Case series of atypical ocular toxoplasmosis.

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Background: *Ocular toxoplasmosis is one of the commonest causes of posterior uveitis worldwide. Its diagnosis can be challenging as it can present with a wide range of clinical signs. This study describes the clinical manifestations, management and outcome of atypical ocular toxoplasmosis seen in different age groups of patients.*

Case Series: *There were three patients in this series. The first case was a 10-year-old child with 1-week history of left eye blurring of vision and seeing a black spot. The second case was a 44-year-old lady who presented with left eye image distortion and floaters for 3 weeks duration while the third case was a 63-year-old lady who presented with left eye blurring of vision for 1-week duration. All patients presented with retinochoroiditis and vasculitis. The first case also had mutton-fat keratic precipitates, iris nodule, anterior chamber inflammation, peripapillary hemorrhage and minimal vitreous haemorrhage. The second case had a retinal scar and the third case had mutton-fat keratic precipitates, anterior chamber inflammation and iris plug. All patinets had positive serology for Toxoplsmosis and were treated with oral trimethoprim/sulfamethoxazole, oral prednisolone and topical steroid.*

Conclusion: *Clinicians may face a challenge when diagnosing atypical ocular toxoplasmosis. Understanding the various manifestations of ocular toxoplasmosis that may occur in the different age groups of patients may help in diagnosing and managing the disease.*

Conflict of interest: *The authors report no conflict of interest.*

Keywords: *atypical, ocular toxoplasmosis, age, case series*

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Introduction

Ocular toxoplasmosis is a disease resulting from infection by an obligate intracellular parasite called Toxoplasma gondii. Ocular inflammation secondary to toxoplasmosis is one of the commonest cause of posterior uveitis worldwide.[1] Diagnosis of ocular toxoplamosis can be challenging as it can present with a wide range of clinical signs. The typical findings include a yellow-white fundus lesion with intense vitreous cells that resemble 'headlights in a fog'. Its clinical hallmark is focal retinochoroiditis adjacent to pigmented chorioretinal scar (Butler et al, 2013). However some patients may present with 'atypical' findings that make diagnosing ocular toxoplasmosis a challenging task. Patients' age may have an influence in the presentations of ocular toxoplasmosis.

Case History

Case 1

A 10-year-old child with no known medical illness presented with 1-week duration of left eye (LE) blurring of vision and seeing a black spot. She denied recent or prolonged fever, loss of appetite, loss of weight, chronic cough, contact with tuberculosis (TB) patients, joint pain, ulcers or skin rashes. She had previous contact with cats but does not own any herself. On further history, the child was born healthy with no history of infection during antenatal and postnatal period in both mother and the child. On her first visit to us, her visual acuity (VA) in the LE was 6/24, 6/18 while her right eye (RE) was 6/6. There was no relative afferent pupillary defect (RAPD). Examination of the RE anterior segment and fundus were unremarkable while LE examination showed mutton fat keratic precipitates, iris nodule, 3+ of anterior chamber cells and 1+ of anterior vitreous cells. Intraocular pressure was 12 mmHg on RE and 10 mmHg on LE. Fundus examination of LE showed retinochoroiditis of 1 disc diameter in the superior retina with vasculitis (Figure 1 a), inferior peripapillary haemorrhage (Figure 1b) and vitreous haemorrhage in the inferior retina. Our impression at that time was LE panuveitis for further investigations. She was started on regular topical dexamethasone and cycloplegic drops.

Laboratory investigations showed normal full blood count and renal profile. Erythrocyte sedimentation rate (ESR) was 24 mm/h and C-reactive protein (CRP) was <0.085 mg/L. Test for anti-nuclear antibody was negative. IgG and IgM Toxoplasma antibodies (IgG and IgM) was positive.

4 days later her anterior chamber cells and keratic precipitates had subsided. However, the fundus examination remained the same. We performed fundus fluorescein angiography (FFA) which showed peripheral vasculitis and hypofluorescent area over the lesion with some hyperfluorescent spots surrounding it (Figure 1c). The lesion did not fluoresce at late phase. There was no capillary fall out or new vessels seen. FFA of RE was normal. Optical coherence tomography (OCT) macula for both eyes were normal.

The child was treated for LE ocular toxoplasmosis. The child weighs 24 kilogram and was started on oral trimethoprim/sulfamethoxazole (Co-trimoxazole) 100 mg BD (4 mg/kg) promptly together with oral prednisolone 15 mg OD which was started 3 days after commencement of oral Co-trimoxazole. The prednisolone dose was tapered down by 2.5 mg weekly. Topical dexamethasone was

started every 2 hourly and reduced by 2 hourly in the subsequent weeks for duration of 8 weeks.

After 6 weeks her LE vision improved to 6/9. Fundus examination showed resolved retinochoroiditis with scarring seen at superior retina (Figure 1 d). Oral Co-trimoxazole and prednisolone was tapered down further. The appearance of the lesion further subsided 2 weeks later.

Case 2

A 44-year-old Malay lady complained of painless left eye (LE) image distortion and floaters for 3 weeks duration. She denied recent or prolonged fever, loss of appetite, loss of weight, chronic cough, contact with tuberculosis (TB) patient, joint pain, ulcers or skin rashes. She does not own any pets but had contact with stray cats occasionally.

On examination, visual acuity of left eye was 6/9 while right eye was 6/6. There was no relative afferent pupillary defect (RAPD). RE anterior segment and fundus examination was normal. LE anterior segment examination was unremarkable apart from anterior vitreous cells of 1+. Intraocular pressure was 14 mmHg in the RE and 12 mmHg in the LE. Fundus examination showed cup-disc-ratio of 0.3 bilaterally with pink disc margin. LE fundus examination showed retinochoroiditis of 1/3 disc diameter size observed at the superior macula with a small scar nasal to it (Figure 2 a). There was also generalized vasculitis seen on the retina. Optical coherence tomographic scan of the macula showed left superior macula retinal thickening.

Laboratory investigations showed normal full blood count, renal profile, liver function test, and random blood sugar. Testing for syphilis was non-reactive. Rheumatoid factor, anti-nuclear antibody and Mantoux test were also negative. Chest x-ray was clear and ESR was 32 mm/h. IgG and IgM Toxoplasma antibodies (IgG and IgM) was positive.

Our impression was LE posterior uveitis secondary to toxoplasmosis. She was promptly started on oral Co-trimoxazole 960 mg BD for 6 weeks and oral prednisolone 20 mg OD which was tapered down 2.5 mg weekly. Low dose steroid was given in this case in view of less inflammation was observed compared to the other cases. She was also started on LE topical dexamethasone QID. She weighs 60 kilogram.

After 6 weeks the retinitis and vasculitis had resolved. There was now a hypopigmented spot observed at the previous retinitis area. The old scar was still seen nasal to it (Figure 2b). Three months later, her vision is stable at 6/6 in both eyes with quiescent LE fundus. A scar was seen on superior macula region.

Case 3

A 63-year-old lady with underlying rheumatoid arthritis and schizophrenia complained of painless LE blurring of vision for 1 week duration associated with redness of the eye. She denied recent or prolonged fever, loss of appetite, loss of weight, chronic cough, contact with tuberculosis patient, ulcers or skin rashes. On examination, her LE visual acuity was 6/40, 6/30 and her RE was 6/6. Reverse RAPD was negative. Examination of LE showed mutton fat keratic precipitates, anterior chamber cells of 4+, iris plug and extensive posterior synechiae. After mydriacaine injection and synechiolysis, fundus examination showed elevated hypopigmented

retinochoroidal lesion of 1.5 disc diameter in size located at the inferior retina with generalized vasculitic changes and presence of vitritis. (Figure 3 a). Anterior segment and fundus examination of the RE was unremarkable. Intraocular pressure of both eyes was 12mmHg.

She was treated as LE ocular toxoplasmosis and started on oral Bactrim 960 mg BD, topical prednisolone 1% every 2H, topical cycloplegic and oral prednisolone 30 mg OD 3 days later. The decision to start oral prednisolone and the appropriate dose to be given has been discussed in details with her psychiatrist in view of her underlying psychiatric illness. She weighs 58 kilogram.

Laboratory investigations showed normal full blood count, random blood sugar and ESR of 24 mm/h. Mantoux test was negative, chest x-ray and VDRL was normal. IgG and IgM Toxoplasma antibodies (IgG and IgM) was positive.

1 week later her LE visual acuity improved to 6/20, reduced anterior chamber cells but with little changes on fundus examination. The prednisolone was tapered down and Co-trimoxazole was continued. After 3 weeks, her LE vision further improved to 6/9, cornea was clear and the retinochoroidal lesion appeared plaque-like and more well-defined with resolving vitritis (Figure 3b). At 4 months, her LE vision was good with visual acuity of 6/9. The anterior chamber was quiet, the retinochoroidal lesion has scarred up and the vitritis has resolved completely (Figure 3c).

Discussion

Ocular toxoplasmosis is caused by infection with an obligate intracellular parasite called Toxoplasma gondii. It was first described in 1923 in an infant with congenital infection (Holland, 2009). It was previously thought that toxoplasmic retinochoroiditis is a disease of newborns only until 1952 when Wilder confirmed the presence of ocular toxoplasmosis in a series of adult patients (Wilder, 1952).

Cats are the primary hosts for toxoplasma (Jasper et al, 2013). The main route of infection is by ingestion of oocytes from cat feces present in soil and sand boxes which may be attached to fruits and vegetables. Contaminated drinking water may be a main route of endemic infections with Toxoplasma gondii. Another route is by ingestion of tissue cysts in raw or undercooked meat from intermediate animals (Park and Na m, 2013). The organism enters the human blood stream via gastrointestinal tract and invades other organs. In congenital infection, transmission from mother to child occurs via the transplacental route (Jasper et al, 2013).

About 25% of the population with Toxoplasma gondii infection present with ocular manifestations which commonly has a 'fluffy' yellow-white appearance with indistinct margins. This signifies an active chorioretinal lesion represented by areas of focal, necrotizing disease (Graff and Russell). Its clinical hallmark is focal retinochoroiditis adjacent to pigmented chorioretinal scar (Butler et al, 2013). Perivasculitis may be present in vessels near the active lesion with focal vitritis overlying and surrounding the lesion (Graff and Russell). These are the typical findings of ocular toxoplasmosis.

Atypical ocular toxoplasmosis might mimic the findings of other ocular diseases. Ocular disease severity can be determined by the parasite genetics

or host factors and age is one of the determining host factor (Wilder, 1952) (Kianersi et al, 2012). Risk of ocular involvement and its severity varies between different age groups (Wilder, 1952). More severe presentation is highly likely in the extremes of age as seen in the third and first case as compared to the second case in these case series. They may also be predisposed to granulomatous anterior uveitis as seen in the 10-year-old child described in the first case who presented with mutton fat keratic precipitates. Older patients have a higher risk of acquiring acute infection of Toxoplasma gondii hence primary retinal lesions were commonly found in the elderly (Bosch-driessen, 2002). They may also present with large or multiple active lesions, severe vitritis and prolonged disease as described in the third case. This could be attributed to the decrease in immunity as they aged (Johnson et al, 1997). In this case series, it has been shown that elderly patients and children may present with more severe features such as intense inflammation and mutton fat keratic precipitates. An elderly patient may also present with posterior synechiae and prolonged inflammation while a child may present with vitreous peripapillary splinter haemorrhages.

As for congenital ocular toxoplasmosis, they usually occur bilaterally and over the macula region. Although it is not specific to congenital infections, the macular region is favoured in this group in view of anatomic and microvascular differences between the macula and peripheral retina in which vascularization of peripheral retina is completed much later (Bosch-driessen et al, 2002) (Holland, 2004).

Toxoplasma gondii antibodies are generally not useful due to high seropositivity for Toxoplasma gondii infection in the general population (Butler et al, 2013). Hence seropositive findings cannot confirm the diagnosis of ocular toxoplasmosis but can confirm previous exposure to the parasite. In most cases, diagnosis is usually made clinically, and the best clue is to recognize its various clinical presentations (Dodds et al, 2008). This is beneficial and helpful especially in low-income countries where blood investigations of Toxoplasma gondii antibodies may not be readily available.

Finally, as ocular toxoplasmosis is a self-limiting disease, it typically resolves over a period of 1-2 months (Butler et al, 2013). Therefore not all cases require treatment. However, in this case series, all patients were treated as the lesions were vision threatening (case 1: involvement of major vessels, case 2: macula involvement, case 3: significant vitritis) with all the three patients showing good response to treatment (Butler et al, 2013). Toxoplasmic retinochoroiditis is usually treated with a course of one or more antimicrobial drugs such as oral Trimethoprim/Sulfamethoxazole (160 mg - 800 mg BD) and concurrent oral corticosteroid (Wilder, 1952) (Holland, 2009). The combination of these antimicrobials is a well-tolerated alternative to its 'classic therapy' which is a combination of Pyrimethamine/ Sulfadiazine (Butler et al, 2013). The function of antimicrobials is to limit the multiplication of parasites during active retinitis while the steroid is used to reduce the risk of tissue damage caused by the associated inflammatory response (Butler et al, 2013) (Wilder, 1952). The duration of treatment is usually 6 weeks however it depends largely on the disease response. The administration of oral corticosteroid may be individualized in certain cases depending on the severity of inflammation and the host immunity status as it can

suppress the immune response to parasites hence increasing the risk of severe disease (Holland, 2009).

Conclusion

Host age influences risk for ocular involvement and the severity of ocular toxoplasmosis. Understanding its various manifestations and the course of disease in different age groups may help clinicians in diagnosing and managing the disease.

Figures

Figure 1a:

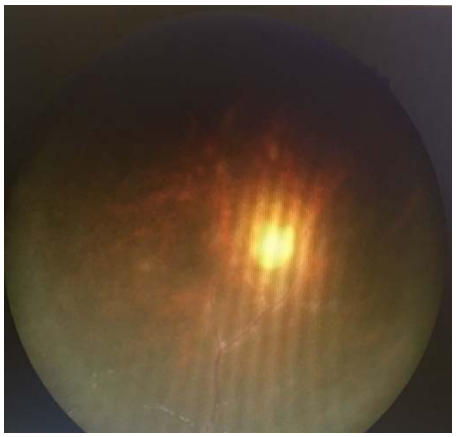


Figure 1b:

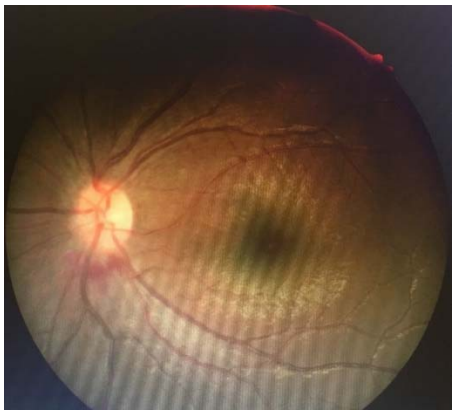


Figure 1c:

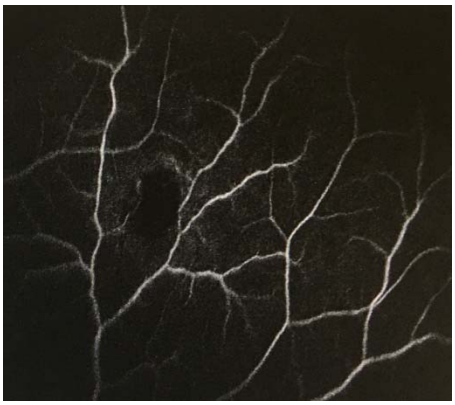


Figure 1d:

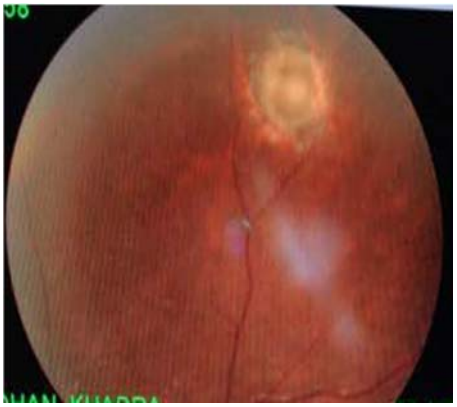
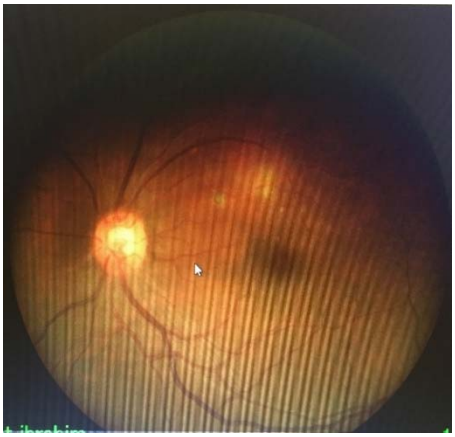


Figure 2a:



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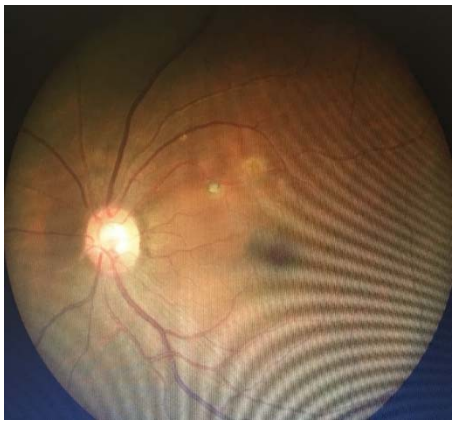

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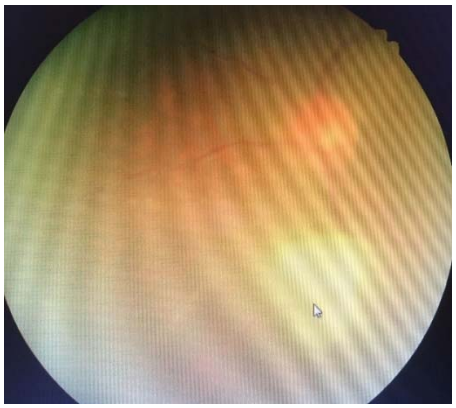

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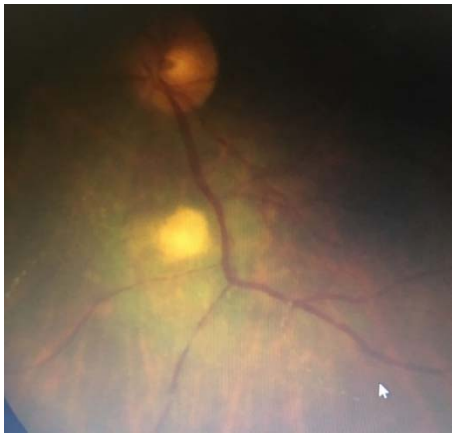

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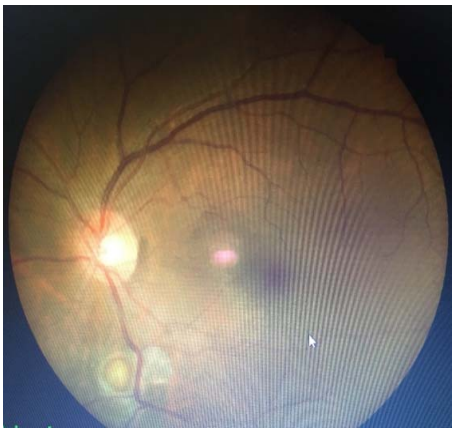

Informed Consent

Informed consent to publish this case series has been obtained from the patients and guardian.

Disclosure of interest

The authors report no conflicts of interest.

References

1. Butler, N.J, Furtado J.M, Winthrop K.L, Smith J.R. (2013). Ocular toxoplasmosis II: clinical features, pathology and management. Clin Experiment Ophthalmol, 41(1): 95-108.
2. Holland, G.N. (2009). Ocular toxoplasmosis: the influence of patient age. Mem Inst Oswaldo Cruz, 104(2): 351-7.
3. Wilder, H.C. (1952). Toxoplasma chorioretinitis in adults. AMA Arch Ophthalmol, 48(2): 127-36.
4. Jasper, S., Vedula, S.S., John S.S, Horo, S., Sepah, Y.J., Nguyen, Q.D. (2013). Corticosteroids as adjuvant therapy for ocular toxoplasmosis. Cochrane Database Syst Rev. 2013; (4):CD007417.

5. Park, Y.H., Nam, H.W. (2013). Clinical features and treatment of ocular toxoplasmosis. Korean J Parasitol. 51(4): 393-9.
6. Graff, J.M., Russell, S.R. (2007) Acquired Ocular Toxoplasmosis: 42-year-old female with "fuzzy" vision for two weeks. EyeRounds.org. Available from: http://www.EyeRounds.org/cases/74-Acquired-Toxoplasmosis-Retina.htm. Published September 14, 2007.
7. Kianersi, F., Naderi Beni, A., Naderi Beni, Z. (2012) Clinical manifestation and prognosis of active ocular toxoplasmosis in Iran. Int Ophthalmol. 32(6): 539-45.
8. Bosch-driessen, L.E., Berendschot, T.T., Ongkosuwito, J.V., Rothova, A. Ocular toxoplasmosis: clinical features and prognosis of 154 patients. Ophthalmology. 109(5): 869-78.
9. Johnson, M.W., Greven, G.M., Jaffe, G.J., Sudhalkar, H., Vine, A.K. Atypical, severe toxoplasmic retinochoroiditis in elderly patients. Ophthalmology. 104(1): 48-57.
10. Holland, G.N. (2004) Ocular toxoplasmosis: a global reassessment. Part II: disease manifestations and management. Am J Ophthalmol. 137(1): 1-17.
11. Dodds, E.M., Holland, G.N., Stanford, M.R., Yu, F., Siu, W.O., Shah, K.H., Ten Dam-van Loon, N., Muccioli, C. Hovakimyan, A., Barisani-Asenbauer T., International Ocular Toxoplasmosis Research Group. (2008) Intraocular inflammation associated with ocular toxoplasmosis: relationships at initial examination. Am J Ophthalmol. 146(6): 856-65.e2.