

Nur-Najwa S^{1,2}, Zunaina E^{1,2}, Ngoo QZ^{1,2}, Muhammed J^{1,2}

Choroidal Tuberculoma as a Presentation of Possible Intraocular Tuberculosis in a Health Care Worker

¹Department of Ophthalmology and Visual Science, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

²Hospital Universiti Sains Malaysia, Jalan Raja Perempuan Zainab II, 16150 Kubang Kerian, Kelantan, Malaysia

*Corresponding author
Ngoo Qi Zhe
henryzhe@usm.my

Received 17th Febr 2022
Revised 25th April 2022
Accepted 29th March 2023
Published Online 29th May 2023

Abstract – Choroidal tuberculoma is a rare form of extrapulmonary tuberculosis that raises a clinical challenge especially when occurring without other manifestations of the disease. This study reports the case of a 37-year-old community nurse who had history of exposure to tuberculosis patient presented with painful blurring of vision in the right eye for one week. Her fundus examination revealed an elevated choroidal mass over the superotemporal region. The diagnosis of possible choroidal tuberculoma was established by positive tuberculin skin test. Laboratory and imaging workup ruled out pulmonary and systemic tuberculosis as well as other possible etiologies. Antituberculosis therapy was started and led to an improved visual acuity and a shrinkage of the choroidal tuberculoma at 2 months of treatment. This is one of the few reported cases of solitary choroidal tuberculoma in a patient with no other sign of systemic tuberculosis.

Keywords – *Choroidal tuberculoma, health care worker, ocular tuberculosis*

1 INTRODUCTION

Tuberculosis (TB) infection is one of the leading causes of morbidity and mortality globally. TB has been recognized as an occupational hazard for health care workers. Meta-analysis from 16 countries showed that the incidence rate ratio for active TB was 2.94 for health care workers compared with the general population [1]. Similarly, Liew et al [2] reported that health care workers in Malaysia are at higher risk of TB infection as compared to the general population. Despite higher risk of TB infection, the fatality rate of TB among health care workers are notably lower than the general population [2].

There are few factors that contribute to the high incidence for TB among health care workers which include exposure to patient with active TB and working in TB laboratory facilities [2]. Risk of infection depended primarily on the concentration of infectious droplet nuclei in the air and duration of exposure to a person with infectious TB disease.

Study done by Liew et al [2] regarding TB infection among health care workers in Malaysia found that paramedic is the occupation category that has the highest risk for TB (44.3%) compared to doctors (13.8%) and other health care workers. They also found that those working in hospital has

a higher risk than those working in community health clinic.

TB is a multisystem disease caused by *Mycobacterium* species that primarily affects the respiratory systems and can also affect other systems including ocular [3]. Extrapulmonary TB among health care workers range from 19.5% to 25% [2,4]. Choroidal tuberculoma is an ocular form of extrapulmonary TB that raises a clinical challenge, especially when occurring without other manifestations of the disease. We report a case of a healthy 37-year-old health care worker with possible ocular TB. The aim of this case report is to create awareness among health providers especially ophthalmologists regarding variable clinical manifestations of intraocular TB along with diagnostic and treatment challenges in managing the cases.

2 CASE REPORT

A previously healthy 37-year-old community nurse presented with right eye blurry vision for one week. It was associated with floaters, eye pain, eye redness and photophobia. However, there was no eye discharges. There were no constitutional symptoms such as chronic cough, hemoptysis, fever, chills, night sweats, and loss of weight. She works as a community nurse for more than 11

years and had history of exposure to TB patient a few years prior eye presentation. Otherwise, she has no history of living in the same house with family members or friends who had TB or past TB infection. She had Bacillus Calmette-Guerin (BCG) vaccination during childhood.

Upon her first examination, the right eye visual acuity was 6/15 and 6/6 in the left eye. The anterior segment examination of the right eye showed presence of granulomatous keratic precipitates with moderate anterior chamber reaction and moderate flare. There was no iris nodule or broad-based posterior synechiae. Fundus examination of the right eye revealed a solitary elevated yellowish choroidal lesion measuring around one-and-a-half-disc diameter with indefinite border over peripheral superotemporal arcade (Figure 1). The optic disc was normal. There was presence of perivascular sheathing with mild vitritis but no retinitis. The fellow eye examination was normal. The intraocular pressure was normal in both eyes. Optical coherence tomography (OCT) of the right macula was normal with no cystoid macula oedema or any subretinal fluid at the fovea region. The patient was planned for fundus fluorescein angiography (FFA), however the FFA machine was out of order during her presentation and follow-up.



Figure 1. Right fundus showed a choroidal tuberculoma (red arrow) approximately one-and-a-half-disc diameter over peripheral superotemporal arcade

Tuberculin skin test was 15 mm. Erythrocyte sedimentation rate was not raised. Chest radiography was normal with no consolidation of the upper zone or hilar enlargement or evidence of a Ghon complex. There was also no mass seen on chest radiography. Sputum for acid fast bacillus was negative. QuantiFERON-TB was not performed because it was not readily available in our centre. Other infective screening for

toxoplasma, syphilis, herpes simplex virus (HSV), cytomegalovirus (CMV), hepatitis, and human immunodeficiency virus (HIV) were negative. The connective tissue disease screening was also negative.

The patient was referred to medical team to rule out any malignancy. Systemic examination showed no mass identified with no hepatosplenomegaly or lymphadenopathy. Breast and pelvic examinations were normal.

A diagnosis of right eye possible ocular TB was made in view of the patient was at a high risk of contracting TB due to occupational exposure and positive tuberculin test. The patient was co-managed with the infectious disease team. Systemic anti-TB intensive phase comprising of isoniazide, rifampicin, ethambutol and pyrazinamide were given for two months, followed by 10 months of maintenance phase. The patient was started on eyedrops prednisolone acetate 1% four hourly and atropine 1% daily for the right eye. Oral prednisolone 20 mg daily (0.5 mg/kg/day) was started two weeks after initiating anti-TB therapy, then was tapered down 5 mg monthly to be completed for four months.

On subsequent follow-up about eight weeks after initiating treatment, right eye vision had improved from 6/15 to 6/9 with resolution of anterior chamber inflammation. Fundus examination of her right eye showed the choroidal tuberculoma was flatter and the size was reduced to one fourth of optic disc size with a more well-defined margin (Figure 2). The anti-TB therapy was continued for up to total 12 months with regular follow up.

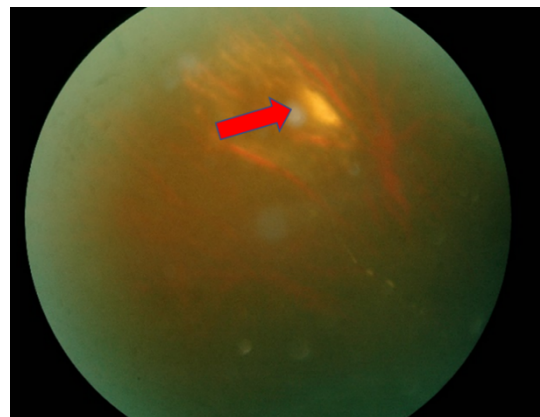


Figure 2. The right fundus showed a flatter choroidal tuberculoma with a more defined margin (red arrow) at eight weeks after initiation of anti-TB therapy

3 DISCUSSION

TB is a global health challenge as it is the second leading infectious cause of mortality worldwide after COVID-19 [5]. The WHO South-East Asia has the highest rate of populations infected with TB [5]. In 2019, an estimated 10 million people worldwide fell sick with TB and a total of 1.2 million people died from TB in 2020 [5]. Health care workers are at a high risk of TB infection. The prevalence of latent TB infection among health care workers in Malaysia was relatively low (10.6%) for an intermediate TB burden country [6].

Rafiza et al [6] in their study showed that the prevalence of latent TB infection was significantly higher among older aged group more than 35 years and employed for 11 years or more. They also found that there was no significant association of latent TB in high-risk group of workers who are exposed to active TB patient regularly with the low-risk group of workers. Beside working place, health care workers that living in the same house with family members or friends who had TB disease is a known risk factor as these individuals share the same air space and are in close contact with each other [6]. Almost half of health care workers infected by TB were paramedics, which consists of assistant medical officers and nurses [2]. Nearly a quarter (25%) of cases were extrapulmonary TB [2]. The finding is consistent with finding from Taiwan, an intermediate TB burden country where 19.5% of TB among health care workers were extrapulmonary [2]. HIV positive and female has been found to increase the risk of extrapulmonary TB among health care workers, though the reason is unclear [2]. In our case report, risk factors that contribute to TB infection mainly were female gender, older age, and occupation as a nurse for more than 11 years. High influx of foreign workers from high TB burden countries [6] is another factor that may contribute to TB infection among health care workers.

Ocular TB is a rare extrapulmonary manifestation of TB which may cause a devastating impact on visual loss in patients diagnosed with the disease. It is still an important cause of uveitis. The most common clinical presentation appears to be posterior uveitis, followed by anterior uveitis, panuveitis, and intermediate uveitis [7].

Multiple choroidal tubercles are the most common intraocular manifestation of tubercular posterior uveitis, which results from hematogenous spread of tubercular bacilli [7]. Choroidal tuberculomas or tuberculous choroidal

granulomas are less common manifestation of intraocular TB. These tuberculomas are solitary elevated yellowish colored mass-like lesions measuring 4 to 14 mm in size, mimicking a tumor. The tuberculoma contains macrophages, epithelioid cells, and multinucleated giant cells and surrounded by T lymphocytes. The tubercle bacilli multiply within a tuberculoma that result in tissue destruction through liquefactive caseous necrosis [7,8]. A tuberculoma as a presenting sign in a patient with no evidence of systemic disease is rare [9,10]. This case has shown a choroidal tuberculoma as a presenting clinical sign in a patient without systemic evidence of TB and a normal chest x-ray finding.

Intraocular TB manifestations can mimic many other ocular inflammatory diseases. Interlandi et al [11] reported a misdiagnosed case of TB tuberculoma with choroidal neovascularization (CNV) at the posterior pole which mimic an exudative age-related macular degeneration (ARMD). Patient's old age along with CNV induced a diagnosis of exudative ARMD. Unresponsiveness to therapy along with positivity of tuberculin skin and interferon-gamma release assay later supported the diagnosis of possible intraocular TB. In another case series review showed varied presentations of ocular TB from conjunctival abscess, sclera-uveitis to occlusive vasculitis [12]. The diagnosis of ocular TB is often challenging due to variable and wide spectrum of presentations and difficulty in obtaining uveal biopsy or intraocular fluids for microbiology examination to provide definitive diagnosis of ocular TB.

Definitive diagnostic of ocular TB is when microbiological confirmation of at least one positive culture from intraocular fluids or confirmation of *Mycobacterium tuberculosis* DNA (MTB DNA) by nucleic acid amplification tests is obtained [13]. The diagnostic methods are expensive, not readily available, and require invasive sample procurement, and difficulty to obtain an adequate sample. Therefore, most cases are diagnosed presumptively and not definitively after excluding other possible etiologies as suggested by Gupta et al [7]. Gupta et al have proposed a newer classification of ocular TB with confirmed, probable, and possible categories for better define intraocular TB for diagnostic purposes [13]. Confirmed intraocular TB is by positive MTB culture from ocular fluids/tissues, whereas probable intraocular TB is diagnosed when there is presence of clinical sign suggestive of intraocular TB with evidence of TB in

chest x-ray or positive TB culture from sputum or extraocular sites and history of exposure to TB or immunological evidence of TB [13]. Possible intraocular TB is diagnosed when there is presence of clinical sign suggestive of intraocular TB with exposure to TB or immunological evidence of TB infection when there is no evidence of TB in chest x-ray or clinical evidence of extraocular TB [13]. In this case report, the patient was diagnosed as possible intraocular TB, based on the presence of choroidal tuberculoma, history of pulmonary TB contact with TB patient and significant tuberculin test measuring over 10 mm.

Imaging technique such as FFA is commonly used, however other modality including OCT scan can be helpful in excluding other diagnoses, especially intraocular tumors. In FFA, expected findings were early hyperfluorescence with a dilated capillary bed, progressive increase in hyperfluorescence, and a pooling of dye during the late phase, corresponding to the surrounding exudative detachment [7]. A less invasive imaging which is OCT may differentiate a choroidal granuloma from other noninflammatory conditions. OCT scan in choroidal tuberculoma shows a distinctive feature of attachment between the retinal pigment epithelial–choriocapillaris layer and the neurosensory retina over the granuloma (“contact” sign) [14]. Unfortunately, in this case the OCT at the choroidal lesion was unable to be performed in view of difficulty in scanning the lesion due to its location at far periphery of the retina.

A purified protein derivative or also named tuberculin skin test has been found to be significant and reliable and cannot be overlooked as a way of diagnosing a possible ocular TB patient [3,15]. A test result of more than 10 mm is reported as positive for those patients living in endemic areas and for employees of high-risk settings (health care workers). Any result of 15 mm is considered a positive result [16]. The newer version of test, QuantiFERON TB GOLD which uses enzyme-linked immunosorbent assay (ELISA) to measure the production of interferon gamma by circulating T cells in whole blood against specific *Mycobacterium tuberculosis* antigens. In contrast, tuberculin skin test measures the hypersensitivity response to purified protein derivative, which contains a mixture of antigens found in *Mycobacterium tuberculosis*, *Mycobacterium bovis* and several other non-tubercular mycobacteria. QuantiFERON TB GOLD is more specific than tuberculin skin test in the diagnosis of TB as it is unaffected by previous

BCG or by non-tubercular mycobacteria [6]. Definitive diagnosis of TB is one our diagnostic challenges as QuantiFERON-TB GOLD is available commercially and not readily available in our centre.

A standard systemic treatment with the first-line combination regimen comprising isoniazid, rifampicin, pyrazinamide, and ethambutol for an initial two-month period followed by a choice of different options over next four to seven months for treatment of TB has been widely accepted [7]. Almost all patients with presumed or confirmed ocular TB who received these treatment regimens between 6 and 15 months demonstrate reduction in intraocular inflammation [7]. However, long term treatment duration, limited knowledge about TB disease, fear of stigma, lack of self-efficacy or motivation to complete treatment are the factors that associate with TB treatment non-adherence and lost to follow up [17].

Failure to recognize TB in the intraocular inflammation may lead to fatal consequences, as the immunosuppressive agents used to manage intraocular inflammation without initiation of anti-TB therapy may lead to sight threatening in patients with active TB. Hence all patient with intraocular inflammation with clinical suspicion of TB should be treated presumptively for TB. As in this case report, a low dose systemic steroid (0.5 mg/kg/day) was initiated two weeks after anti-TB therapy started. The low dose steroid was initiated to reduce the ocular tissue damage caused by the delayed type of sensitivity. However, there was no significant difference found in the outcome between patients treated with anti-TB therapy alone and those with concomitant systemic corticosteroid [18]. Most patients with intraocular TB receiving anti-TB therapy showed low recurrence rates with more than half showed improvement in visual acuity [18].

Anti-TB therapy are frequently associated with ocular toxicity. Among anti-TB therapy, ethambutol is the most commonly implicated drug causing optic neuropathy. Symptoms of optic neuritis typically begin three to six months after the start of ethambutol therapy. Toxic effects are dose related, they occur in 5% to 6% of patients receiving a daily dose of 25 mg/kg and are rare with a daily dose not exceeding 15 mg/kg when taken more than two months [19]. Optic neuritis caused by ethambutol is mostly reversible when the drug is discontinued promptly [19]. Hence it is important to have regular assessments of visual status of the patient and health education should be given to patient regarding visual side effects.

Beside the challenges in terms of long-term side effect of the TB treatment, the emergence of multidrug resistant TB is also the factors that lead to poor treatment respond and this condition contribute as one of the risk factors to TB infection among health care workers [6].

4 CONCLUSION

This case report is one of the rare cases of choroidal tuberculoma being the presenting sign of TB without systemic involvement in a healthy individual. A high index of suspicion for ocular TB should be maintained in health care worker in intermediate TB burden area presenting with choroidal tuberculoma. Wide spectrum of clinical manifestations of intraocular TB, difficulty to obtain ocular specimen, no definitive diagnosis, poor compliance to treatment, long term side effect of TB drugs, and emergence of multidrug resistant are the diagnostic and treatment challenges.

REFERENCES

- [1] Uden L, Barber E, Ford N, Cooke GS. Risk of tuberculosis infection and disease for health care workers: an updated meta-analysis. *Open Forum Infect Dis*. 2017; 4:ofx137.
- [2] Liew SM, Khoo EM, Ho BK, Lee YK, Mimi O et al. Tuberculosis incidence and factors associated with mortality among health care workers in Malaysia. *Asia Pac J Public Health*. 2019; 31(1): 61-71. doi: 10.1177/1010539518817980.
- [3] Testi I, Agrawal R, Mehta S, Basu S, Nguyen Q et al. Ocular tuberculosis: Where are we today? *Indian J Ophthalmol*. 2020; 68(9): 1808. doi:10.4103/ijo.IJO_1451_20.
- [4] Pan SC, Chen YC, Wang JY, et al. Tuberculosis in healthcare workers: a matched cohort study in Taiwan. *PLoS One*. 2015; 10: e0145047.
- [5] Glaziou P, Sismanidis C, Floyd K, Raviglione M. Global epidemiology of tuberculosis. *Cold Spring Harb Perspect Med*. 2014; 5(2): a017798. doi: 10.1101/cshperspect.a017798.
- [6] Rafiza S, Rampal KG, Tahir A. Prevalence and risk factors of latent tuberculosis infection among health care workers in Malaysia. *BMC Infect Dis*. 2011; 11: 19. doi: 10.1186/1471-2334-11-19.
- [7] Gupta V, Gupta A, Rao NA. Intraocular tuberculosis--an update. *Surv Ophthalmol*. 2007; 52(6): 561-87. doi: 10.1016/j.survophthal.2007.08.015.
- [8] Gurung HM, Gurung K, Gurung A, Maharjan I, Shrestha E et al. Choroidal tuberculoma in a healthy immunocompetent patient. *Nep J Oph*. 2021; 13(2): 202-206. doi.org/10.3126/nepjoph.v13i2.34049.
- [9] Arej N, Fadlallah A, Chelala E. Choroidal tuberculoma as a presenting sign of tuberculosis. *Int Med Case Rep J*. 2016; 9: 365-368. doi:10.2147/IMCRJ.S119703
- [10] Ying JEJ, Tang CS, Hanapi MS, Ngoo QZ, Hitam WHW. Unilateral choroidal tuberculoma as an initial manifestation of presumed ocular tuberculosis: a case report. *Rev Bras Oftalmol*. 2021; 80(4): e0017.
- [11] Interlandi E, Pellegrini F, Pavesio C, De Luca M, De Marco R et al. Intraocular tuberculosis: a challenging case mimicking wet age-related macular degeneration. *Case Rep Ophthalmol*. 2021; 12: 519-524. doi: 10.1159/000512578.
- [12] Ui Lyn L, Nadras I, Choo Mee Y, Nadarajah G, Oli Mohamed S. et al. Case series of ocular tuberculosis; the great masquerader. *J of Biomed & Clin Sci*. 2018; 3(2): 1-5.
- [13] Gupta A, Sharma A, Bansal R, Sharma K. Classification of intraocular tuberculosis. *Ocul Immunol Inflamm*. 2015; 23(1): 7-13. doi:10.3109/09273948.2014.967358
- [14] Aksoy FE, Altan C, Basarir B. Multimodal imaging of a choroidal granuloma as a first sign of tuberculosis. *Photodiagnosis Photodyn Ther*. 2020; 29:101580. doi: 10.1016/j.pdpdt.2019.101580.
- [15] Elangovan S, Govindarajan S, Mayilvakanam L, Gunasekaran N. Clinical profile and treatment response of patients with ocular inflammation due to presumed ocular tuberculosis: A retrospective study. *Turk J Ophthalmol*. 2019; 49(4): 188-193. doi:10.4274/tjo.galenos.2019.05874
- [16] Wardani HR, Mertaniasih NM, Soedarsono S. Risk factors of latent tuberculosis infection in healthcare workers at hospitals in Jember city Indonesia. *Afr J Infect Dis*. 2020; 15(1): 34-40. doi: 10.21010/ajid.v15i1.4.
- [17] Tola HH, Tol A, Shojaeizadeh D, Garmaroudi G. Tuberculosis treatment non-adherence and lost to follow up among tb patients with or without HIV in developing countries: a systematic review. *Iran J Public Health*. 2015; 44(1): 1-11.
- [18] Kee AR, Gonzalez-Lopez JJ, Al-Hity A, Gupta B, Lee CS et al. Anti-tubercular therapy for intraocular tuberculosis: A systematic review and meta-analysis. *Surv Ophthalmol*. 2016; 61(5): 628-53. doi: 10.1016/j.survophthal.2016.03.001.
- [19] Aggarwal R, Sethi P, Duvesh RK, Sethi HS, Naik M et al. Ocular toxicity of anti-tubercular drugs. *DJO* 2021; 31: 35-38.