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Case Series of Ocular Tuberculosis; The Great Masquerader

Abstract— Tuberculosis, an ancient disease, still thrives today as the leading infection caused by *Mycobacterium tuberculosis*. Diagnosis of ocular tuberculosis poses a great challenge due to the varied clinical presentations. We report 3 cases of primary ocular tuberculosis with varied presentations: conjunctival abscess, sclera-uveitis and occlusive vasculitis. There were no symptoms suggestive of pulmonary tuberculosis in all cases. All patients presented with acute, unilateral painful red eye. The first case had good visual acuity (VA) OD (6/9) with a swollen upper lid, localized perilimbal-hemorrhagic conjunctival swelling superiorly, keratic precipitates and mild anterior chamber reaction. The posterior segment was normal. The second case had a VA of 6/60 OD. There was presence of conjunctival injection, keratic precipitates, posterior synechiae and anterior chamber reaction of 1+. A few days later, there was a progression to vitritis OU and hyperemic optic disc OD with choroidal folds, cystoid macula edema and a positive T sign on B scan ultrasonography. The third case had VA of 6/6 OU, AC reaction of 2+ OD. There was multiple peripheral choroiditis with peripheral vasculitis seen in the posterior segment OU. Fundus fluorescein angiography (FFA) showed peripheral periphlebitis in all 4 quadrants OU. All 3 cases had positive Tuberculin Skin Test (Mantoux test) results which were more than 20mm. Anti-tuberculous treatment was promptly started and all patients showed significant clinical improvement. This case series highlights the diverse clinical presentations of ocular tuberculosis. A high clinical index of suspicion led to prompt initiation of anti-tuberculous therapy which resulted in good clinical outcomes for all cases.

***Keywords*— Conjunctival abscess, infection, occlusive vasculitis, ocular, sclera-uveitis, tuberculosis.**

1 INTRODUCTION

Tuberculosis (TB) is an ancient disease which still thrives today as the leading infectious disease-related mortality worldwide [1]. *Mycobacterium tuberculosis*, an acid-fast, tubercle bacillus is the causative agent. About 85% of patients with TB present with pulmonary complaints whereby the lungs are the most common site for the development of TB. Extrapulmonary TB can occur as part of a primary or late, generalized infection [1].

The term "Primary ocular TB" refers to an infection by *Mycobacterium tuberculosis* that can affect any part of the eye (intraocular, superficial or surrounding the eye), with or without systemic involvement. "Secondary ocular TB" is defined as ocular involvement as a result of seeding by hematogenous spread from a distant site or direct invasion by contiguous spread from adjacent structures, like the sinuses [2].

Ocular tuberculosis can affect both the anterior and posterior segments of the eye and also the ocular adnexa. Chansangpetch *et al*. reported an unusual progression of tuberculous iridocyclitis which mimicked phacolytic glaucoma to nodular scleritis without evidence of extraocular tuberculous infection [3]. Diagnosis of ocular tuberculosis is indeed a great challenge in the ophthalmology field with such diversified clinical presentations.

2 METHOD

This was a retrospective case series of three cases of primary ocular tuberculosis with different clinical presentations in Hospital Tengku Ampuan Rahimah, Klang, Selangor, Malaysia in the year 2017. Patients' case notes were reviewed for demographic details (age and gender), anterior segment and fundus photographs, blood

investigations, and ocular examination were analyzed. All patients had a Tuberculin Skin Test (Mantoux test) performed.

3 RESULTS

All three cases ranging from 14-year-old to 51-year-old presented with no signs, symptoms or radiological evidence of pulmonary tuberculosis. They all presented with unilateral acute painful red eye. All had positive Mantoux test results (ranging from 20mm to 33mm).

3.1 Case 1

A 29-year-old female with no previous co-morbid, complete immunisation, no history of tuberculosis exposure nor any high risk behaviour, presented with injected, painful right eye associated with photophobia for a week. Her visual acuity was 6/9 OD and 6/6 OS. The right upper lid was swollen with two small vesicular-like skin lesions and there was a localized hemorrhagic and tender conjunctival swelling measuring 5mm x 4mm at 10 o'clock adjacent to the limbus (Figure 1). There were fine non-granulomatous keratic precipitates and occasional cells in the anterior chamber with the absence of any corneal lesions, iris nodules, rubeosis iridis or posterior synechiae. Otherwise, intraocular pressure and posterior segments OU were normal. She was treated as right upper lid herpes simplex infection with anterior uveitis with the subconjunctival nodule. Oral Acyclovir 400mg 5 times per day was commenced with topical Gutt Dexamethasone ophthalmic suspension 0.1% 4 times a day and Gutt Moxifloxacin 4 hourly over the right eye. The next day, the subconjunctival nodule appeared yellowish beneath the hemorrhagic lesion. The diagnosis was revised to right anterior uveitis with localized scleritis and subconjunctival abscess. Oral Ciprofloxacin 500mg twice a day and oral Ibuprofen 400mg twice a day were added. She was admitted for intensive treatment with intravenous Ciprofloxacin 400mg twice a day with Gutt Moxifloxacin hourly round the clock for an infective conjunctival abscess due to persistent eye pain and ulceration of the nodular lesion (Figure 2). The topical steroid was withheld. Erythrocyte sedimentation rate was raised at 53mm/hr. Mantoux test was performed to rule out ocular tuberculosis. The other blood investigations including infective screening for human immunodeficiency virus (HIV), hepatitis B and C viruses and syphilis infection were negative and chest X-ray was unremarkable.

In view of Mantoux test reading after 72 hours was 33mm, anti-tuberculous treatment was commenced. Three weeks post commencement of Ethambutol, Isoniazid, Rifampin (Rifampicin) and Pyrazinamide (Akurit-4) intensive phase of anti-tuberculous therapy showed resolution of conjunctival abscess with only minimal conjunctival injection at that site (Figure 4).

Figure 1: Anterior segment photograph of the right eye showing localized hemorrhagic area and conjunctival swelling measuring 5mm x 4mm at 10 o'clock next to the limbus during pre-treatment presentation.

Figure 2: A week after treating lesion as an infective cause the conjunctival lesion to be ulcerated.

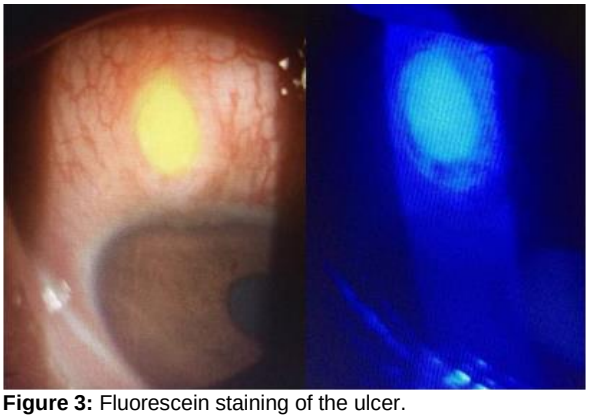

Figure 3: Fluorescein staining of the ulcer.

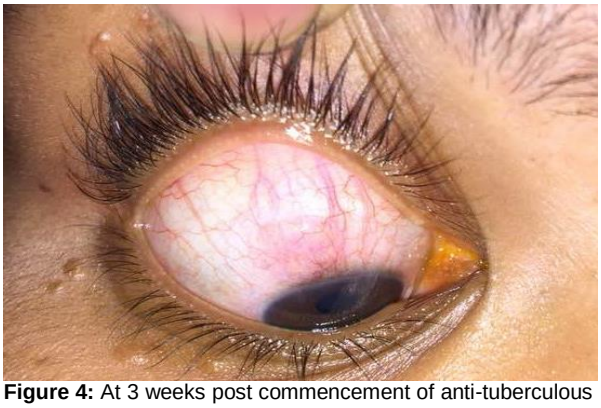

Figure 4: At 3 weeks post commencement of anti-tuberculous therapy.

3.2 Case 2

A 51-year-old female with underlying diabetes mellitus, hypertension, dyslipidemia, history of Bacille Calmette-Guerin (BCG) vaccination but denied exposure to tuberculosis or previous Mantoux test, had acute blurring of vision 6/60 (Pinhole 6/36) OD for 2 days associated with pain, redness and tearing while 6/9 OS. On examination OD there was non-granulomatous keratic precipitates and anterior chamber reaction of 1+, posterior synechiae at 4 o'clock but normal posterior segment findings and normal eye findings OS. The patient was started on topical Gutt Dexamethasone ophthalmic suspension 0.1% 4 hourly, Gutt Levofloxacin four times a day and Gutt Atropine twice a day OD. The working diagnosis then was right anterior uveitis. When reviewed 5 days later, the patient was noted with vitritis with hyperemic optic disc, choroidal folds and cystic macula edema OD. Otherwise, there were no choroiditis, retinitis or vasculitis. OS had fine non-granulomatous keratic precipitates and vitritis. B scan showed T sign for posterior scleritis. Mantoux reading was 25mm but TB quantiferon test was negative. The diagnosis was revised to bilateral sclera-uveitis and oral Ibuprofen 400mg twice a day was added. Despite undergoing treatment for 2 weeks, only the anterior segments OU became quiet but vitritis OU and choroidal folds OD persisted. The diagnosis of presumed ocular TB was made and the patient was treated as TB sclera-uveitis and anti-tuberculous therapy was commenced. Oral Ibuprofen was withheld. Five days later oral prednisolone 1mg/kg/day was started and was tapered accordingly. Fundus Fluorescein Angiography (FFA) showed no evidence of capillary nonperfusion or cystoid macula edema (Figure 5).

Three months' post-commencement of anti-tuberculous medication, her VA improved to 6/9 OU, with normal quiet anterior segments and resolved vitritis, choroidal folds and cystoid macular edema.

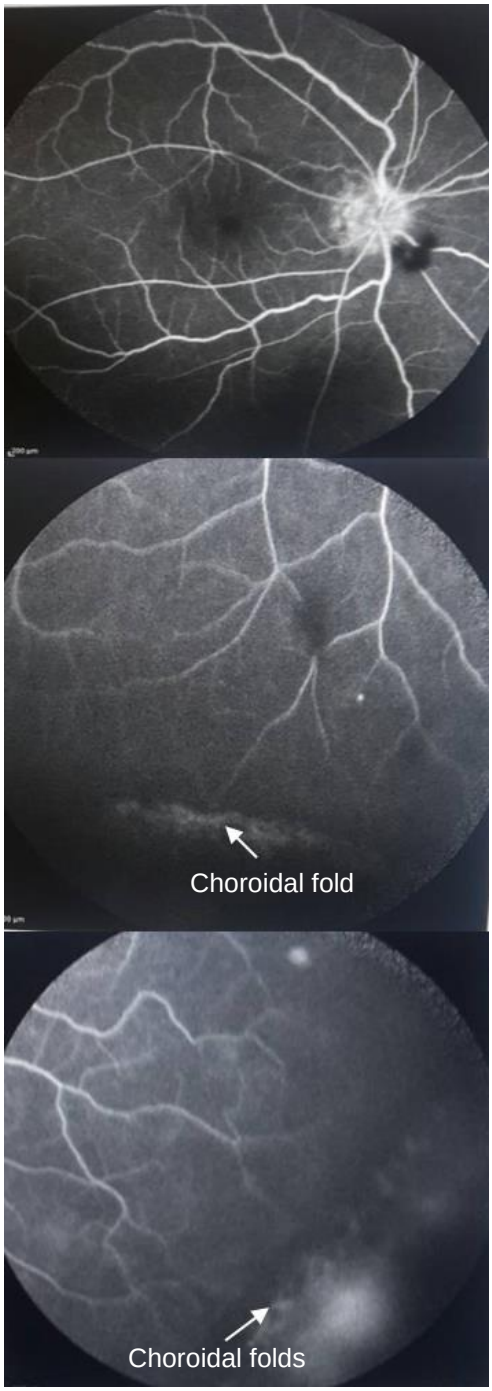

Figure 5: Fundus fluorescein angiography of the right eye with the presence of choroidal folds.

3.3 Case 3

A 14-year-old healthy male, with complete immunization but had a history of frequent pulmonary tuberculosis exposures by visiting his family member who had passed away due to pulmonary tuberculosis 4 years prior, presented with right eye pain and redness for a week. VA OU was 6/6. On examination, there was nasal injection and AC reaction of 2+ OD, with normal anterior segment findings OS. The posterior segment showed multiple peripheral choroiditis with peripheral vasculitis in all four quadrants OU. FFA revealed hot disc, phlebitis in all 4 quadrants, area of capillary non perfusion with new vessels superior nasally but absence of cystoid macular edema OD; and there was phlebitis in all 4 quadrants, absence of area of capillary nonperfusion and cystoid macular edema OS. He was started on Gutt Dexamethasone ophthalmic suspension 0.1% 4 times a day, Gutt Ciprofloxacin 4 times a day and also Gutt Homatropine 2% 3 times a day OD. His Mantoux reading was 20mm and TB Quantiferon was positive for Tuberculosis. Diagnosis of bilateral occlusive vasculitis secondary to ocular tuberculosis was made (Figure 6).

He was started on anti-tuberculous treatment and underwent FFA guided panretinal photocoagulation to treat areas of non-perfusion. After completion of 9 months of anti-tuberculous therapy, both eyes were quiescent.

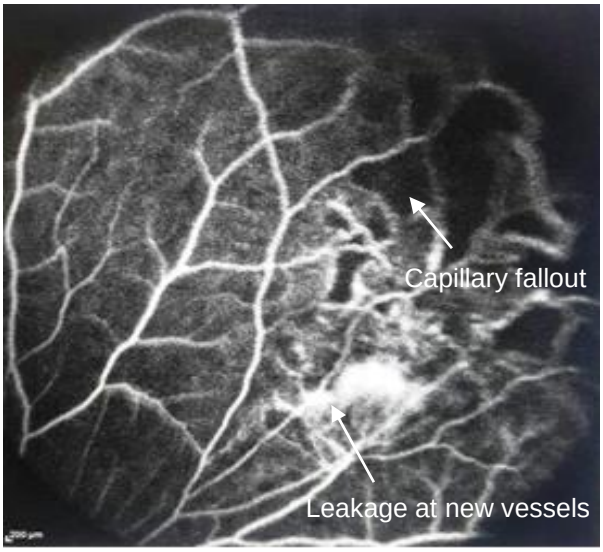

Figure 6: Fundus fluorescein angiography of the right eye showed phlebitis; superior nasal leakage at new vessels and capillary fallout.

4 DISCUSSION

According to the World Health Organization (WHO), there was an estimated 10.4 million people suffering from Tuberculosis in 2016 with mortality as high as 1.3 million among Human Immunodeficiency Virus (HIV)-negative people and an additional 374,000 deaths among HIV-positive people. About 6.3 million incident cases were notified in 2016 and extrapulmonary TB represented 15% of the total [4].

Extrapulmonary TB diagnosis, particularly ocular tuberculosis, is a challenge due to various clinical presentations and no pathognomonic ocular findings. The ocular manifestations of tuberculosis vary from involvement of the lid and adnexa, orbital cellulitis, dacryoadenitis, periocular lymphadenopathy to phlyctenules, conjunctival granuloma, scleritis, and iridocyclitis in the anterior segment. The posterior segment can present in the form of vitritis and optic neuritis. Sometimes ocular TB can be the only manifestation of the serious underlying systemic active tuberculosis [5,6]. Our patients' presentations varied from conjunctival abscess, sclera-uveitis to occlusive vasculitis. Primary conjunctival abscess in ocular tuberculosis is a rare presentation in developed countries. Eyre's review in 1882 of over 30 years on 206 cases of conjunctival tuberculosis had classified these presentations into four types; ulcerative, nodular, hypertrophic granulomatous and pedunculated. His review showed that unilateral, palpebral conjunctiva and upper lid was the most common presentation [7,8]. However as shown in case 1, an unusual unilateral bulbar conjunctival abscess not resolving with antibiotic treatment should still include ocular tuberculosis as a differential diagnosis.

Case 1 and 2 both presented with non-granulomatous keratic precipitates which are non-typical for tuberculous infection. Granulomatous uveitis of tuberculosis usually presents with mutton-fat keratic precipitates and iris nodules (Koeppe and Bussaca). Damodaran *et al.* reported that tuberculous sclera-uveitis may rarely masquerade as an ocular tumor [9].

In case 3, the patient had unilateral anterior uveitis but bilateral multiple peripheral choroiditis with peripheral vasculitis in all four quadrants. Nayak *et al.* reported similar presentation of a patient with unilateral retinal periphlebitis, retinal and pre-retinal hemorrhages and areas of capillary non-perfusion and a serpiginous-like choroiditis in the other eye which underwent remission of anti-tuberculous treatment. They concluded that retinal

vascular involvement especially if occlusive and associated with inflammation is quite suggestive of ocular tuberculosis [10].

To make a definitive diagnosis of ocular tuberculosis, microbiologic evidence should be obtained; for example, via aqueous or vitreous sampling. However, sampling of a viable organism is usually inadequate and may cause another ocular morbidity. Mantoux test (TST; tuberculin skin test) is not specific due to the possibility of false positive results in those previously vaccinated with Bacillus Calmette–Guérin (BCG) or in non-tuberculous mycobacteria infection [11]. However, it is the most feasible.

Polymerase chain reaction technique and interferon-gamma- release assays (IGRAs) tests provide more sensitive and specific results but are costly and may not be easily available in all centers [12]. In endemic countries whereby all newborns receive BCG vaccination, IGRAs are useful in detecting latent tuberculosis infection as the test is not affected by BCG vaccination status.

TB is an important differential diagnosis of ocular infection in the endemic area. Clinical examination and investigation results all are important in leading to diagnosis and to avoid the delay in starting treatment as this could lead to devastating consequences.

5 CONCLUSION

This case series highlights the diverse clinical presentations of ocular tuberculosis in the absence of systemic tuberculosis. A high index of suspicion is required especially in endemic countries with such an alarming infectious rate. A thorough investigation is needed to identify the primary source of infection and followed by prompt anti-tuberculous therapy commencement for good clinical outcome as shown in the three cases above.

CONFLICTS OF INTEREST

The authors report no conflicts of interest in this retrospective case series.

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