Toxoplasma retinitis following intravitreal injection of triamcinolone acetonide: A case report and review of literature

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The aim of this study was to report a case of atypical toxoplasma retinochoroiditis following intravitreal triamcinolone acetonide (IVTA) injection and to review the literature pertaining to toxoplasma retinochoroiditis following intravitreal injection of corticosteroid. Clinical data were collected from a 64-year-old male who developed toxoplasma retinitis 2 months after IVTA. A review of the literature was conducted to identify additional reports on similar cases. A 64-year-old male, known diabetic with nonproliferative diabetic retinopathy in both the eyes and optic atrophy in the left eye, presented with atypical retinitis inferior to the disc following IVTA. Real-time polymerase chain reaction and serology confirmed the toxoplasma etiology, and the patient was started on anti-toxoplasma therapy along with oral corticosteroid leading to regression of the lesion by 3 months. A high index of suspicion and proper microbiological diagnosis with appropriate antimicrobial therapy can aid in the management of toxoplasma retinochoroiditis following intravitreal injection of corticosteroid.

Key words: Diabetes, toxoplasmosis, triamcinolone

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/ijo.IJO_142_18

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Manuscript received: 28.01.18; Revision accepted: 24.04.18

Intravitreal corticosteroids have been in use for various conditions such as diabetic macular edema, vein occlusions, pseudophakic cystoid macular edema, and a variety of uveitic diseases. Common adverse events include cataract formation and steroid-induced glaucoma, endophthalmitis, vitreous hemorrhage, and retinal detachment. There have been reports of infective uveitis following injection of intravitreal corticosteroids in recent years.[1-4] Although majority of them reported a viral etiology,[1,4-7] rare presentations of acute syphilitic posterior placoid chorioretinitis[2,8] and toxoplasma retinochoroiditis[3,9] following intravitreal injection of corticosteroid have been reported.

Typical toxoplasma lesions include unilateral focal retinochoroiditis at the border of a preexisting pigmented retinochoroidal lesion and overlying vitritis. However, atypical lesions may consist of large areas of retinal necrosis or retinochoroiditis without adjacent preexisting pigmented retinal scar or retinochoroiditis in both the eyes. Such atypical lesions are seen in elderly individuals and in those with underlying immunodeficiency due to various causes.[10]

We report an unusual case of an atypical toxoplasma retinochoroiditis after intravitreal triamcinolone acetonide (IVTA) injection in an elderly diabetic patient. A detailed review of the literature on PubMed was conducted using such terms as intravitreal, corticosteroid, toxoplasma retinochoroiditis, and ocular toxoplasmosis. Additional studies were also looked for from the bibliographies of the retrieved articles.

Case Report

A 64-year-old male presented to our uveitis clinic with complaints of blurring of vision in the right eye of 10-day duration. He was a known diabetic for 14 years and documented to have nonproliferative diabetic retinopathy in both the eyes and optic atrophy (due to probable ischemic optic neuropathy) in the left eye for 4-year duration. IVTA

Cite this article as: Ahmed A, Sudharshan S, Gopal S, Majumder PD, Biswas J. Toxoplasma retinitis following intravitreal injection of triamcinolone acetonide: A case report and review of literature. Indian J Ophthalmol 2018;66:1205-8.

Table 1: Review of literature of cases of ocular toxoplasmosis following intravitreal corticosteroid

Author	Age/sex	Immune status	Indication for intravitreal corticosteroid	Intravitreal corticosteroid	Duration between intervention and infection (days)	Comorbidity
Rush and Seth[9]	42/male	Immunocompetent	Autoimmune panuveitis	IVTA	60	Multiple sclerosis
	30/male	Immunocompetent	Toxoplasma retinochoroiditis	IVTA	42	Nil
Nóbrega and Rosa[3]	84/male	immunocompetent	CNVM	PDT, IVTA 4 mg	30	Nil
Olson *et al*.[17]	74/male	Immunocompetent	Iridocyclitis and vitritis	Dexamethasone Implant	42	Nil
Reported case	64/male	Immunocompetent	DME	IVTA 4 mg	60	Diabetes mellitus

CNVM: Choroidal neovascular membrane, DME: Diabetic macular edema, IVTA: Intravitreal triamcinolone acetonide, PDT: Photodynamic therapy

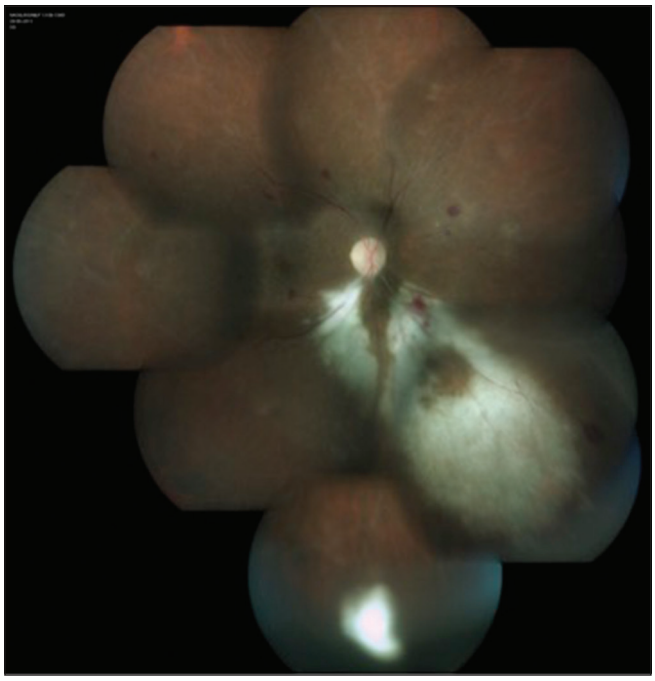

Figure 1: Montage fundus photograph of the right eye showing a large, whitish, fluffy lesion inferior to the disc and inferonasal quadrant. A clump of residual intravitreal triamcinolone acetonide is seen in the inferior vitreous

was administered in his right eye for clinically significant macular edema (CSME) 2 months back. On examination, his best-corrected visual acuity (BCVA) in the right eye was 6/18, N6, and in the left eye was counting fingers at 2 m. Slit-lamp examination of his right eye revealed pseudophakia with minimal anterior chamber reaction. Intraocular pressure (IOP) of the right eye, measured with applanation tonometry, was 27 mmHg. Anterior segment examination of the left eye was within normal limits including a normal IOP. Fundus examination of the right eye revealed a large area of retinitis inferior to the disc with few hemorrhages [Fig. 1]. Left eye posterior segment examination revealed optic atrophy. Optical coherence tomography revealed an epiretinal membrane (ERM) and retinal thickening inferonasal to fovea with shallow subretinal fluid [Fig. 2]. A provisional diagnosis

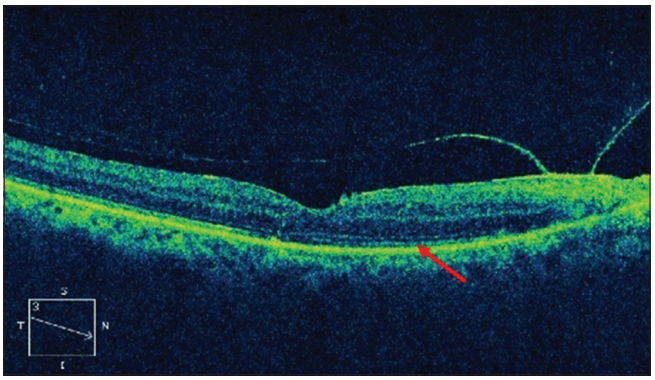

Figure 2: Optical coherence tomography showed a posterior vitreous detachment along with an epiretinal membrane. Foveal contour is noted with retinal thickening and subretinal fluid inferonasal to the fovea

of atypical necrotizing retinitis due to infectious etiology was considered. Routine blood investigations were normal and he tested negative for human immunodeficiency virus 1 and 2. Polymerase chain reaction (PCR) of aqueous aspirate from his right eye was positive for *Toxoplasma gondii* genome with the sequence (B1-5′TCT TTA AAG CGT TCG TGG TC 3′) and negative for herpes simplex, varicella zoster, and cytomegalovirus genomes. Enzyme-linked immunosorbent assay (ELISA) test in serum for antibodies to *T. gondii* was also positive for IgG antibodies (410 IU/ml). A diagnosis of necrotizing retinitis due to toxoplasma in the right eye was made, and the patient was started on a multidrug regimen of oral clindamycin 300 mg four times per day and combination of sulfamethoxazole and trimethoprim (double strength, 800 mg sulfamethoxazole and 160 mg trimethoprim) twice per day. Oral steroids at a dose of 1 mg/kg/day were initiated 2 days after initiating anti-toxoplasma treatment. Serial follow-up at 4 weeks showed a regressing lesion [Fig. 3]. The retinitis had completely resolved 3 months after initiation of treatment. At final follow-up, 20-month postfirst visit, the patients' BCVA was 6/12, N6, and no recurrences have been noted till date.

Discussion

There have been anecdotal reports of fulminant toxoplasma retinochoroiditis following systemic and depot corticosteroid administration.[11-13] Furthermore, there are few reports of using

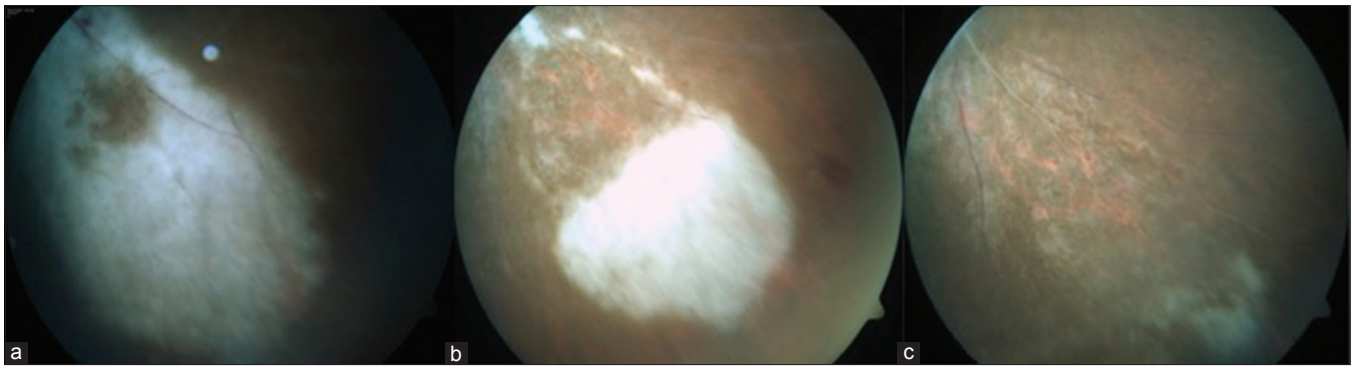

Figure 3: Serial monitoring of the lesion shows progressive resolution. (a) At presentation. (b) At 1 month. (c) Three months after presentation

intravitreal corticosteroid as adjunct in the management of severe cases of toxoplasma retinochoroiditis.[14,15]

Toxoplasmic retinochoroiditis can present in atypical forms, especially in immunocompromised state. Elderly patients can be at risk of more severe involvement due to waning immune system.[3,4] In our patient, advanced age and the uncontrolled glycemic status could have led to an immunocompromised state. In a report by Takakura *et al*.,[16] 12 of the 30 patients, who developed viral retinitis following intraocular or periocular steroid injection, were diabetics and the authors postulated that the diabetic vasculopathy facilitated the entry of the microorganism into the retina leading to the development of retinitis.

Four cases of toxoplasma retinochoroiditis following intravitreal injection of corticosteroid have been reported in literature [Table 1].[3,9,17] Olson *et al*. reported a case of toxoplasma retinochoroiditis in a 74-year-old male, who was treated with intravitreal dexamethasone for iridocyclitis and vitritis refractory to topical difluprednate. The patient developed severe anterior chamber inflammation with raised IOP and fundus examination revealed vitritis, retinal vasculitis, and retinitis. As was seen in our patient, majority of the cases reported in literature presented with retinitis following intravitreal injection of corticosteroid and was initially diagnosed as viral retinitis.

Toxoplasmic retinochoroiditis may mimic viral retinitis early phase of ocular involvement because of its predominant retinal involvement, which subsequently involves choroid to manifest as retinochoroiditis.[18]

PCR testing of intraocular fluids and ELISA for anti-toxoplasma antibodies can help establish the diagnosis in atypical presentations as was seen in our patient. Treatment with multidrug regimen of anti-toxoplasma therapy along with tight diabetic control helped resolution of inflammation and restoration of vision.

Intravitreal corticosteroids, due to their immunosuppressive actions, suppress host immunity and may lead to release of *T. gondii* from intraretinal cyst resulting in ocular disease with enormous tissue destruction.

IVTA which was given in our patient for the management of CSME probably led to local immunosuppression and subsequent development of *de novo* toxoplasma retinitis as he had no evidence of old toxoplasmic scars which could indicate reactivation of latent disease.

Rush and Seth[9] described two cases of fulminant toxoplasmic retinochoroiditis and exerted a caution on treating conditions such as panuveitis with intravitreal corticosteroid, particularly in population with higher prevalence of toxoplasmosis.

Nóbrega and Rosa[3] reported a case of reactivation of a toxoplasma satellite lesion in a 84-year-old-male which had developed adjacent to an atrophic scar post-IVTA and photodynamic therapy for presumed choroidal neovascular membrane secondary to age-related macular degeneration.

Conclusion

This case report and review of literature aims to elevate awareness of the possibility of the rare occurrence of toxoplasma retinochoroiditis in patients receiving intravitreal corticosteroid. It is important to have proper glycemic control when planning IVTA. Clinicians need to carefully monitor the patients following administration of intravitreal medication and diagnosis of toxoplasma retinochoroiditis should be kept in mind while dealing with retinitis mimicking viral retinitis. Proper microbiological diagnosis aided by the use of newer laboratory investigations such as real-time PCR, and rapid, effective, and appropriate antimicrobial therapy can prevent devastating complications in infectious posterior uveitic diseases in such cases.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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