rapid detection of the mycobacterial genome (Kotake et al, 1994).<sup>11</sup>

In the past, the PCR studies were based on single-target PCR with low positivity rates; now with multi-target PCR, the results are shown to have high sensitivity (73%) and specificity (100%). Hence, routine use of PCR is gaining popularity as early diagnosis and treatment leads to improved clinical outcome (Balne et al, 2014).

Regarding treatment, Anti tubercular Therapy (ATT) is said to reduce disease recurrence and help in preventing active disease by 80-90 % even in those with latent Tb (Ang et al, 2017; Oluleye, 2013).

The American Thoracic Society recommends prescribing four drugs (isoniazid 5 mg/kg/day, rifampicin 450-600mg/day, ethambutol 15 mg/kg/day, and pyrazinamide 25-30 mg/kg/day) for 8 weeks, followed by two drugs (rifampicin and isoniazid) for at least another 18 weeks (American Thoracic Society, 2003).

There have been controversies regarding the duration of treatment as some studies have recommended a longer duration of 9-18 months of therapy for ocular tuberculosis; (Ang et al, 2012). But no clear evidence has been shown to follow the longer duration of treatment (Sanghvi et al, 2011).

In eyes with no definitive intraocular evidence of aetiology, empirical treatment with ATT may be considered, and responsiveness to ATT may indicate the correct diagnosis. According to a study done in the UK, in 70.3% of patients the uveitis disappeared with empirical treatment of ATT for 6 months (Babu et al, 2009).

It is important to liaise with infectious disease specialist or pulmonologist to manage the case

of intraocular tuberculosis, as many of these ATT drugs are notorious to cause distressing side effects (Agrawal et al, 2017).

Concomitant corticosteroids can be used to reduce inflammation and macular oedema (Shakarchi, 2015).

It is based on the theory that some of the inflammatory processes could be secondary to a type IV hypersensitivity reaction to tubercular proteins.

The dose of steroids is 1 mg/kg/day, with tapering regimen over six to twelve months. But there have been controversies regarding the use of steroids in the treatment of IOTB (Shakarchi, 2015).

Despite the advancement in diagnostic technology, the management of IOTB remains controversial with no clear guidelines. To have a proper diagnosis and to reduce morbidity with significant visual loss, the ophthalmologists and internists have to work together, establish guidelines and determine the best treatment course for this potentially debilitating disease.

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