Review Article

Tuberculosis (TB) – An Ophthalmic Perspective

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It is estimated by the World Health Organization (WHO) that one-third of the world's population is infected by Mycobacterium tuberculosis. Ophthalmologists should be aware of the ocular features and management strategies so that they can not only gauge the burden of the diseases in their population but also control it effectively. Following are the updates, which are important from ophthalmic point of view.

PATHOGENESIS

Tuberculosis (TB) is a chronic infection caused by mycobacteria, Mycobacterium tuberculosis. After entry of the organisms in the body, most persons remain asymptomatic, but the infection persists permanently in a latent or dormant state. Active disease occurs when microorganisms begin replicating and it is usually when the immune system fails. The epidemic of human immunodeficiency virus (HIV) infection may have contributed to the increase in TB in the western countries.

OCULAR INVOLVEMENT

Different ocular tissues can be involved (Table 1).
Lid, Conjunctiva and lacrimal sac: Lupus vulgaris may spread from the face to the skin of the lids as translucent nodule that ulcerates. Lid tuberculosis (with negative tuberculin reaction) may present as basal cell carcinoma[1] and tarsitis can be mistaken as chalazion. Chronic unilateral conjunctivitis is in the form of a conjunctival mass or ulceration associated with regional lymphadenopathy. Tuberculous dacryocystitis can lead to fistula formation.

Sclera, Uveal tissue, Optic Nerve and Retina: TB associated uveitis (TAU) may present as anterior uveitis,[2] either granulomatous or nongranulomatous, choroiditis, or choriodal tubercles / tuberculoma. Tuberculoma of the choroid may be confused with a choroidal melanoma[3] or metastatic tumor.[4] Hypopyon is a rare manifestation of TAU[5]. TB is responsible for half of the cases of infectious uveitis in Pakistan,[6] 6% of uveitis cases in Spain[7] and 5% of anterior uveitis cases in India[2]. In scleritis cases, 1% had TB[8]. Infective causes should be suspected in cases of scleritis which progress despite treatment[9]. Disseminated TB has been observed to present as irido-ciliary granuloma in an immune competent patient.[10] Central nervous system TB can lead to bilateral papilloedema causing the branch retinal vein occlusion (BRVO),[11] horizontal gaze palsy, and papill edema with unilateral sixth nerve paresis.[12] For intra-retinal white infiltrates associated with hemorrhage and vitritis, initial diagnostic considerations include infectious causes (cytomegalovirus retinitis, syphilis, toxoplasmosis, tuberculosis), inflammatory (retinal vasculitis associated with autoimmune disease or hyperco-agulable states) or malignant (intraocular lymphoma) diseases.[13] Presumed tubercular cases include a case of

retinal vasculitis with serpiginous-like choroiditis in the other eye[14] and a case of combined optic neuropathy with central retinal artery occlusion without systemic infection.[15]

Tuberculous optic neuropathy may manifest as papillitis, neuroretinitis, or optic nerve tubercle and visual recovery from tuberculous optic neuropathy is common, if the appropriate treatment is given (Davis EJ et al 2012).[16] Ocular TB (choroidal tuberculoma) may be associated with cerebral abscesses that respond to anti TB treatment[17] or multiple pigment epithelial detachments progressing to a large serous detachment of the macula (patient had positive T-spot test).[18]

Table 1: Frequency of involvement of different eye tissues/ part Tuberculosis (TB) += rare involvement, ++= moderate involvement, +++=frequent involvement.

Tissues / parts of the eye involved by tuberculosis	Frequency
Adnexa	+
Conjunctiva	+
Sclera	+
Cornea	+
Lens	-
Anterior uvea	++
Intermediate uvea	+
Posterior uvea	+++
Retina	+++
Optic nerve	++
Extraocular muscle	+
Orbit	+
CNS	++

Reactivation of latent Mycobacterium tuberculosis may occur especially in patients on long term systemic immunosuppressive treatment.[9] Chronic immune suppression (due to corticosteroids and immunosuppressive agents) to reduce inflammation in patients with posterior or panuveitis is a risk factor for systemic infections. Choroidal tuberculoma associated with tuberculosis has been reported in a patient with ocular Behçet disease[19]. Sarcoidosis is rare in children but should be included in differential diagnosis of TB.[20]

MANAGEMENT

The diagnosis of ocular tuberculosis can be confirmed by finding caseating granuloma, acid-fast bacilli which are detected by histopathologic staining methods of ocular tissues and on isolation of the organism on Lowenstein – Jensen (LJ) medium or by polymerase chain reaction (PCR). In the histopathologic specimens, microscopy reveals a paucity of organisms and often there are only 1 or 2 organisms near a giant cell or near an area of necrosis.[21]

PCR is an excellent test for the detection of organisms that are difficult to culture or that take long time to grow, such as Mycobacterium tuberculosis.[22] PCR using different gene targets can help in the diagnosis of extrapulmonary tuberculosis (EPTB) including the ocular TB.[23] Nested PCR has been found positive in tubercular ampiginous choroiditis[24]. Subjects with uveitis associated with TB who respond to anti-TB therapy do not have an active ocular tuberculous infection, but rather an autoimmune-related ocular inflammation that may be triggered by TB.[25] MTB genome was demonstrated in more than 50% of vitreous fluid samples with significant bacillary load, indicating that half of patients with so-called Eales' disease are indeed cases of tubercular vasculitis.[26] A modified loop – mediated isothermal amplification (LAMP) assay has been used for detection of the Mycobacterium tuberculosis complex and claimed to have high specificity, high sensitivity, simplicity, and superiority in avoidance of aerosol contamination.[27]

Two interferon gamma release (IFN-c) assays (IGRA) are commercially available: T SPOT-TB (Oxford Immunotec, Oxford, UK) and Quanti FERON TB Gold In-Tube (QFT – IT; Cellestis, Valencia, California, USA. These assays are highly sensitive and specific. Uveitis patients have higher M tuberculosis infection rate and grade of intensity response than healthy control subjects detected by ELISPOT-IFN-gamma (ELISPOT – MTP).[28] QuantiFERON®-TB Gold test has been found to be useful in diagnosis of ocular TB.[29] A combination of clinical signs, IGRA and tuberculin skin test (TST) has been recommended to diagnose TAU.[30] Others have proposed that a combination of Schirmer test > 10 mm, retinal

vasculitis with areas of multiple, pigmented chorioretinal atrophy along blood vessels, and positive Mantoux test may be used clinically to differentiate tubercular from sarcoid uveitis in Indian population.[31]

In presumed TB a therapeutic trial of anti TB drugs (isoniazid, rifampin, pyrazinamide and ethambutol) can be given for 2 – 4 weeks. If the response is good, full anti TB course should be given (ethambutol for 2 months to prevent optic neuropathy and the rest for 6 months). TAU with latent TB responds to anti-TB therapy.[32] Some believe that anti-tubercular treatment is not required in latent tuberculosis[33]. Antituberculosis drugs are known to cause decreased vision.[34] Anti-tuberculosis drug, rifabutin induced uveitis[35] should be kept in mind and especially in AIDS patients[36] to avoid useless and potentially invasive interventions in these fragile people. Visual acuity, contrast sensitivity, and multifocal ERG are sensitive tests to detect ethambutol toxicity in subclinical stages[37]. Continued progression of choroiditis lesions after initiating antituberculosis treatment in tubercular serpiginous – like choroiditis is an indication for increased immunosuppression with continuation of antituberculosis treatment which results in good outcome.[38]

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