

A case of solitary choroidal tuberculoma with highly positive tuberculin skin test and negative interferon gamma release assays

Lin Zhou¹, Bin Hu², Zhu-Ping Xu³

¹Department of Ophthalmology, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu 610072, Sichuan Province, China

²Department of Ophthalmology, Chengdu Tianfu New District People's Hospital, Chengdu 641400, Sichuan Province, China

³Department of Ophthalmology, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China

Correspondence to: Zhu-Ping Xu. Department of Ophthalmology, West China Hospital, Sichuan University, Address 37, Guo Xue Lane, Chengdu 610041, Sichuan Province, China. xuzhuping@scu.edu.cn

Received: 2023-06-30 Accepted: 2023-12-01

DOI:10.18240/ijo.2024.05.23

Citation: Zhou L, Hu B, Xu ZP. A case of solitary choroidal tuberculoma with highly positive tuberculin skin test and negative interferon gamma release assays. *Int J Ophthalmol* 2024;17(5):969-972

Dear Editor,

Tuberculosis (TB) is an infectious disease which has been considered as a global public health emergency problem during the past 25y. The World Health Organization has estimated that approximately one-third of the world's population are infected by TB. However, only 10% of patients with TB is symptomatic. TB can affect multiple organs throughout the body. Eighty percent of those infected are pulmonary TB. Ocular TB can occur with or without lung or other systemic TB. It is a rare extrapulmonary form of the disease and occupied about 3.5%–5% of all of the TB. It should not be disregarded as its potential influence on vision loss. The intraocular and/or extraocular structures could be impacted by ocular TB^[1]. Uvea was the most common affected structure^[2]. Broad posterior synechiae, retinal vasculitis with or without choroiditis/scars, or rechristened tuberculous multifocal serpiginous choroiditis showed could be detected in approximately 90% patients with TB uveitis^[3]. Tuberculin skin test (TST) and immunodiagnostic test [interferon gamma

release assays (IGRA)] have been globally used to help the diagnosis of TB^[3]. It had been reported that IGRA was more sensitive and accurate than TST^[4]. While in our study, we report a 42-year-old male suffered solitary choroidal tuberculoma without systemic TB showing positive TST and false negative IGRA.

Ethical Approval This study was approved by West China Hospital Sichuan University and it followed the tenets of the Declaration of Helsinki. The informed consent was obtained from the subject.

A 42-year-old male was admitted to our Ophthalmic Center with complain of blurred vision in the left eye for two months. The best corrected visual acuity was 20/20 and 6/20 in the right and left eye, respectively. No abnormality was detected in the anterior segment of both eyes. While slit-lamp examination revealed cells (++) in vitreous of the left eye. A triangular-shaped solitary yellowish choroidal nodules (the size was approximately of 1×0.5 disc) was located at the supertemporal of the optic disc and below the temporal vascular arcade in the fundus of in the left eye. Autofluorescence showed hypofluorescence of the mass and surrounded with hyperfluorescence. Fundus fluorescein angiography showed early hypofluorescence with late hyperfluorescence of the mass and leakage (Figure 1). A lobulated, homogeneous, hyporeflective thickening of choroid with size of 1786 μm×554 μm and subretinal fluid involving the macular were detected by optical coherence tomography. "Contact sign" which represented the attachment between retina pigment epithelium-choriocapillaris layer and the neurosensory retina over the granuloma could be detected as well (Figure 2).

A complete medical history (history of present illness, past surgical history, family medical history, social history, allergies, and medications the patient was taking or may have recently stopped taking) was inquired. The patient was in good overall health, with no noteworthy medical history. Systemic investigations including laboratory and imaging modalities were performed. High-resolution computed tomography scan of the chest was performed and produced negative result. Blood and urine routine, immunological

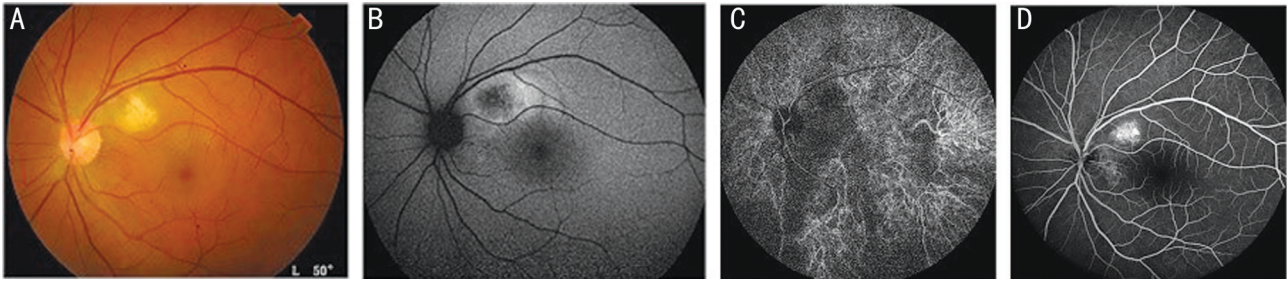


Figure 1 Multimodal imaging (color fundus photograph, corresponding fundus autofluorescence imaging and fundus fluorescein angiography) of the left eye at his first examination A: Color fundus photograph at presentation showed a triangular-shaped solitary yellowish choroidal nodules (the size was approximately of 1×0.5 disc) in the left eye. It was located on the supertemporal of the optic disc and below the temporal vascular arcade. B: Choroidal nodules present as hyperautofluorescent with central hypoautofluorescence was shown on the corresponding fundus autofluorescence imaging. C: The hypofluorescence of the choroidal nodules was observed in the early stage of fundus fluorescein angiography. D: Hyperfluorescence of the mass and leakage was detected in the late stage of fundus fluorescein angiography.

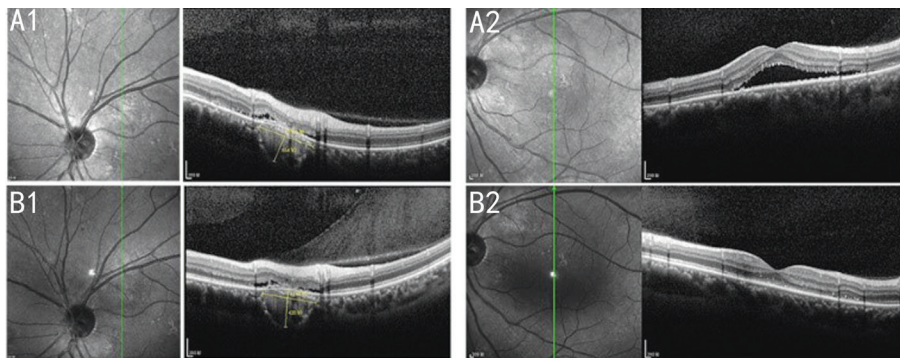


Figure 2 Optical coherence tomography scans of the tuberculoma and macular at his first examination and after treatment for 3mo A1, A2: The mass and subretinal fluid involving the macular at his first examination; B1, B2: The decreased size tuberculoma and completely absorbed subretinal fluid at the macular after treatment for 3mo.

indexes, hepatic and renal function, syphilis serology, TORCH [toxoplasmosis, rubella cytomegalovirus, herpes simplex, and human immunodeficiency virus), tumor-specific growth factor, sarcoidosis screen (angiotensin converting enzyme, normal liver enzyme tests) and TB screen TST and IGRA] were performed to give a definite diagnosis. The TST revealed an induration of 25 mm, while IGRA was negative. He had not been exposed to TB, and had not received the Bacillus Calmette-Guérin (BCG) vaccine previously.

Based on the high-resolution computed tomography scan of the chest and other laboratory evaluation, the presence of lung and other systemic tuberculosis was ruled out by the respiratory physician. A diagnosis of solitary choroidal tuberculoma was established.

The differential diagnosis for choroidal tuberculoma encompassed various potential causes of choroidal nodules, such as choroidal nodule caused by systemic sarcoidosis, metastatic choroidal tumor and nodular posterior scleritis and choroidal hemangioma. Because of the negative results of the high-resolution computed tomography scan of the chest, the normal range of the angiotensin converting enzyme, and the normal results of the liver enzyme tests

(aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, or gamma-glutamyl transferase), the solitary choroidal nodule caused by systemic sarcoidosis was ruled out. Based on a normal high-resolution computed tomography scan and the normal range of the tumor-specific growth factor, no primary or secondary malignancy was found prior to the use of anti-tubercular medication. We could exclude the possibility of choroidal tumor metastases. Early hypofluorescence with late hyperfluorescence of the mass in the fundus fluorescein angiography could exclude the diagnosis of choroidal hemangioma. The middle-aged male patient in the study did not complain of any eye pain and the laboratory tests including blood and urine routine and immunological indexes were normal. We might rule out the diagnosis of nodular posterior scleritis.

Anti-tubercular treatment was recommended by the respiratory specialist. Initial phase of two months of isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by continuation phase of four months of isoniazid and rifampicin were administered. The administration and monitoring of the anti-tubercular treatment were overseen by the respiratory physician. In addition, oral prednisolone was administered, with a starting

dose of 1 mg/kg·d (55 mg/d for our patient). Prednisone was tapered after two weeks and the gradual tapering schedule for corticosteroids was as per earlier guidelines^[5]. After three months of the treatment of anti-tubercular treatment and oral corticosteroids, the best corrected visual acuity of the left eye was improved to 8/20. The subretinal fluid was absorbed completely. Though the size of the tuberculoma had no significant changes based on the fundus examination, a decrease of the tuberculoma size (from 1786 μm×554 μm to 1740 μm×420 μm) revealed on the optical coherence tomography. To sum up, following the anti-tuberculosis treatment, the patient experienced a notable enhancement in vision, accompanied by a considerable reduction and improvement in the choroidal mass.

Our case presented with typical clinical manifestations of choroidal tuberculoma, with highly positive TST, negative IGRA and normal high-resolution computed tomography scan of the chest. High-resolution computed tomography scan of the chest was performed but produced negative result. However, the negative result could not rule out the possibility of ocular TB. It had been reported that approximately two thirds of patients with extrapulmonary TB have no history of pulmonary TB^[3]. In addition, comprehensive ocular examination and systemic investigations had excluded the possibility of choroidal nodule other than choroidal tuberculoma. What's more, the obvious therapeutic effect of anti-tuberculosis treatment indicates the definitive diagnosis of solitary choroidal tuberculoma.

IGRA might be false negative in our case with solitary choroidal tuberculoma. TST and IGRA are the main approaches for the diagnosis of TB infection. As TST might be interrupted by the BCG vaccination and non-tuberculous mycobacterial infections, IGRA was reported to be more accurate and specific than TST^[4]. While a recently published Meta-analysis in 2019 showed that IGRA was not superior to TST and the specificity of IGRA was lower than TST with induration larger than 25 mm^[6]. Additionally, Nguyen *et al*^[7] reported that 12.3% TB infected patients could be IGRA negative among the 3825 patients with TB. Older age, non-Hispanic white race, human immunodeficiency virus co-infection, and longer time to TB treatment were significantly associated with false-negative IGRA results. To summarize, TST was still an irreplaceable, cheap and sensitive method for the diagnosis of TB.

Collaborative Ocular TB Study Consensus Group set up an international, expert led consensus initiative for the treatment of ocular TB. The initiation of anti-tubercular treatment was recommended for the patients with ocular TB, even only one positive immunologic evidence, a positive TST or IGRA. The positive radiologic investigation is not required for the usage of the drugs. The indication of corticosteroid for the ocular

TB remains controversial. Corticosteroids were effective for the control of ocular inflammation, 93% reduction in the odds of visual impairment could be detected in patients with uveitis. However, no significant difference could be observed in ocular outcome of these affected individuals receiving anti-tuberculosis therapy and corticosteroids cooperated with anti-tuberculosis therapy in a Meta-analysis involving 1917 patients with ocular TB^[8]. The choroidal tuberculoma with no active systemic infection in our case was recommended starting at a dose of 1 mg/kg·d (55 mg/d for our patient) and produce good response.

In our case, no other systemic TB except choroidal tuberculoma were detected. It was a rare event that a total of nine cases of choroidal tuberculoma without systemic evidence of TB had been reported to our knowledge^[9-14]. The details of two cases reported in 2013 could not be summarized as the unavailability of the full article. For the remaining cases, the male-to-female ratio is 5:2, the mean age is 35.14±9.08 (24–42) years old. Decreased vision was the most common main complaint and two patients suffered with floaters. The vision varies from hand moving to 20/50. Choroidal mass (0.3 to 4 disc in diameter) with retinal detachment could be detected in all these patients. TST is positive in seven cases of report solitary choroidal tuberculoma including our patient. In one case, the diagnosis was confirmed after histopathological examination of the enucleated eye. In another case, DNA amplification by polymerase chain reaction on aqueous humor sample confirmed the diagnosis of TB.

In conclusion, solitary choroidal tuberculoma with false negative IGRA results and positive TST is observed in our case. A comprehensive medical history, physical examination, and analysis of the complete examinations are necessary for the doctor to get a definitive diagnosis. Nevertheless, laboratory tests are not flawless, and false-positive or false-negative results might happen at any time. When using the laboratory tests, we ought to exercise caution and judgment. This can help mitigate potential harm from spurious results.

ACKNOWLEDGEMENTS

Foundation: Supported by Natural Science Foundation of Sichuan Province (No.2022NSFSC1370).

Conflicts of Interest: Zhou L, None; Hu B, None; Xu ZP, None.

REFERENCES

- 1 Gupta V, Testi I, Agrawal R, Mehta S, Basu S, Nguyen Q, Pavesio C. Ocular tuberculosis: where are we today? *Indian J Ophthalmol* 2020;68(9):1808.
- 2 Abdismadov A, Tursunov O. Ocular tuberculosis epidemiology, clinic features and diagnosis: a brief review. *Tuberculosis* 2020;124:101963.
- 3 Tungsattayathitthan U, Boonsopon S, Tesavibul N, Dharakul T, Choopong P. Interferon-gamma release assays in tuberculous uveitis: a comprehensive review. *Int J Ophthalmol* 2022;15(9):1520-1528.

- 4 Nasiri MJ, Pormohammad A, Goudarzi H, Mardani M, Zamani S, Migliori GB, Sotgiu G. Latent tuberculosis infection in transplant candidates: a systematic review and meta-analysis on TST and IGRA. *Infection* 2019;47(3):353-361.
- 5 Jabs DA. Immunosuppression for the uveitides. *Ophthalmology* 2018;125(2):193-202.
- 6 Auguste P, Madan J, Tsertsvadze A, Court R, McCarthy N, Sutcliffe P, Taylor-Phillips S, Pink J, Clarke A. Identifying latent tuberculosis in high-risk populations: systematic review and meta-analysis of test accuracy. *Int J Tuberc Lung Dis* 2019;23(11):1178-1190.
- 7 Nguyen DT, Teeter LD, Graves J, Graviss EA. Characteristics associated with negative interferon- γ release assay results in culture-confirmed tuberculosis patients, texas, USA, 2013–2015. *Emerg Infect Dis* 2018;24(3):534-540.
- 8 Kee AR, Gonzalez-Lopez JJ, Al-Hity A, *et al*. Anti-tubercular therapy for intraocular tuberculosis: a systematic review and meta-analysis. *Surv Ophthalmol* 2016;61(5):628-653.
- 9 Arej N, Fadlallah A, Chelala E. Choroidal tuberculoma as a presenting sign of tuberculosis. *Int Med Case Rep J* 2016;9:365-368.
- 10 Berinstein DM, Gentile RC, McCormick SA, Walsh JB. Primary choroidal tuberculoma. *Arch Ophthalmol* 1997;115(3):430-431.
- 11 Levecq LJ, De Potter P. Solitary choroidal tuberculoma in an immunocompetent patient. *Arch Ophthalmol* 2005;123(6):864-866.
- 12 Sarvananthan N, Wiselka M, Bibby K. Intraocular tuberculosis without detectable systemic infection. *Arch Ophthalmol* 1998;116(10):1386-1388.
- 13 Alaraj AM, Al-Dhibi H, Al-Mezaine HS, Abu El-Asrar AM. Solitary presumed choroidal tuberculomas masquerading as choroidal tumors. *Saudi Med J* 2013;34(1):86-90.
- 14 Mansour AM, Haymond R. Choroidal tuberculomas without evidence of extraocular tuberculosis. *Graefes Arch Clin Exp Ophthalmol* 1990;228(4):382-383.