

TUBERCULOSIS AND THE EYE

C. M. Chuka -Okosa

Department of Ophthalmology, University of Nigeria Teaching Hospital (U.N.T.H) Enugu, Nigeria

ABSTRACT

Objectives:

1. To refresh knowledge on the epidemiology, pathogenesis, clinical features, investigations and treatment of ocular tuberculosis;
2. To highlight the ocular complication of tuberculosis.

Method: Through an internet search and review of current literature on tuberculosis and its ocular complications, the information relevant to the objectives was obtained.

Conclusions: TB can affect any structure in the eye and adnexae. Ocular TB is not easy to diagnose because most times there is no concurrent active systemic tuberculosis. However, once TB is confirmed, treatment is generally the same as for systemic TB. Topical steroids are given in addition, in cases like phlyctenulosis. Early diagnosis and treatment of ocular TB can prevent blindness or severe ocular morbidity. With the growing epidemic of HIV and the consequent increased risk of developing TB, ophthalmologist and eye care workers are, therefore, advised to heighten their suspicion of ocular TB.

Key words: Mycobacteria; Tuberculosis; Eye

INTRODUCTION

Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*, which is a member of a group of closely related organism in the *M. tuberculosis* complex (*Mycobacterium africanum*, *mycobacterium bovis*, *mycobacterium microti* and *mycobacterium tuberculosis*).^{1,2} It is one of the oldest disease in the world. Lesions of bone typical of TB (Potts disease) were evident in Europe from Neolithic times (8000 BCE), in ancient Egypt (1000 BCE) and in the pre-Columbian New World.¹ However, the first ocular lesion of tuberculosis, the tubercular iris nodule was first described in 1711.³ As of several years ago it was generally accepted that the incidence of tuberculous infection was declining. But in recent years it has re-emerged as a serious public health problem. TB is currently the leading infectious cause of morbidity and mortality worldwide^{4,5} and also a global emergency as declared by WHO⁶. With this current situation the possibility of a higher prevalence of tuberculous eye disease or ocular tuberculosis has also been raised. Ocular tuberculosis, which indicates any infection by *Mycobacterium tuberculosis* or any of the *Mycobacterium* species, in, on or around the eye³

This paper will discuss the epidemiology, pathogenesis, clinical features, investigations and treatment of ocular tuberculosis.

EPIDEMIOLOGY

The number of TB cases worldwide corresponds with economic conditions; the highest incidences are

seen in the countries of African, Asia and Latin America that have the lowest GNP³(GROSS NATIONAL PRODUCT). Worldwide, there are approximately 8-10million new cases of TB every year, 95% in developing countries.⁶ Nearly 3 million people die from TB each year; 98% infection-related deaths occurring in the developing world⁶. Ocular TB involving any of the tissues of the eye is uncommon.⁷ Dutt and associates⁸ reported ophthalmic involvement in only 3 of 402 sites of extrapulmonary TB. Donahue⁹ found that 1.4% of more than 10,000 patients in one sanatorium were treated for ocular TB between 1940 and 1966. Ayanru¹⁰, in his series of 1987 uveitis patients seen in Benin City, Nigeria, reported only one case of TB uveitis. The choroid is probably the most commonly infected intraocular structure. Woods¹¹ estimated that the choroid is involved in about 1% of patients with pulmonary TB. Tuberculosis accounted for less than 1% of uveitis in a more recent study in Los Angeles¹². Eyre reported a prevalence of conjunctival TB of 1 in 2500 among patients with ocular complaints, compiled in an area with a high rate of TB¹³. Phlyctenular keratoconjunctivitis occurs in up to 35% of patients in populations with high rates of *M. tuberculosis* infection, such as Alaskan Eskimos.¹⁴ It occurs most commonly in the first and second decades of life, and girls are made more commonly affected than boys. In contrast, Donahue⁹ found only 6 cases of phlyctenular conjunctivitis in 10,524 patients with TB. The impact of the AIDS epidemic on rates of ocular TB remains unclear. There are few published reports of ocular TB in HIV-infected patients with extrapulmonary TB. Shafer et al¹⁵ and Small et al¹⁶

Correspondence: Dr. C.M. Chuka-Okosa

reported no cases of ocular TB in their HIV-infected series. Nevertheless, it is reasonable to expect that ocular TB in HIV-infected patients will become more frequent as their life expectancy increases

PATHOGENESIS ¹⁷⁻¹⁸

Ocular manifestations in TB may be attributed to either infection or non-infectious immunologic reactions.

Infection: Ocular involvement in tuberculosis due to infection may occur in one of three ways:

Primary exogenous infections of the eye (Primary ocular TB) are rare but may occur in the lids or in the conjunctiva. Other external tissues that may rarely become infected include the cornea, sclera, and lacrimal sac. At the implantation site the organism causes a minimal acute polymorphonuclear inflammatory response in the tissues during the first 10 days. Within the first 24 hours the polymorphonuclear phagocytose organisms but do not kill them, and they drain these viable organisms into the regional lymph nodes where lesions develop, causing nodal enlargement. The typical TB lesion is the tubercle. This appears as a pinhead-sized white or grayish

Secondary infections of the eye (Secondary ocular TB) may occur by direct extension from surrounding tissue or by contamination with patient's own sputum. By far the most common form of ocular involvement result from **haematogenous dissemination** from a distant site (Secondary ocular TB). The uvea, iris, ciliary body and choroid is the tissue most frequently involved because of its great vascularity.

Immune Reactions⁷: to tuberculo-protein may cause phlyctenulosis, interstitial keratitis, and possibly retinal vasculitis.

TUBERCULOSIS OF THE EYE (OCULAR TUBERCULOSIS)

Tuberculosis can affect disease occurs as a result of haematogenous dissemination, whereas external disease may occur from either exogenous or endogenous sources.

CLINICAL FEATURES:

TUBERCULOSIS OF THE ADNEXAE

EYELID¹:

Though rare the skin of the eyelid can be affected with tuberculosis (cutaneous TB) in various ways

PRIMARY INOCULATION TB (TUBERCULOUS CHANCRE): result from direct introduction of mycobacterium into the skin or mucosa of an individual who was not previously infected with TB or was immunized with the Mycobacterium bovis strain Bacilli Calmette Guerin (BCG). Since mycobacteria do not penetrate intact skin, initiation of infection almost follows an injury, usually in children.

TB VERRUCOSA CUTIS: is an indolent warty plaque that occurs after direct inoculation of TB into

the skin of individuals previously infected with Mycobacterium Tuberculosis or Mycobacterium bovis. TB verrucosa cutis can result from accidental exposure to tuberculous tissue in high-risk group such as physicians, pathologists and laboratory workers. Farmers, butchers and veterinarians contract this form of re-infection TB from tuberculous cattle. Individuals also contract this lesion after contact with tuberculous sputum. Lesions are usually solitary, and regional nodes are not affected unless secondary bacterial infection occur. Spontaneous resolution with scarring can occur.

MILIARY TB OF THE SKIN: This is a rare manifestation of fulminant military TB resulting from haematogenous spread of mycobacteria to multiple organs. The disease occurs predominantly in children and may be coincident with other infections such as measles. Lesions erupt as small (millet-sized) red macules or papules. Purpura, vesicles and central necrosis are common. Affected patients are gravely ill, and prognosis is poor.

SCROFULODERMA (TUBERCULOSIS COLLIQUATIVE CUTIS): This results from breakdown of skin overlying a tuberculous focus. Lesions present as firm, painless, subcutaneous nodules that gradually enlarge and suppurate then form ulcers and sinus tracts in overlying skin. Typical ulcers have undermined edges and a floor of granulation tissue. Spontaneous healing can occur but takes years and is accompanied by the formation of hypertrophic scars.

METASTATIC TUBERCULOUS ABSCESS (TUBERCULOUS GUMMA): This is a variant of scrofuloderma that occurs following haematogenous spread of mycobacteria to skin in tuberculin-sensitive individuals. Painless, fluctuant subcutaneous abscesses form singly or at multiple sites, then break down into fistulas and ulcers resembling scrofuloderma. These lesions typically occur in malnourished children or in severely immunosuppressed patients.

LUPUS VULGARIS: This is a chronic and progressive form of cutaneous TB that occurs in tuberculin-sensitive patients. Lesions usually are solitary, and more than 90% involve the head and neck. Small, sharply marginated, red-brown papules of gelatinous consistency (apple-jelly nodules) slowly evolve by peripheral extension and central atrophy into large plaques. However, many clinicians in Asian countries who see large numbers of this entity have questioned the descriptive term 'apple jelly nodules' since this is not seen in many pigmented patients. Reappearance of new nodules within previously atrophic or scarred lesions is characteristic. Conjunctival mucosa may be involved primarily or by extension. Lesions of lupus vulgaris often persist for years before diagnosis is made and they can be

disfiguring. In long standing lupus vulgaris, squamous cell carcinoma can occur and be confused with the disease itself.

CONJUNCTIVA²:

Tubercular infection of the conjunctiva is very rare. It can be primary or secondary. Conjunctivitis may start slowly with a conjunctival granuloma; present as an acute purulent conjunctivitis or as a pseudomembranous conjunctivitis. One important clue that a patient may have tuberculous conjunctivitis is the presence of lymphadenitis, which is usually absent in other viral, bacterial and allergic conjunctivitis.

TUBERCULOSIS OF THE ORBIT¹⁹⁻²¹

Orbital involvement in TB can involve any of the orbital tissue including the bone, periosteum and lacrimal gland. Orbital tuberculosis may occur as a result of haematogenous spread of infection from a distant site or by direct extension of infection from adjacent sinus, the lacrimal apparatus or the eye itself. **ORBITAL PERIOSTITIS:** This is the most common form of orbital tuberculosis. It tends to occur during the first two decades of life when bony growth is still active. In the vascularised spongy tissue of the outer margin of the orbit, the infection may smolder for weeks to months producing local erythema and oedema involving the lids and conjunctiva. A cold abscess may form and discharge chronically through a cutaneous fistula.

TUBERCULOMA OF THE ORBIT: Is a rare manifestation of tuberculosis usually occurring in middle age. It could also occur in a child. The patient presents with a painless proptosis and depending on the location of the mass it could be axial or non-axial.

ORBITAL ABSCESS: This is also a rare manifestation

TUBERCULOSIS OF THE LACRIMAL GLAND: Tuberculosis rarely involves the lacrimal gland. The patient could present with a painful superotemporal orbital swelling.

TUBERCULOSIS OF THE EXTRAOCULAR MUSCLES

Tuberculosis involving the extraocular muscle is a very rare presentation though a number of cases have been reported. A tuberculoma of the extraocular muscle could present as a painful swelling over the corresponding part of the eye with associated restriction of ocular motility involving the muscle

TUBERCULOSIS OF THE EYE

CORNEA:

Primary infection of the cornea is very rare. Corneal involvement is usually due to a hypersensitivity or cross-reaction whereby the immune system mistakenly attacks proteins in the cornea, which are similar to those on mycobacteria.

PHLYCTENULAR KERATOCONJUNCTIVITIS^{2,7}:

This is the most common form of external ocular TB. Tuberculosis was once the leading cause of phlyctenular keratoconjunctivitis, but is now a much less common cause than staphylococcus specie. The two causes cannot be distinguished clinically. The pathophysiology of tuberculous phlyctenular keratoconjunctivitis is unclear, but presumably is due to delayed hypersensitivity to foreign (mycobacterium) protein which predominantly affects malnourished older children and is more common in girls. Phlyctenulosis rarely occurs in patients with active pulmonary TB, which may be related to the impairment of cellular immunity in patients with systemic disease. A conjunctival phlycten usually presents as a small pinkish-white nodule, starting astride the limbus. But it may occur anywhere on the bulbar conjunctiva. It has prominent vessels extending towards the fornix. These lesions become gray and soft over several days. It may resolve spontaneously or it may extend onto the cornea and very occasionally it may give rise to severe ulceration and even perforation. Corneal phlyctenules begin at the limbus as an elevated nodule with a trailing sheath of dilated vessels. The central area undergoes necrosis over several weeks. A healed cornea phlycten usually leaves a triangular limbal-bases scar. Recurrent lesions may progress centrally, but do not cross the central cornea. In populations with a high prevalence of TB, phlyctenulosis is common. Furthermore, the incidence of positive tuberculin skin test is much higher in patients with corneal opacities than in those without.

DIFFERENTIAL DIAGNOSES: Staphylococcal phlyctenules, bacterial ulcers, marginal ulcers, inflamed pingueculae, and vernal keratoconjunctivitis

INTERSTITIAL KERATITIS⁷: This is thought to be due to a cross-reaction. It is unilateral and painless. Clinically, it runs a prolonged course with multiple attacks. The infiltration is usually peripheral and sectoral, sparing the central cornea. The superficial and middle layers of the cornea stroma are usually affected; vascularisation follows with the vessels usually being located in the anterior stroma. It has been suggested that tuberculous interstitial keratitis, in contrast to syphilitic interstitial keratitis, is usually unilateral and more anterior, with more frequent attacks.

OTHERS: Other manifestations of cornea TB are kerato-conjunctivitis with stromal infiltration or an extension of scleral or uveal tract TB.

SCLERA AND EPISCLERA:

SCLERITIS/SCLERAL GRANULOMA: Scleritis can be diffuse, posterior or nodular and associated with localized granuloma development. Deep nodular scleritis is due to direct infection of the sclera by the mycobacteria. Clinically, the scleritis presents as one more painful indurated nodules which appear fixed to the sclera and are associated with marked injection.

Focal, necrotizing anterior scleritis is most common presentation of TB scleritis. The nodules eventually turn yellow as they necrose, and ulceration eventually follows. There could also be associated conjunctival ulceration. Scleral perforation may occur. Tuberculous scleritis is usually not several painful. Adjacent interstitial keratitis may be present if the infection is near the limbus. Physical examination may reveal regional preauricular and submandibular lymphadenopathy. Tuberculous scleritis should be suspected when a necrotizing lesion occurs in a patient with a positive chest x-ray or PPD skin test. Scrapings that reveal acid-fast bacilli and a positive culture are confirmatory, but a negative result does not rule out the diagnosis.

DIFFERENTIAL DIAGNOSES: Infectious scleritis caused by agents such as varicella-zoster virus or *Aspergillus* spp, syphilis or other bacterial infection; scleritis associated with systemic vasculitis.

EPISCLERITIS: This is a result of hypersensitivity reaction to mycobacterium protein.

UVEA:

UVEITIS: This is the most common ocular manifestation of TB, usually presenting as a chronic anterior uveitis, a panuveitis or as a choroiditis. Both direct infection and delayed hypersensitivity reactions have been implicated in the pathogenesis of the uveitis. TB uveitis is rarely seen in patients with active pulmonary TB. Generally, it accounts for about 0.2% of all uveitis cases². Up to 32% of childhood uveitis in developing countries may be due to TB²². TB uveitis can affect any age-group; has no gender predilection; is chronic in a majority of the cases; is granulomatous in most presentation (some, however, present as non-granulomatous uveitis); is unilateral in a majority of cases and involves both anterior and posterior segments. Where granulomatous anterior uveitis develops, it presents with mutton-fat keratic precipitates (KP) and iris nodules. However, in some cases, instead of mutton-fat keratic precipitates there might be large greasy-appearing cellular deposits on the corneal endothelial surface. The classic inferior distribution of KP appears in the lower one third of the cornea, known as the Arit triangle. Millitary TB may cause seeding of the iris with development of small, gray nodules surrounded by a network of fine blood vessels. Such lesions must be distinguished from sarcoid nodules, which are larger and more pink. In rare cases, a conglomerate tubercle of the iris grows rapidly, involves the cornea by direct extension, and cause painful glaucoma or even perforation. The choroiditis in ocular TB could be diffuse, focal or multifocal. With its high blood flow the choroids is a common site for tuberculous involvement. Tuberculosis has been suggested as a possible cause of serpiginous choroiditis²³⁻²⁵. This is a chronic, recurrent, progressive disorder that primarily involves the choroids and choriocapillaris. It is characterized by gray-white lesion that shows

centrifugal spread. This gray lesion turns pale in few weeks, while the active edge advances further and eventually results in the development of multiple jigsaw puzzle-shaped areas of chorioretinal atrophy. Laatikainen and Erkkila²⁴ hypothesized that a tubercular allergic cause may play a role, at least in patients who have had tuberculosis in the past.

TUBERCULOMAS OF THE UVEAL TRACT: Especially those of the ciliary body²⁶ have a chronic course and tend to occur in young adults rather than children. The patients may have an old healed pulmonary tuberculosis focus, or when they present with their ocular symptoms, an active lesion may be found. In the rare instance of a tuberculoma in the macular region, vision loss may be permanent despite treatment²⁷.

CHOROIDAL GRANULOMAS (TUBERCLES): Choroidal tubercles and tuberculomas are common clinical presentation of ocular TB. While TB uveitis is rarely associated with or without inflammation, is strongly correlated with systemic disease, and is an indicator of hematogenous spread of mycobacteria. It is also possible to see choroidal granulomas in patients who are not symptomatic from choroidal tubercles are unilateral. They can range in size from 1/6 to several disc sizes in diameter; are found around the posterior pole and are usually less than 5, although there are cases of 50-60 + lesions. The lesions appear yellow-white early on, and become pigmented as time passes. They have indistinct borders. Occasionally, they can be associated with an overlying serious retinal detachment. A marked anterior uveitis and retinal vasculitis may occur rarely. In general, however, these reactions are uncommon. Choroidal haemorrhages and subretinal neovascularisation have also been described. Whereas choroidal tubercles are generally small and multiple, tuberculomas are usually solitary and may measure up to 7mm in diameter.

DIFFERENTIAL DIAGNOSES: Syphilis, toxoplasmosis, sarcoidosis, melanoma, metastatic carcinoma (choroidal tumours), retinoblastoma.

COMPLICATIONS OF TB UVEITIS:

Include raised IOP/secondary glaucoma: anterior or posterior synechiae; iris granulomas; cataract; cystoid macular edema; retinal and choroidal scarring

UVEITIS ASSOCIATED WITH TUBERCULIN SKIN TESTING: This is a peculiar clinical entity. It is a bilateral granulomatous anterior uveitis that responds to topical and oral steroids. The few reported cases did not find evidence of systemic TB, and resolved without the need for anti-tuberculous medications.

RETINA:

The retina is rarely involved primarily. Where it is affected, it normally spreads from adjacent choroids, although haematogenous spread from a more distant site is also possible.

RETINITIS: Retinal lesions are of either a focal tubercle or massive retinitis nature. The clinical features of tuberculous retinitis include vitreous opacification and gray-white retinal lesions.

RETINAL VASCULITIS:

Is characterized by moderate vitritis, severe ischaemic oeriphlebitis and peripheral retinal capillary closure leading to neo-vascularisation

Secondary changes in the retinal vessels overlying choroids tubercular masses have been reported. Possible causes of retinal vasculitis in patients with TB include haematogenous dissemination of infection, inflammation from adjacent choroidal lesions, or hypersensitivity reactions.

EALES'DISEASE: This is a rare disorder that is not associated with *Mycobacterium tuberculosis* specifically, but with a positive tuberculin skin test (there are cases of Eales' disease without positive tuberculin skin tests). It is characterized by recurrent vitreous haemorrhages in healthy young adult males. Retinal periphlebitis is the prominent finding, along with peripheral capillary nonperfusion. In few cases where pathology was examined, there was no evidence of mycobacterium infections. This disease may have multiple causes. Rapid improvement of retinal vasculitis following treatment with antituberculous chemotherapy is consistent with an infectious cause in some cases. Elliot²⁸ suggested that the haemorrhage and exudation in Eales' disease result from local reaction in a vessel wall sensitised to tuberculo-protein.

DIFFERENTIAL DIGNOSES: Sarcoidosis; syphilis; Behcet's disease; multiple sclerosis, sickle cell disease and idiopathic retinal vaculitis.

TB PANOPHALMITIS: Acute tuberculous panophthalmitis usually occurs in children or severely ill adults. The ocular involvement and duration of symptoms is relatively short (1-2 months) and the ocular diagnosis is frequently missed. McMoli et al³⁰ reported a case of TB panophthalmitis which presented as a localized episcleral mass and was wrongly diagnosed and treated as retinoblastoma.

TB ENDOPHTHALMITIS: Tuberculous endophthalmitis is a highly destructive process with rapid onset resulting from direct infection of interocular structures. Granulomatous uveitis and painful glaucoma are present. Tuberculous endophthalmitis may be mistaken for syphilis, retinoblastoma, pseudotumor, or metastatic carcinoma.

TUBERCULOSIS AND CRANIAL NERVES :

Optic Nerve:

PAPILLITIS: Optic nerve inflammation can occur alone or as part of uveitis, it can also be involved through direct infiltration as part of tuberculous meningitis

DISC OEDEMA/PAPILLOEDMA: Disc oedema may occur alone or in conjunction with other posterior segment inflammation. Any intracranial lesion due to TB may cause papilledema.

Facial Nerve:

Facial nerve inflammation can occur from haematogenous dissemination from a distant site.

Neuroophthalmic Disesse:

Meningitis is the most common cause of neuroophthalmic disease in patients with TB. HIV-infected patients are at increase risk of tuberculous meningitis, but the clinical manifestation and outcoMe do not appear different from those in patients without HIV infection.

Sixth and, less frequently, third cranial nerve palsies may occur as a result of increased intracranial pressure.

A variety of papillary abnormalities may occur. Optic nerve involvement may take the form of chiasmatic crchnoiditis, papilloedema, or optic neuritis. Tuberculous meningitis is a far more common cause of optic neuritis than is tuberculous retinal periphlebitis.

In tuberculous meningitis, vasculitis involving the pontine lenticulostriate and thalamopenetrating arteries may occur and cause small infarcts in the basal ganglia and brainstem. These infarcts can lead to stroke and cortical blindness.

OCULAR TB AND HIV³

Tuberculin skin testing is not reliable in HIV infected patients. There are many case-reports of HIV patients with biopsy or culture-proven systemic TB who do not respond to tuberculin skin testing³.

Ocular TB manifestations are the same as in immunocompromised patients, and disseminated choroiditis is the most common one. Their immunocompromised status retards recovery of ocular complications. Drug malabsorption is additionally a common problem in HIV infected individuals mandating longer therapy.

DIAGNOSIS OF OCULAR TB

History (Clinical Diagnosis):

Patients with ocular TB rarely have overt systemic manifestations. This can lead to difficulties in establishing the diagnosis.

Occasionally, a history of previous TB exposure or positive skin test for TB will be found.

The patients may come from an area where there is high incidence of TB. Patients with ocular TB rarely have fever, cough, or sputum production.

In 1966, Duke-Elder and Perkins³¹ stated that a "positive diagnosis of ocular TB can be made in those case of miliary or proliferative lesions in which there is no evidence of other disease liable to cause a granulomatous uveitis and which exhibit tuberculous

disease elsewhere, particularly if specific therapy induces a favourable response."

A high index of suspicion is required.

LABORATORY DIAGNOSIS^{3,7}:

Microscopy, Culture And Sensitivity: Definitive diagnosis is achieved by identifying the Mycobacteria tuberculosis organisms in ocular tissue or fluid. Through pars plana vitrectomy, vitreous is collected and subjected to microscopy, culture and sensitivity.

BIOPSY: Diagnosis of superficial granulomata with Langhans giant cells and acid-fast bacilli. Organisms are rarely obtained from ocular specimens. Easily accessible sites include the eyelid, conjunctiva, lacrimal gland, and sclera choriorretinal biopsy: A team of specialist published a report of diagnosis TB choroiditis by choriorretinal biopsy, using standard three-port pars plana vitrectomy technique³. Postoperatively, the patient did well, vision improved from CF to 20/70, with an epiretinal membrane as the only post-operative consequence³.

PCR (Polymerase Chain Reaction) testing: This technique amplifies even very small portions of a predetermined target region of Mycobacterium tuberculosis-complex DNA. The test uses an automated system that can rapidly detect as few as one organism in the fluid. It has shown sensitivity of nearly 90% in pulmonary disease. More recently, PCR has been used to diagnosis ocular TB. Aqueous and vitreous specimen may be used to make the diagnosis. False-positives are an expected difficulty when using this test because of its extreme sensitivity.

Skin Tests: The Mantoux test is the preferred and standard skin detecting TB. It is commonly used to diagnose ocular TB although there is no statistically significant correlation between ocular lesions and Mantoux sensitivity:

A positive response (induration of 10mm or more) confirms that patient had been exposed to Mycobacterium tuberculosis maybe as an infection or as vaccination (BCG).

However, a person who has been exposed to Mycobacterium tuberculosis maybe as an infection or as vaccination (BCG).

However, a person who has been exposed to Mycobacterium tuberculosis, due to weakened immune response from e.g. age, steroids or HIV, may not make a positive reaction to the test.

A Mantoux test showing induration of less than 5mm in diameter (negative reaction) does not rule out the possibility of ocular TB.

Patients with proven ocular TB have been reported to have insignificant or negative PPD skin tests. Reports exist also of TB uveitis patients with induration less than 10mm or even erythema alone who have responded favourably to antituberculous therapy.

A common dilemma in diagnosis and treatment may arise in cases of patients with TB uveitis with positive Mantoux test. It is important to remember that not every patient with such findings needs treatment with

antituberculous drugs (The treatment of proven active TB infection is different from prophylaxis in Mantoux-positive patients without evidence of active TB.) Roseenbaum and Wernick³¹ calculated that a patient with uveitis and a positive PPD but no other signs of TB has only a 1% probability of having active TB.

There is no proof of the theory that increased intraocular inflammation following tuberculin testing indicates that the ocular lesion is tuberculous.

Furthermore, there is a risk of tuberculin skin test-induced uveitis in the absence of TB.

Radiological Investigations:

Chest X-rays: are also useful in detecting active signs of TB infection (infiltrations, sometimes with evidence of cavitation or pleural effusion) or evidence of previous infection. However, a negative finding does not rule out the possibility of ocular TB. Patients with orbital TB usually have pulmonary evidence of TB.

*X-ray of the orbit: Orbital radiographs reveal bony erosion in orbital TB.

Use Of Therapeutic Trials For Diagnosis:

Abrams, Schlaegel and associates^{32,33} have advocated the Isoniazid therapeutic test for diagnosis of suspected tuberculous uveitis. Isoniazid is given in a dose of 300mg daily for three weeks. If there is dramatic improvement of the inflammatory signs, a presumptive diagnosis is made and full course of multiple drug antituberculous therapy is instituted. The value of this test is unsubstantiated.

Limitations:

The clinician must distinguish between a therapeutic effect of the INH and a natural fluctuation in the course of chronic uveitis of some other origin;

The diagnostic value of therapeutic trials is diminished by the increased prevalence of drug-resistant strains of *M. tuberculosis*, including those causing ocular disease;

The use of a single drug is not acceptable; even a course of therapy as short as 3 weeks can result in resistance of organisms, although development of resistance is rare, if the infection involves a small number of organisms value of

Adjunctive Tests⁷:

These include: Fluorescein angiography of choroidal tubercles. Ultrasonography of choroidal tubercles; Elevated levels of lactate dehydrogenase or soluble antigen fluorescent antibody from aqueous specimens in eyes with choroidal tubercles have been reported; The radioactive phosphorus test may be positive for a choroidal tubercle, so that it simulates a choroidal melanoma.

TREATMENT

A. MEDICAL^{2,6,8,12}

Systemic Treatment:

Tuberculosis and the eye. C.M.Cuka-Okosa

ANTITUBERCULOUS THERAPY: Once ocular TB is confirmed systemic treatment with antituberculous therapy is commenced immediately, since it will last at least 6 months, and will sometimes require up to 2 years. There is no difference between the treatment for pulmonary tuberculosis and that given for ocular tuberculosis. The three basic therapeutic principles in the treatment of TB also apply in the treatment of ocular TB:

- I. Any regimen must contain multiple drugs to which the Myc. Tuberculosis is susceptible (this is because TB is resistance to INH and Rifampicin);
- II. The therapy must be taken regularly and
- III. The therapy must be continued for a sufficient period of time.

*Usually, a three-drug therapy is recommended with Rifampicin + Isoniazid + pyrazinamide at least for two months, followed by Rifampicin and INH for another 4 months, or a total of 6 months of therapy.

*If it is known in the region that INH resistance is more than 4%, four-drug therapy with Rifampicin + INH + Prazinamide + Ethambutol or Streptomycin is recommended.

*After the first two months Ethambutol and Prazinamide are discontinued because of their optic nerve and liver toxicity respectively. A course of antituberculous therapy could be intermittent or daily but it lasts for 6 months except in special cases where it lasts longer.

* In HIV-positive patients, treatment is given for 9 months because of their high relapse rate. Alternative drug regimens are used in treating HIV positive patients because Rifampicin is not used with protease inhibitors which are a part of the HAART regimen used in the treatment of HIV. Drugs like Rifabutin are used in place of Rifampicin.

*Direct-observed-therapy (DOT) is recommended for the treatment of ocular tuberculosis as poor patients' compliance is the most common reason for treatment failure in tuberculosis. DOT involves the direct monitoring of the patient taking the pills by a health care worker. Following treatment with the systemic antituberculous therapy, choroidal tubercles become larger, paler, and more distinct with time, leaving behind sharply demarcated scars.

Corticosteroid Therapy: There is no role for systemic corticosteroid therapy in the treatment of infectious ocular TB.

Topical Treatment:

Tuberculous phlyctenulosis: In addition to treatment of underlying TB, treatment of tuberculous phlyctenulosis consists of topical corticosteroids tapered over one week. Cycloplegic agents are also helpful. Conjunctival lesions causing mild symptoms may respond to topical astringents. Mucopurulent discharge suggests secondary bacterial infection and should be treated with topical antibiotics.

Tuberculous interstitial keratitis: Treatment consists of topical corticosteroids and cycloplegics. Antituberculous drugs are indicated for the systemic

treatment, but have no effect on the ocular disease. However, resolution of sclerokeratitis is usually achieved with systemic antituberculous chemotherapy alone.

* TB Uveitis: After TB uveitis has clearly responded to the antituberculous therapy, topical or depot corticosteroids may be considered to decrease the local inflammatory response and improve visual function. Oral corticosteroids should be avoided. Patients undergoing treatment for uveitis require close monitoring for both therapeutic response and drug toxicity by the treatment ophthalmologist as well as a physician.

Surgical¹²:

Surgery is not required for treating ocular TB. When surgery is planned, it is usually directed to treating side-effects of the disease or for the rehabilitation of vision.

Occasionally, a surgical biopsy of conjunctiva, vitreous, choroids, or sclera may be required to help establish the diagnosis or to rule out other potential diagnostic aetiologies.

Cataract in a patient with TB could either be an age-related one or a complication of tuberculous uveitis. The definitive treatment is cataract extraction.

SPECIAL CONSIDERATIONS FOR CATARACT SURGERY:

Cataract surgery should not be performed in a patient with tuberculous uveitis until all inflammation has been completely controlled, cell-free, for a period of at least 3 months. Younger patients, noncompliant patients, and patients with severe ocular damage should be cell free for 6 month prior to elective surgery.

Modern small incision, phacoemulsification techniques are preferred. Extracapsular surgery produces unwarranted excess inflammation in these tuberculous eyes due to the large incision size and requirement for sutures.

Attention should be paid to the posterior capsule and the in-the -bag placement of the IOL to avoid postoperative complication in these eyes.

IOLs should be made of highly bio-inert materials. These are acrylic and hydrophilic materials. PMMA and Silicone lenses are not acceptable. The former have a higher posterior capsular opacification rate and may have a higher bioadhesion to inflammatory cells and bacteria. The second-generation silicone polymers and hybrid collamer (silicone and collagen) materials may prove to be more biocompatible.

Concomitant pars plana vitrectomy for uveitis cataract implantation may provide more complete visual rehabilitation for patients who complain a lot about floaters. It can be performed immediately after implantation with an intact posterior capsule.

ELECTIVE PARS PLANA VITRECTOMY: INDICATIONS:

Those patients with TB uveitis who complain bitterly of floaters.

In addition, the vitreous gel is believed to provide capacitance for inflammatory debris, cell, and mediators. Removal of the core vitreous, therefore, may benefit patients with uveitis by reducing the need for long-term inflammatory medications.

Prophylaxis: Progressive vitreous opacification and organization in more severe cases of TB uveitis may predispose to cyclitic membrane formation and subsequent retinal detachment. Elective vitrectomy guards against this.

CONCLUSIONS

1. Although rare, ocular TB when present can cause severe ocular morbidity or blindness if not managed promptly
2. Without a high index of suspicion, even when present it even be missed because the patients rarely have concurrent systemic disease.
3. With the increasing incidence of HIV and AIDS and the longer life expectancy with better drugs, it will be no surprise if the incidence of ocular TB also increases. Ophthalmologists should heighten their level of suspicion for the ocular complications of HIV AND AIDS.

REFERENCES

1. **Meltzer, M.S.; Nacy, C.A.:** Cutaneous tuberculosis <http://www.emedicine.com/derm/topc/134.tm>
2. **Wilkins, Lightman, S.:** Ocular manifestations of HIV and TB <http://www.optometry.co.uk> module 4 part 6:26-32.
3. **Samson, C.M:** Ocular tuberculosis. <http://www.uveitis.org/medical/articles/case/ocular-tuberculosis.htm>.
4. **Mahler, D.; Raviglione, M.C.:** The global epidemic of tuberculosis: A World Health Organisation perspective. In: sclossberg D, ed. Tuberculosis and non-tuberculous mycobacterial infections, 4th rd. Philadelphia WB Saunders, 1999, chapter 10:104-15.
5. **Dye, C; Scheele, S.; Dolin, P. et al:** Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country WHO. Global surveillance and monitoring project. JAMA 1999; 282: 677-686.
6. **Cunningham, E.T.; Rathinam, S. R.:** Editorial TB or not TB? Perennial question. Br J Ophthalmol 2001; 85: 127-128.
7. **Dunn, J. P.; Helm, C,J.; Davidson, P. T.:** Tuberculosis J.S. Pepose; G.N. Holland; K. R. wilhemos Externabular infection and Immunity St. Louis Missouri, Mosby; 1996: 1405-1420.
8. **Dutt, A. K.; Moers, D.; Stead, W. W.:** Short-course chemotherapy for extrapulmonary tuberculosis: nine years' experience. Ann Inter Med 1986; 104:712.
9. **Donahue, H.C.:** Ophthalmologic experience in a tuberculous sanatorium. Am J. Ophthalmol 1967; 64: 472-478.
10. **Ayanru, J. O.:** The problem of uveitis in Bendel State of Nigeria: experience in Benin City. BJO 1977; 16:655-659.
11. **Woods, A. C.:** Ocular tuberculosis. In: Sorsby A, ed.: Modern ophthalmology Philadelphia J.B. Lippincott, 1972; 105-140.
12. **Schlaegel, T.F. Jr; O'conner, G.R.:** Tuberculosis and syphilis. Arch ophthalmol Clin 1981; 17:87-108.
13. **Henderly, D. E.; Genstler, A. J.; Smith, R.E.; Rao, N.A.:** Changing patterns of uveitis. Am J Ophthalmol 1987; 103: 131-136.
14. **Eye, J.N.H.:** Tuberculosis of the conjunctiva. Lancet 1912; 1: 1319.
15. **Thygeson, P.:** Observation on nontuberculous phlyctenular keratoconjunctivis. Trans Am Acad Ophthalmol Otolaryngol 1954; 58: 128-132.
16. **Shafer, R.W.; Kim, D. S.; Weiss, J.P.; Quale, J.M.:** Extrapulmonary tuberculosis in patients with human immunodeficiency virus infection. Medicine 1991; 70:384-309
17. **Small, P.M.; Schecter, G. f.; Goodman, P.C. et al:** Treatment of tuberculosis in patients with advanced human immunodeficiency virus infection N. Eng J Med 1991; 324: 289-294.
18. **Davies, P. D. O.; Girling, D.J.; Grange, J. M.:** Tuberculosis and its problems in developing countries. In: Weatherall, D.J.; ledingham, J.G.G. Warrell, D. A. eds. Oxford Textbook of Medicine. New York, Oxford University Press 1996: 638-665.
19. **Cotton, R.E.:** Lecture notes on pathology. 4th ed. London: Blackwell scientific publications, 1992: 374-376.
20. **Khalil, M.; Lindley, S.; Matouk, E.:** Tuberculosis of the orbit. Ophthalmology 1985; 92: 1624-1927.

21. **Sheridan, P. H.; Edman, J.B.; Starr, S.E.:** Tuberculosis presenting as an orbital mass. *Pediatrics* 1981; 67: 874-875.
22. **Spoor, T.C.; Harding, S.A.:** Orbital tuberculosis. *Am J Ophthalmol* 1981; 19: 644-647.
23. **Sen, D.K.:** Endogenous uveitis in Indian children: analysis of 94 cases. *J Pediatr Ophthalmol* 1977; 14: 25-32.
24. **Laatikainen, L.; erkkila, H.:** Serpiginous choroiditis. *Br J Ophthalmol* 1974; 58: 777-783.
25. **Moorthy, R.S.; Jampol, L. M.:** Posterior uveitis of unknown cause. In: Yanoff, M.; Duker, J. S.; Augsburger, J.J. et al, eds. *Ophthalmology*. London: Mosby Int Ltd.; 1999: chap. 16.
26. **Barondes, M.J.; Sponsel, W. E.; Steves, T. S.; Plotnik, R. D.:** Tuberculous Choroiditis diagnosed by Chorioretinal endobiopsy (letter0. *Am j Ophthalmol* 1991; 112: 460-1
27. **Ni, C.; J.J.; Robinson, N. L. et al:** Uveal tuberculosis. *Int Ophthalmol Clin* 1982; 22(3): 103-124
28. **Goldbery, M.F.:** Presumed tuberculous maculopathy. *Retina* 1982; 2:47-50
29. **Elliot, A.:** Recurrent intraocular haemorrhage in young adults (Eale's disease): a report of thirty-one cases. *Trans Am Ophthalmol SOC* 1954; 52:811.
30. **McMoli, T. E.; Mordi, V. P. Grange, Abiose, A.:** Tuberculous Panophthalmitis: *J Pediatr Ophthalmol Stabismus* 1978; 15(6): 383-385.
31. **Duke-Elder, S.; Perkins, E.S.:** System of Ophthalmology: diseases of the retina, vol. 10, St. Louis Mostby 1967.
32. **Rosenbaum, J.T.; Wernick, R.:** The utility of routine screening of patients with uveitis for systemic lupus erythematosus or tuberculosis: a baycuian analysis. *Arch Ophthalmol* 1990; 108: 1291-1293.
33. **Abrams, J.; Schlaegel, A.B; Schlaegel, T.F. Jr.:** The role of the Isoniazid therapeutic test in tuberculous uveitis. *Am J Ophthalmol* 1982; 511-515.
34. **Schaegel, T. F. Jr.; O'connor, G. R.:** Tuberculosis and syphilis. *Arch Ophthalmol* 1981; 99: 2206-2207.