A rare case of ocular toxoplasmosis complicated by both retinal detachment and choroidal neovascularization in an immunocompetent patient

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Background: To report an unusual case of ocular toxoplasmosis complicated by both retinal detachment and choroidal neovascularization in the same eye of an immunocompetent patient

Results: A 74-year-old gentleman of oriental origin presented with a 3-month history of reduced vision in the left eye: best corrected visual acuity was 6/6 in the right eye and 6/24 in the left eye. Clinical examination revealed no signs of systemic illness. The anterior segment in the left eye showed pigmented granulomatous keratic precipitates. Anterior chamber was deep with 3+ cells; no hypopyon. Both eyes were pseudophakic with clear media. Posterior segment of the left eye showed dense vitritis, with 2 areas of retinitis. No retinal breaks were visible. Serum Toxoplasmosis antibodies IgM was negative, but IgG was positive at 3.584. Vitreous tap was negative for CMV, HSV1, HSV2, and VZV DNA. Vitreous PCR for toxoplasmosis was not available at the time. He was started on oral Prednisolone 1 mg/kg, oral Bactrim (Sulfamethoxazole and Trimethoprim), and topical prednisolone acetate 1% (PredForte) 4-hourly. Visual acuity in the affected eye was 6/9 at 8 weeks post initiation of treatment. He subsequently developed retinal detachment which was operated with a visual outcome of 6/18. Unfortunately, he then developed choroidal neovascularization, and despite anti-VEGF treatment, did not regain his vision. .

Conclusion: Prompt diagnosis of atypical presentation of ocular toxoplasmosis may aid management and subsequent preservation of visual function.

Conflicts of interest: The authors report no conflicts of interest.

Keywords: Toxoplasmosis, Retinal detachment, Choroidal Neovascularization

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Background

Toxoplasma gondii is an obligate intracellular protozoa capable of infecting humans and other mammals. It has a worldwide distribution and is known to infect up to one third of the world's population.[1] The etiological spectrum of infectious uveitis differs throughout the world because of various factors including geographic and demographic factors.[2] This case describes a case of presumed ocular toxoplasmosis complicated by retinal detachment and choroidal neovascularization.

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Case history

A 74-year-old gentleman of oriental ori-

gin with underlying hypertension, benign prostatic hyperplasia, and a non-functioning pituitary adenoma, presented with a 3 month history of reduced vision in the left eye. He was initially treated with Predforte and Azarga prior to presenting at our centre for a second opinion.

Both eyes were pseudophakic, performed at a private center, without any known complications. He denies any history of prodromal flu-like illness, tinnitus, chronic cough, night sweats, or fevers. He also denies any ulcers or joint pains. There was no history of penetrating eye injury. He lives at home with his wife and 3 children, all of whom are healthy. They do not have any pets at home. He retired from being a consultant designer at age 60. He gave a history of recent travel to Philippines a month prior to presentation. He is an ex-smoker and his regular medications were Losartan 50 mg OD, Amlodipine 10 mg OD, and Simvastatin 10 mg ON.

Clinical examination revealed no signs of systemic illness. There were no skin changes such as rashes or alopecia. At presentation, best corrected visual acuity was 6/6 in the right eye and 6/24 in the left eye. The anterior segment in the left eye showed pigmented granulomatous keratic precipitates (Figure1). Anterior chamber was deep with 3+ cells; no flare or hypopyon were visible. Both eyes were pseudophakic. Posterior segment of the left eye showed dense vitritis, with 2 areas of retinitis – superior nasal (Figure 2) and inferior nasal. No retinal breaks visible. Infective screen for HIV, Hepatitis B, and Hepatitis C were negative. Rapid Plasma Reagin (RPR) testing was non-reactive and Treponema Pallidum Particle was not detected. Serology for Toxocariasis was negative. Serum Toxoplasmosis antibodies IgM was negative, but IgG was positive at 3.584. Mantoux test was 13mm, but serum PCR for TB was negative. Vitreous tap was negative for CMV, HSV1, HSV2, and VZV DNA. Vitreous PCR for toxoplasmosis was not available at the time.

He was started on oral Prednisolone 1 mg/kg od, which was tapered by 10 mg every 5 days, oral Bactrim (Sulfamethoxazole 800mg and Trimethoprim 160mg), and PredForte 4-hourly. He had a raised IOP of 23 mmHg and was started on Timolol. Upon follow-up, he responded well to the above treatment, and the oral Prednisolone and PredForte were tapered down. Oral Bactrim was continued. Visual acuity in the affected eye was 6/9 at 8 weeks post initiation of treatment.

However, after completion of the oral Prednisolone regimen, the patient noticed a reduction in vision, and 8 days later presented with a 360° exudative retinal detachment (RD) with a visual acuity of 6/18. Anterior chamber activity was 1-2+ with minimal vitritis. He was restarted on oral Prednisolone 1 mg/kg. He returned the following day with a sudden drop in visual acuity to perception of light, with a bullous RD involving the macula (Figure 3), which was confirmed with a B-scan. A trans pars plana vitrectomy (TPPV) with silicone oil was performed, no retinal break(s) seen intraoperatively. At one month post-op, he underwent another surgery for removal of silicone oil as he was found to have raised intraocular pressure. Three months post retinal detachment surgery, his best corrected visual acuity improved to 6/18 (Figure 4).

Two months later, vision in the affected eye reduced to counting fingers. A yellow central macular lesion was noted and subsequently developed into a fibrotic scar. This lesion was appeared at a different location from the previously described areas of retinitis. The optic disc appeared pale. An immune reaction was suspected and he was restarted on oral Prednisolone regime in a tapering manner (Figure 5). However the fibrotic scar remained the same but developed neovascularization

around the lesion (Figure 6). Choroidal neovascularization (CNV) was suspected and a fundus fluorescein angiography was performed which showed subfoveal leakage corresponding to the lesion shown in Figure 7. He was then given 3 consecutive intravitreal injections of Bevacizumab and his OCT (Figure 8) showed resolution of the subretinal fluid but his vision remained blurred at counting fingers.

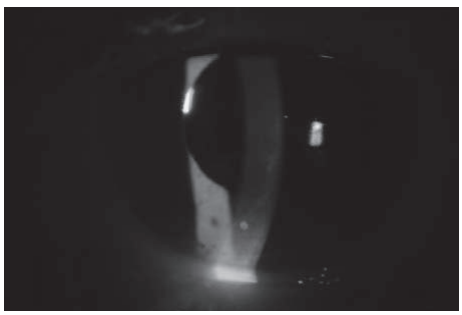

Figure 1: Anterior segment showing resolving keratic precipitates.

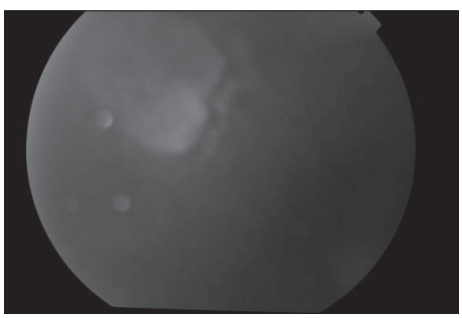

Figure 2: Fundus photo showing superior nasal lesion.

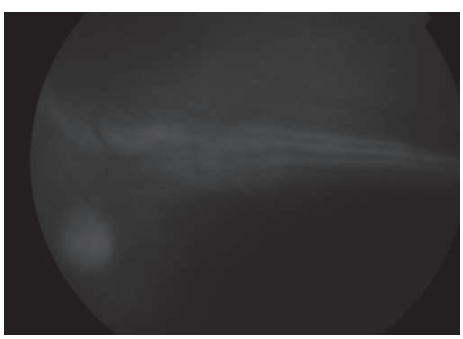

Figure 3: Retinal detachment with dense vitritis.

On the last follow-up, two years after the initial treatment for ocular toxoplasmosis, the retina is flat with no recurrence of disease and the subfoveal choroidal neovascularization remained inactive with no further improvement of vision.

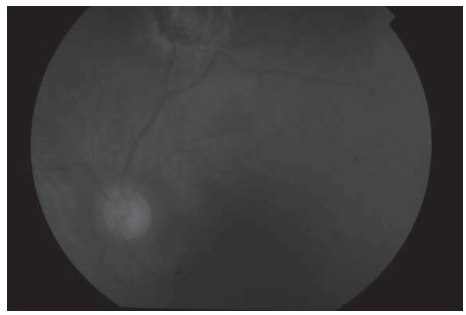

Figure 4: Fundus photo of affected eye 11 weeks post TPPV.

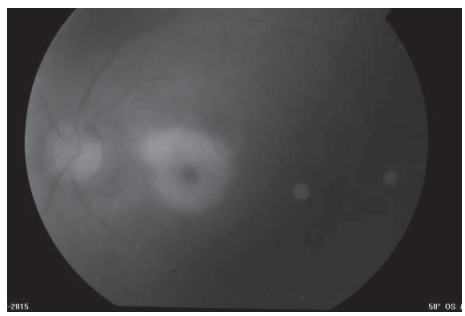

Figure 5: Fibrotic scar at macula.

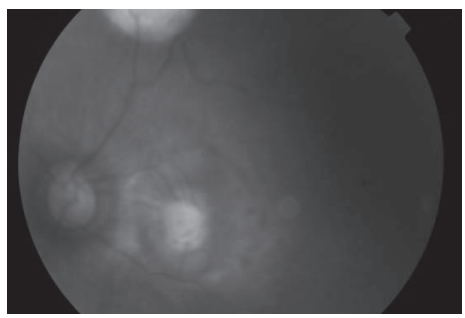

Figure 6: Foveal edema with surrounding neovascularization.

Discussion

Ocular toxoplasmosis, a disease caused by the parasite Toxoplasma gondii, an obligate intracellular protozoan. It is one of the most frequently identifiable causes of

uveitis worldwide. In fact, Toxoplasma gondii infection is the most common cause of infectious posterior uveitis in non-immunocompromised individuals, second only to cytomegalovirus retinitis in patients with HIV/AIDS.[3] While cats are the definitive hosts, humans serve as intermediate hosts to Toxoplasma gondii and approximately 33% of the human population worldwide is infected by the parasite. Fortunately, ocular manifestations are generally found in only 2% of those infected.[4, 5]

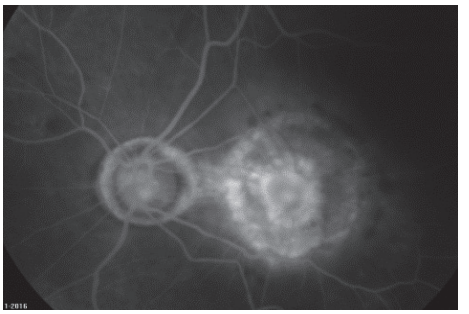

Figure 7: A fundus fluorescein angiography showing subfoveal leakage.

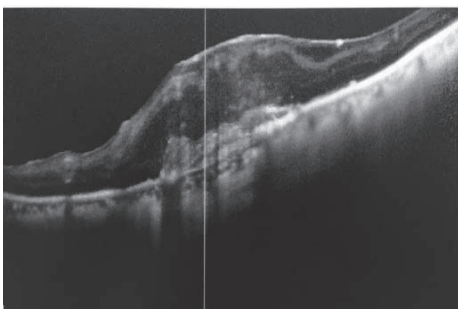

Figure 8: Heidelberg OCT of macula.

Typical presentation of ocular toxoplasmosis includes a characteristic finding of unilateral and focal retinochoroiditis with an adjacent healed retinochoroidal scar. Vitreous inflammation may also be present. Rarely, especially in patients with immune compromise, ocular toxoplasmosis presents atypically as aggressive retinal choroiditis.[6,7] Patients with ocular toxoplasmosis often describe blurred or hazy vision and floaters, with absence of pain. Up to 20% of patients have acute ocular hypertension at presentation.[8] On fundus examination, most commonly there will be unilateral bright white-yellow retinal lesions. Retinal hemorrhages are usually absent. Significant vitritis is a common finding.[8] Anterior chamber spill over may also occur.

Although diagnosis is most often made clinically, based on characteristic fundus lesions, laboratory investigations aid in confirming the diagnosis, especially for atypical presentations. An initially incorrect diagnosis with prolonged empiric treatment may be harmful by delaying appropriate treatment resulting in suboptimal visual outcomes. Use of corticosteroids without simultaneous antitoxoplasmosis treatment may result in more rapid progression of the chorioretinitis. Polymerase chain reaction amplification of toxoplasmic DNA is faster than culture, requiring only small amounts of intraocular fluid. However, an intracellular organism such as Toxoplasma gondii would not usually be expected to be floating freely in intraocular fluid.[9] IgM antibodies will rise early post-infection and remain detectable for less than one year, while IgG antibodies will appear within the first two weeks post-infection and remain detectable for life. Because these antibodies are highly sensitive markers of the disease state, antibody testing is helpful in ruling out toxoplasmosis when the result is negative.[10]

Ocular Toxoplamosis presenting typically is a self-limiting disorder, usually resolving within 6 weeks to 2 months. It is not established that antibiotics improve short-term disease course or long-term visual outcomes in the immunocompetent persons compared to observation or placebo[11]. Bactrim (trimethoprim-sulfamethoxazole) 160/800 mg twice daily has been shown to be equivalent to the traditional triple-therapy regimen of Pyrimethamine, Sulfadiazine, and Folinic acid. Level I ev-

idence backs intermittent treatment every few days with Bactrim to significantly reduce the risk of recurrence of retinochoroiditis.[12] Concomitant prednisolone therapy of 0.5 to 1 mg/kg daily is also often used to reduce inflammation, although there is limited evidence from randomized clinical trials demonstrating their effectiveness as an adjuvant therapy.[13,14] However, steroids should not be used as monotherapy (without antibiotics), or in the immunocompromised patient due to the high probability of inducing fulminant retinochoroiditis.[15]

A study by Faridi et al of 35 eyes of 28 patients diagnosed with ocular toxoplasmosis showed that 11.4% of patients developed RD which led to severe vision loss despite successful RD repair.[16] A study of 150 patients with ocular toxoplasmosis by Bosch-Driessen et al showed that 6% had RD and a further 5% had retinal breaks. It was noted that intraocular inflammation in eyes preceding the RD or retinal breaks was severe. It was also noted that the frequency of myopia was significantly higher in eyes with retinal detachment and breaks as compared to those without detachment or breaks.[17] The patient described in this case is not known to be myopic although both eyes were pseudophakic, and the inflammation sustained during his attack of ocular toxoplasmosis was no more severe than what was usually expected. Despite this he still developed retinal detachment followed by choroidal neovascularization following the initial acquired retinitis due to toxoplasmosis.

Choroidal neovascularization is a rare complication of ocular toxoplasmosis, which usually arises secondary to retinochoroiditis and macular scarring.[18] Increased expression of vascular endothelial growth factor (VEGF), compromise in the Bruch membrane, and inflammation secondary to toxoplasmosis infection may contribute to the formation of neovascular disease.[19] A study by Rasier et al showed that intravitreal VEGF concentrations were significantly elevated in vitreous samples of patients with RD.[20] The CNV lesion in the patient described in this case is located at the macula, away from the original 2 lesions of retinitis – superior nasal and inferior nasal. It may be postulated that the CNV may be a complication of the inflammation from the original insult of retinitis, or secondary to the operated RD, or a combination of both. Toxoplasma gondii has been shown to express VEGF in tissue culture. This justifies specifically targeting VEGF when treating CNV in ocular toxoplasmosis. Benevento et al showed that CNV lesions occurring as a complication of ocular toxoplasmosis were successfully treated with intravitreal Ranibizumab and antiparasitic therapy.[21] Korol et al showed that intravitreal Aflibercept has been shown to have a positive clinical effect and was well tolerated for the treatment of CNV associated with chorioretinitis including those secondary to Toxoplasmosis gondii.[22] Verteporfin photodynamic therapy (V-PDT) has been shown to be effective and safe in treating subfoveal choroidal neovascularization associated with ocular toxoplasmosis.[23] Adan et al reported a case of ocular toxoplasmosis with subfoveal choroidal neovascularization. The patient underwent pars plana vitrectomy and submacular surgery with subsequent improvement of visual acuity and resolution of metamorphopsia.[24] The patient in this case developed what was thought to be an immune reaction 2 months post retinal detachment surgery. Although he was treated with Bactrim and Prednisolone, he still progressed to develop choroidal neovascularization. Intravitreal Bevacizumab was used in this case and the neovascularization resolved after 3 doses.

This case illustrates a case of ocular toxoplasmosis in an immunocompetent individual. He was treated adequately with Bactrim and Prednisolone yet subsequently

still developed RD followed by subfoveal CNV. Despite surgical intervention for the retinal detachment and anti-VEGF treatment for the choroidal neovascularization, his vision unfortunately remains poor.

Conclusion

It is important for vigilant examination of patients with ocular toxoplasmosis to aid early identification of potential complications like retinal detachment and choroidal neovascularization. One needs to be aware of such devastating complications as in some unfortunate cases as demonstrated here, despite adequate intervention, the outcome remains poor.

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