Infectious chorioretinitis in an immunocompetent patient: A diagnostic dilemma

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A 44-year-old male presented with a history of defective vision in the right eye for the past 5 months with the previous history of tubercular cervical lymphadenitis. On examination, right eye revealed panuveitis with dense vitritis and chorioretinitis in the superotemporal quadrant. His Mantoux test was positive (25 mm × 25 mm induration), QuantiFERON-TB Gold was test positive, aqueous aspirate was positive for *Mycobacterium tuberculosis* genome, negative for viruses and toxoplasma, and hence he was initiated on four-drug antitubercular therapy (ATT) with oral steroids. On follow-up, he had worsening of vitritis and intravenous methylprednisolone was given suspecting paradoxical reaction to ATT; however, a repeat AC tap was positive for toxoplasma B1 genome, IgG antitoxoplasma antibody was also positive in serum and aqueous; hence, we switched to systemic antitoxoplasma therapy. He underwent a therapeutic vitrectomy along with intravitreal clindamycin and dexamethasone for persistent vitreous membranes and vitritis. The patient responded well to the treatment with a reduction in vitritis and scarring of the lesion.

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/ijo.IJO_190_17

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Manuscript received: 15.03.17; Revision accepted: 19.07.17

Key words: Chorioretinitis, Goldmann-Witmer coefficient, polymerase chain reaction, toxoplasmosis

Ocular toxoplasmosis usually presents as a focal necrotizing retinochoroiditis with adjacent scar associated with significant inflammation in typical cases and diagnosed mainly on clinical grounds in typical cases.[1] In areas that are highly endemic for both tuberculosis (TB) and toxoplasmosis, patients may present immunologic evidence of both latent infections, and in the absence of characteristic features, the differential diagnosis depends on polymerase chain reaction (PCR) of intraocular fluids.[2] Seropositivity for toxoplasmosis is common worldwide and hence IgG positivity is useful in supporting the diagnosis and not confirming it.[3] The various conditions which mimic ocular toxoplasmosis are TB, necrotizing retinitis, *Bartonella*-associated neuroretinitis, intraocular lymphoma, punctate inner choroidopathy, and multiple evanescent white dot syndrome.[4] We present a case of ocular toxoplasmosis which mimicked TB and was diagnosed based on PCR of aqueous humor, intraocular antibody production, and clinical judgment.

Case Report

A 44-year-old male presented with complaints of defective vision in the right eye for the past 5 months, was diagnosed previously as posterior uveitis, and treated with two courses of oral steroids and systemic antiviral for 2 weeks by his local ophthalmologist. He had a history of childhood TB in the form of cervical lymphadenitis and had taken antitubercular therapy (ATT) 25 years back. Previous investigations showed Mantoux positivity with induration of 25 × 25 mm with 5 tuberculin units. High-resolution computed tomography was within normal limits, and QuantiFERON-TB Gold test was positive. His HIV status was negative. His best-corrected visual acuity (BCVA) was 20/40 and 20/20 in the right and left eye, respectively.

Cite this article as: Ganesh SK, Ali BS, Madhavan HN. Infectious chorioretinitis in an immunocompetent patient: A diagnostic dilemma. Indian J Ophthalmol 2017;65:1043-6.

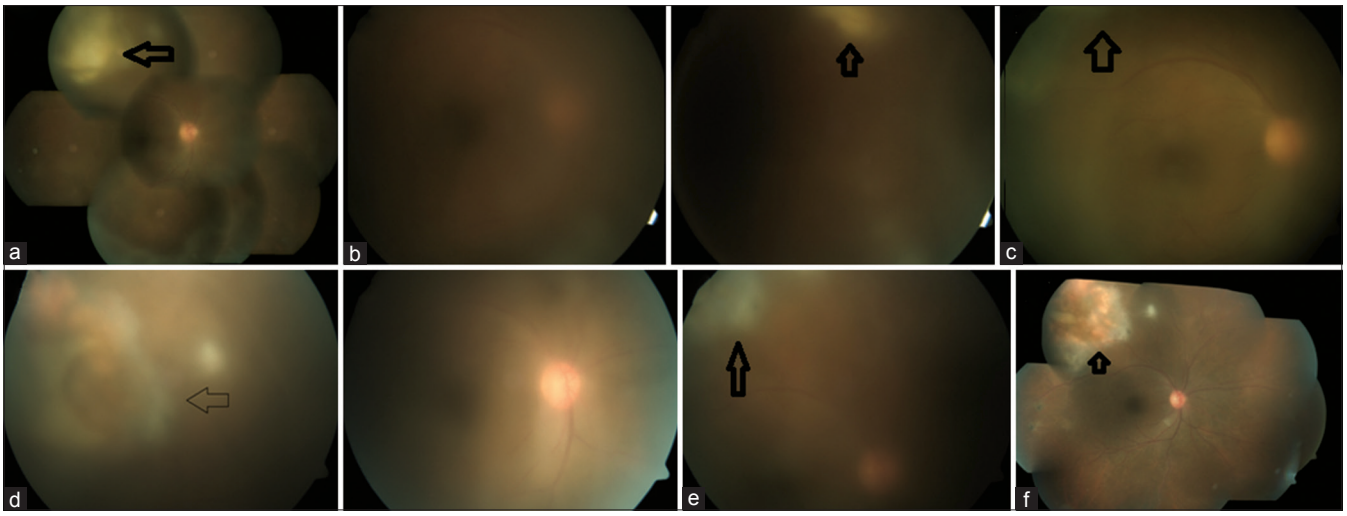

Figure 1: (a) Fundus right eye showing chorioretinitis in the superotemporal arcade along with dense vitritis at initial presentation. (b) At second visit, fundus showing dense vitritis with persistent chorioretinitis after 2 months of antitubercular therapy. (c) After third dose of intravenous methylprednisolone, fundus right eye showing reduction in inflammation. (d) At third visit, fundus showing increase in vitritis along with persistent chorioretinitis with necrosis. (e) After therapeutic vitrectomy and intravitreal clindamycin and dexamethasone, fundus showing clearing of vitritis. (f) fundus of right eye showing complete resolution of lesions with clearing of vitritis

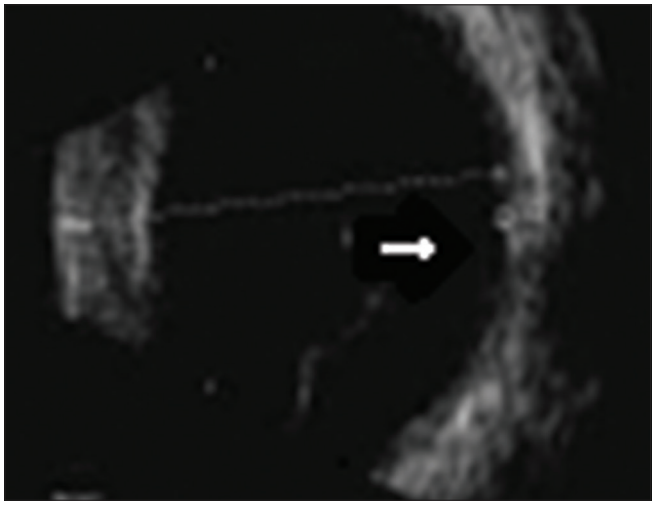

Figure 2: Ultrasonography right eye showing subtle retinochoroidal elevation noted posteriorly in the superotemporal quadrant with moderate surface and internal reflectivity with a peripapillary choroidal thickness of 1.8 mm

Slit lamp examination showed fresh granulomatous keratic precipitates in the right eye with 2 + cells in anterior chamber and anterior vitreous and fundus showed chorioretinitis in the superotemporal quadrant with dense vitritis [Fig. 1a]. B-scan ultrasonography showed subtle retinochoroidal elevation noted posteriorly in the superotemporal quadrant with moderate surface and internal reflectivity with a peripapillary choroidal thickness of 1.8 mm [Fig. 2]. PCR of aqueous aspirate for herpes simplex virus, varicella zoster virus, cytomegalovirus, and toxoplasma was negative; real-time-PCR (RT-PCR) for *Mycobacterium tuberculosis* (MTB) genome (MPB64) was positive and detected five copies/ml of DNA [Fig. 3a]. Serum IgG antitoxoplasma antibody was positive, whereas IgM negative. A presumed diagnosis of ocular TB was made and after obtaining chest physician advise; patient was started on four-drug ATT along with oral steroids.

Two months later, his BCVA was 20/63 and 20/20 in the right and left eye, respectively. Slit lamp examination showed 2+ vitreous cells and fundus showed persistent chorioretinitis with dense vitritis [Fig. 1b]. Paradoxical reaction to ATT was suspected, and the patient was started on intravenous methylprednisolone (IVMP) 1 g for 3 days. AC tap was repeated which showed positivity for toxoplasma B1 genome by nested PCR [Fig. 3b] and IgG for toxoplasma was positive in aqueous. Following IVMP inflammation regressed, lesions on the retina appeared flat [Fig. 1c]. The patient was started on systemic antitoxoplasma therapy and ATT was discontinued.

One month later, his BCVA was 20/63 and 20/20 in the right and left eye, respectively. Fundus examination revealed vitreous membranes persistent chorioretinitis [Fig. 1d]. The patient was continued on systemic antitoxoplasma therapy and steroids. Due to the persistent vitritis and plenty of vitreous membranes and nonresolving lesions, patient underwent therapeutic vitrectomy along with intravitreal clindamycin (1 mg/0.1 ml) and dexamethasone (400 μg) along with the vitreous biopsy. PCR of the biopsied specimen showed negativity for viruses, toxoplasma, and MTB genome. The patient was advised to continue the oral antitoxoplasma therapy. The patient responded well to the treatment and showed clearance of vitritis along with scarring of lesions [Fig. 1e]. One month later, at the last visit lesions resolved, his BCVA was 20/32 and 20/20 in the right and left eye, respectively [Fig. 1f].

Discussion

As classified by Gupta *et al.*, our patient showed positivity for both tuberculin skin test and QTB assay, RT-PCR of aqueous showed positivity for MTB genome, and fundus showed peripheral chorioretinitis with previous evidence of extrapulmonary TB (biopsy-proven cervical lymph node TB), and hence we considered a diagnosis of presumed ocular TB and started the patient on ATT with systemic steroids.[2] The patient, however, did not respond well to the treatment and had worsening vitritis, a paradoxical reaction to ATT was

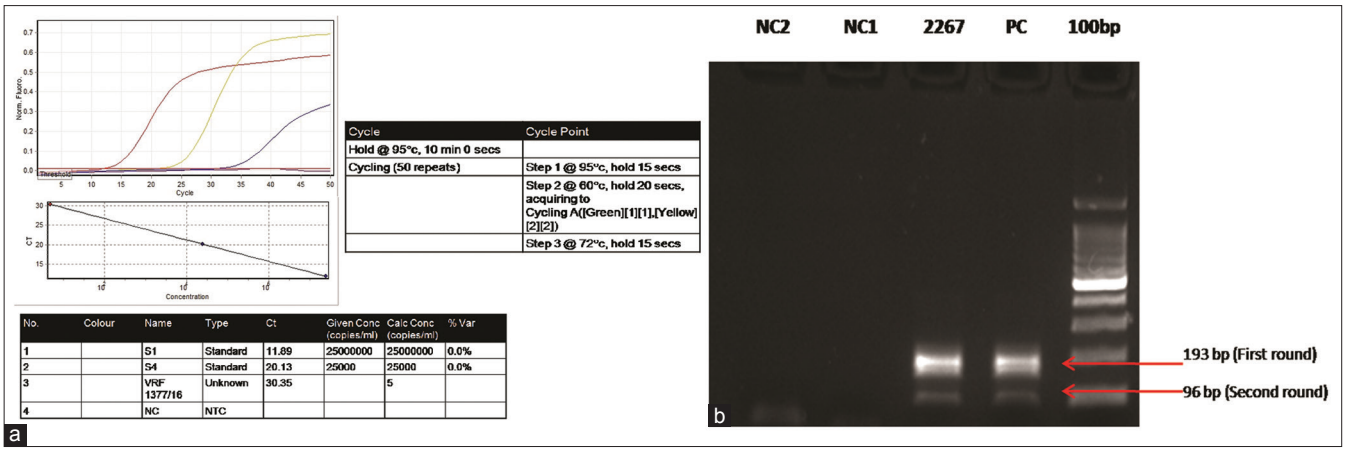

Figure 3: (a) *Mycobacterium tuberculosis* real-time polymerase chain reaction results of patient's sample – Genosens real-time polymerase chain reaction kit – 5 copies of *Mycobacterium tuberculosis* DNA/ml. (b) Agarose gel electrophoretogram of the second round of nested polymerase chain reaction using nested primers targeting the B1 gene of *Toxoplasma gondii* genome: NC2: Negative control II round; NC1: Negative control I round; 2267/16: Aqueous aspirate sample positive for *Toxoplasma gondii*; PC: DNA from tachyzoites of standard RH strain of *Toxoplasma gondii*; 100 bp: Molecular weight marker

suspected, and the patient was given IVMP 1 g for 3 days. After IVMP, lesions persisted while the vitritis appeared to regress. Hence, a repeat AC tap was done which showed nested PCR positivity for toxoplasma B1 genome, IgG anti-toxoplasma antibody positivity in aqueous and serum, and hence systemic antitoxoplasma therapy was added. Although patient responded well to the antitoxoplasma therapy, he had persistent vitreous membranes obscuring vision. Thus, we advised a therapeutic vitrectomy along with intravitreal clindamycin and dexamethasone. However, the vitreous biopsy was negative for toxoplasma, MTB, and viruses. The patient responded very well to the treatment with a reduction in inflammation and lesions scarred. The patient did not require multiple courses of intravitreal clindamycin as systemic antitoxoplasma therapy was continued. Kishore *et al.* published the first evidence of the use of intravitreal clindamycin might be effective, in the form of a case report in 1998 and a retrospective case series including four patients in 2001.[5] Soheilian *et al*. found no statistical difference between intravitreal clindamycin with dexamethasone and triple therapy in a study of 68 patients.[6] Papadopoulo *et al*. demonstrated the efficacy of therapeutic vitrectomy in severe toxoplasmosis retinochoroiditis associated with dense vitritis.[7] De Groot-Mijnes *et al*. showed that with PCR alone, diagnosis was missed in 65% of cases of ocular toxoplasmosis, whereas intraocular antibody production contributes more toward the diagnosis of toxoplasmosis.[8] In a study by Gupta *et al*., sampling and quantitative analysis of MTB DNA by RT-PCR, they correlated the MTB DNA genome with the site of analysis with less numbers of 4.53×10^4 copies in active subretinal mass lesion (vitreous sample) compared to 1.76×10^6 copies in retinal pigment epithelium cells by Vasconcelos-Santos *et al*.[2,9,10] They justify the need to correlate the DNA load with clinical presentation in terms of morphology and severity of tubercular uveitis in a larger set of patients.

We believe that in our case, systemic TB in the form of cervical lymphadenitis, treated 25 years back, created a dilemma in the diagnosis. Repeat PCR of the aqueous after 2 months of ATT showed positivity for both toxoplasma B1 genome as well as intraocular anti toxoplasma antibody production, which contributed more toward the diagnosis of toxoplasmosis. Our patient responded initially well to systemic antitoxoplasma therapy. Due to the presence of persistent vitreous membranes, we attempted therapeutic vitrectomy. We believe, probably the systemic antitoxoplasma therapy, along with intravitreal clindamycin and the therapeutic vitrectomy helped in the resolution of lesions. Our case evoked a diagnostic challenge and demonstrated the importance and limitations of PCR of ocular fluids, especially in areas endemic for TB.

Conclusion

Ocular toxoplasmosis manifesting as infectious chorioretinitis in an immunocompetent patient may simulate TB. PCR of aqueous humor, intraocular antibody production, and clinical judgment may help in the diagnosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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