Quantitative polymerase chain reaction analysis of serpiginous choroiditis with biopsy-proven testicular tuberculosis

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We report a case of a 47-year-old male patient presenting with diminution of vision in the left eye. The left eye fundus showed yellowish lesions with indistinct geographical margin extending over the posterior pole just abutting the macula, suggestive of diffuse choroiditis. The patient gave a history of testicular swelling for the past 2 years. Aqueous tap for polymerase chain reaction analysis was positive for IS6110 mycobacterial tuberculosis (TB) genome, and a biopsy of testicular sac was suggestive of tubercular epididymitis. A diagnosis of TB-multifocal serpiginoid choroiditis was established and was managed with anti-tubercular therapy and systemic steroids.

Key words: Multifocal serpiginoid choroiditis, polymerase chain reaction, testicular tuberculosis

Serpiginous choroiditis (SC) is characterized by a geographic pattern of inflammation involving the peripapillary area and overlying retinal pigment epithelium (RPE), causing irreversible damage to the photoreceptors.[1] It can present either as classic SC or serpiginous-like choroiditis (SLC) and the recent terminology described for it is multifocal serpiginoid choroiditis (MSC). Identification of the spectrum of tuberculosis (TB)-SLC is of great concern as it is more common in TB-endemic areas, with a unilateral presentation.[2,3] TB association with SC was described by Hutchinson and later by others.[4-6] The TB-associated disease was re-labeled as MSC in a large series of 105 patients.[5]

Genitourinary TB (GUTB) occurring in the kidney, ureter, testis, and epididymis can spread through blood-borne infection and accounts for <0.5% of all patients with extrapulmonary TB and 1.5% of all patients with pulmonary TB.[3] The association of GUTB with SC is barely reported.[3] We herein report a case of MSC proven with real-time polymerase chain reaction (PCR) and biopsy of testicular tissue in an immunocompetent patient suggestive of tubercular etiology.

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Case Report

A 47-year-old, Asian Indian male presented with blurring of vision in the left eye for the past 4 months. The best-corrected visual activity was 6/6, N6 in the right eye and 6/12, N10 in the left eye. The right eye findings were unremarkable. The left eye had nil aqueous and vitreous cells with normal optic disc and retinal vascular. However, there were yellowish areas of diffuse choroiditis with indistinct geographical margin, extending over the posterior pole just abutting the macula and extending along the superior arcade up to the equatorial retina, suggestive of SC [Fig. 1]. The fundus fluorescein angiography showed hypofluorescent patches with irregular, poorly defined borders during the early phase with a prominent hyperfluorescence at mid-phase, followed by prominent leakage at in the late phase [Fig. 2]. Fundus autofluorescence showed hyperfluorescence at the margins of the lesions, suggestive of active lesions. The optical coherence tomography showed normal foveal contour in both eyes. A clinical diagnosis of SC was established, and to identify any associated etiology, the PCR analysis of aqueous fluid was performed and sent for real-time and nested PCR analysis for the detection of MPB64 and IS6110 mycobacterial TB (MTB) genome. The PCR result was positive for IS6110 MTB genome by nested primers, and the real-time/quantitative PCR detected 363,345 DNA copies of MTB using Artus Qiagen Kit (Hilden, Germany) [Fig. 3].

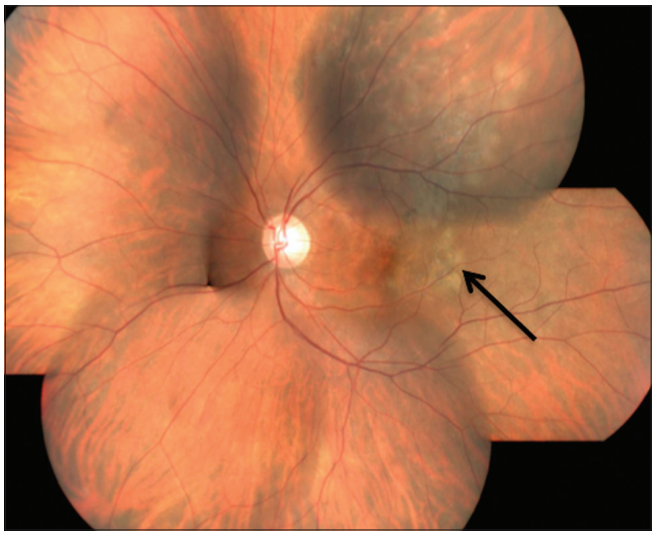

Figure 1: Montage fundus photograph of the left eye showing yellow diffuse lesion suggestive of active choroiditis (black arrow)

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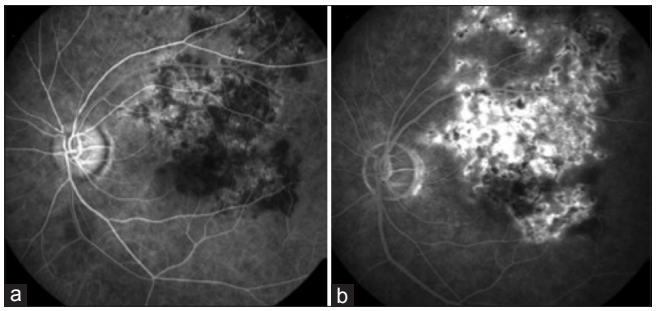


Figure 2: (a) The early hypofluorescent patches with irregular, poorly defined borders, (b) late phase with prominent leakage through the lesion

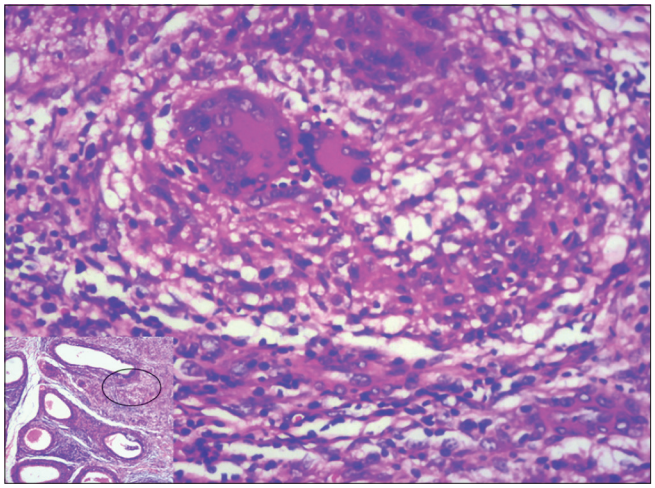


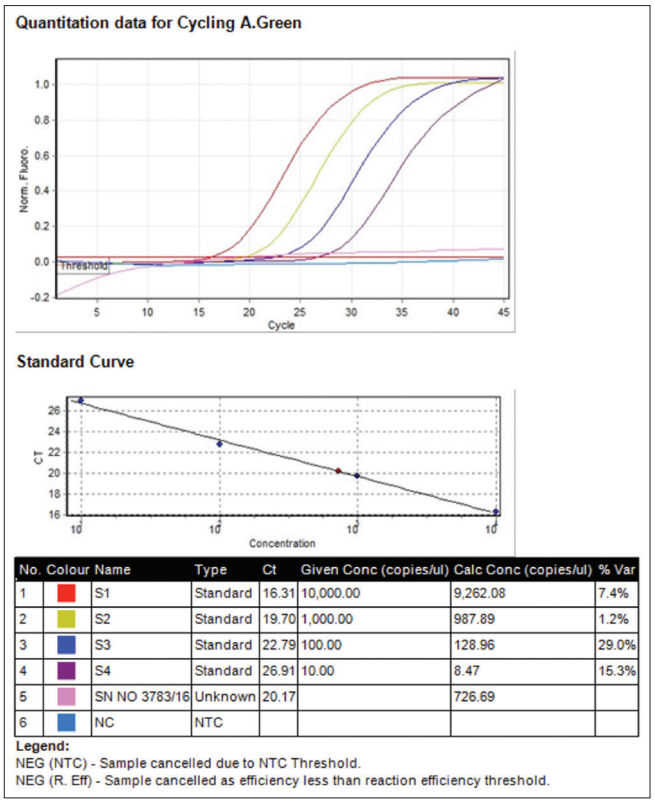
Figure 4: Histopathology slide of the testicular sac showing a granuloma with multiple giant cells surrounded by lymphocytes, plasma cells, and epithelioid cells with surrounding areas of caseation (H and E, ×200)

On systemic evaluation, the patient had normal chest radiogram but had a history of testicular swelling for the last 2 years. A biopsy tissue from the testicular sac was obtained which showed a granuloma with multiple giant cells surrounded by lymphocytes, plasma cells, and epithelioid cells with surrounding areas of caseation, suggestive of tubercular epididymitis [Fig. 4]. The patient had undertaken anti-tubercular treatment with rifampicin and isoniazid (300 mg), pyridoxine, prednisolone (20 mg), and losartan 50 mg for 4 months and stopped on his own a year back.

Based on the PCR findings of aqueous aspirate and biopsy of the testicular sac, the diagnosis of TB-MSC was established, and under the guidance of a physician, the patient was restarted on anti-tubercular therApy(ATT) for 9 months along with azathioprine 50 mg three times for with tablet prednisolone 40 mg in a tapering dose, and there was resolution of the size of retinal lesion in 2-month follow-up.

Discussion

Ocular TB incidence ranges from 1.4% to 5.74% and affects the choroid as an extrapulmonary spread by hematogenous spread from a primary complex or as a latent infection.[1,2] PCR for MTB has been established with a specific role in the detection of ocular fluid.[3] Recent surge in the prevalence of TB with extrapulmonary involvement more so in the developing countries accounts for 20% of GUTB.[3,6] Gupta *et al*.[7] reported



No.	Colour	Name	Type	Ct	Given Conc (copies/ul)	Calc Conc (copies/ul)	% Var
1		S1	Standard	16.31	10,000.00	9,262.08	7.4%
2		S2	Standard	19.70	1,000.00	987.89	1.2%
3		S3	Standard	22.79	100.00	128.96	29.0%
4		S4	Standard	26.91	10.00	8.47	15.3%
5		SN NO 3783/16	Unknown	20.17		726.69	
6		NC	NTC				

Legend:
NEG (NTC) - Sample cancelled due to NTC Threshold.
NEG (R. Eff) - Sample cancelled as efficiency less than reaction efficiency threshold.

Figure 3: Real-time polymerase chain reaction using Artus Qiagen Kit (Hilden, Germany) detected 363,345 deoxyribonucleic acid copies of mycobacterial tuberculosis

a case of "positive PCR for MTB from the vitreous and epididymal fluid in a patient of choroidal tuberculoma and epididymitis" and concluded that PCR-based assay for MTB as a specific modality and prompt response to anti-TB therapy substantiates the diagnosis of tuberculoma of the eye.[7] Mohan *et al*. reported a case of cytomegalovirus and MTB PCR-positive case of MSC with radiological evidence of cerebral TB.[8]

The pathogenesis of TB-associated MSC remains unclear, and our case may represent a reactivation of dormant foci of mycobacteria in RPE cells. Khanamiri and Rao had mentioned that TB-related MSC has a prominent inflammatory cellular reaction in the vitreous, usually with a cellular reaction in the anterior chamber. However, our experience was unique as the presentation was the absence of aqueous and vitreous cellular reaction and the decrease of vision was attributed to macular involvement.[1] We believe that in a TB-endemic country like ours, the possibility of association of SC with TB should be looked for and the chances of extrapulmonary manifestations even from the GU should be ruled out. This report highlighted the evidence-based case of real-time PCR and biopsy-proven testicular TB and managed with antitubercular therapy and the immunosuppressive steroid therapy regimen on the tapering dose for early resolution.

Conclusion

In TB-endemic countries, TB as the possible etiology for SC can be ruled out with the aqueous tap for MTB genomes on PCR as it serves as a sensitive diagnostic modality and helps for early treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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