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Typically active ocular toxoplasmosis: a case report



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ABSTRACT

Background: Ocular toxoplasmosis, a potentially blinding and non-curable disease with a progressive and relapsing course, is the most common cause of infectious posterior uveitis. Infection may be congenital or acquired through ingestion of uncooked meat, contaminated vegetables, or water of different parasite *Toxoplasma gondii*.

Case Presentation: We report a case of a 58-year-old female who came with blurred vision and floaters in her left eye for a month. She had contact with cats, birds, and dogs, as well as eaten raw food before. On examination, anterior segments were normal with visual acuity of 6/6 in the right eye and 6/9 in the left eye. Fundus examination revealed a vitreous haze with a yellow-white exudate located between pupil and macula. Since the disease's progress may lead to recurrence and potential blindness, it must

be recognized clinically, and treatment should be started as early as possible, especially in the active period. Our patient was treated with oral trimethoprim (160 mg)/sulfamethoxazole (800 mg) twice daily and topical eye drops of prednisone four times daily on the left eye. These drugs were prescribed instead of sulfadiazine/pyrimethamine, which is classical and standard therapy. After 4 weeks, the fundus examination showed the toxoplasmic lesion was significantly decreased in size, and vitreous haze was improved.

Conclusion: Trimethoprim-Sulfamethoxazole regimens as the alternative option for active ocular toxoplasmosis also shows significant improvement with less adverse effect.

Keywords: retinochoroiditis, toxoplasma, trimethoprim, sulfamethoxazole

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INTRODUCTION

Ocular toxoplasmosis represents the most common cause of infectious retinochoroiditis in many countries, approximately 23-30% of the population worldwide.^{1,2} It is a potentially blinding, progressive, recurring, and non-curable disease caused by the intracellular parasite *Toxoplasma gondii*. Infection mainly occurs by eating raw or undercooked meat containing tissue cysts of *T. gondii* or by eating food or drinking water contaminated by the oocysts spread by cats as the definitive hosts. Ocular toxoplasmosis can be congenital, acquired, or recurrent. It may be active or inactive in the form of a scar affecting the posterior fundus. Typical symptoms are blurred vision, floaters, and metamorphopsia.^{1,2} It mostly presents as focal necrotizing retinitis involving the inner retinal layers appearing as a circular whitish fluffy lesion with surrounding retinal edema, localized or diffuse vitritis, and granulomatous anterior uveitis. In healthy patients, the retinitis heals within 1-4 months of treatment and is replaced with a sharply demarcated atrophic scar with pigmented borders. Currently, there is no absolute treatment approach for the disease, but classic treatment for ocular toxoplasmosis consists

of triple therapy: Pyrimethamine, sulfadiazine, and prednisone with additional folic acid to prevent bone marrow suppression.^{2,3} However, a combination of trimethoprim-sulfamethoxazole as an alternative treatment option was shown recently to have similar efficacy to classical therapy in a randomized clinical trial.

CASE PRESENTATION

A 58-year-old female came with complaints of blurred vision and floaters in the left eye for a month. She had contact with cats, birds, and dogs, as well as eaten raw food prior to her current condition. Visual acuity in the right eye was 6/6 and 6/9 in the left eye with normal intraocular pressure in both eyes. Mild clouding of the lens in the left eye was found. Fundus examination revealed a vitreous haze along with a yellow-white exudate located between the optic disc and macula. Spectral-domain optical coherence tomography (SD-OCT) showed hyper-reflectivity on the retinal layer and disorganized retinal structure. Moreover, a thickened choroid under the active lesion was also noted. On laboratory examination, the serum titers of IgG antibodies against *Toxoplasma gondii* was found to

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be >300 IU/mL (normal ≤ 4 IU/mL). Based on the clinical features and laboratory findings, a diagnosis of toxoplasma retinochoroiditis was made.

The patient was treated with oral trimethoprim (160 mg)/sulfamethoxazole (800 mg) twice daily and topical eye drops of prednisone four times daily on the left eye. After 4 weeks of treatment, the visual acuity of the left eye was 6/9, and intraocular pressure was stable. Fundus examination and photography demonstrated a decrease in vitreous opacity, and the toxoplasmic lesion was smaller in size. The course of oral trimethoprim/sulfamethoxazole was continued for another 4 weeks. The patient was advised to visit the clinic every week, and then after the disease subsided, she was advised for a regular six-monthly to yearly follow-up to detect recurrences.



Figure 1. Vitritis and yellow-white exudates showed in fundus photography (before treatment)

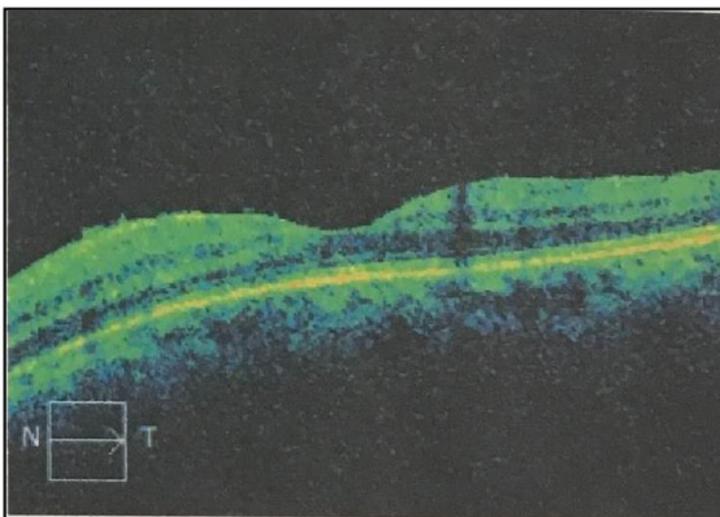


Figure 2. SD-OCT showed hyper-reflectivity on the retinal layer and thickened choroid

DISCUSSION

Toxoplasma gondii is an obligate, intracellular, protozoan parasite that caused retinochoroiditis in humans. The prevalence of the disease varies based on geographic regions and environments, i.e., climates, eating habits, and hygiene status, approximately 25-30% of the worldwide population.^{1,2} Cats are the definitive hosts of *Toxoplasma gondii*, while humans and other species may serve as intermediate hosts. The main route of transmission is ingestion of oocysts from the cat feces in the soil or tissue cysts in uncooked meat. Oocysts in contaminated vegetables, fruits, and water can also be the route of infection. Congenital infection in the fetus occurs via the placenta bloodstream. Other modes of transmission include blood transfusion and organ transplantation with an infective form of the parasite.^{3,4} Once the parasites reach the eye, they make a focus inflammation and result in developing retinitis.⁵ The lesion classically begins in the superficial layer of the retina, but as the inflammation progresses, the deeper retinal layer, as well as the choroid and sclera, can become involved.^{1,2} Host immune response then will induce the transformation of the parasite form, from tachyzoites to bradyzoites and their encystment. The cysts remain inactive in the scar for a long period. However, when the cysts rupture, they release organisms into the surrounding retina; thus, reactivation of the retinitis may occur. The reactivation of retinitis occurs at the border of old scars.^{5,6}

As a potentially blinding disease, ocular toxoplasmosis must be recognized clinically, and treatment should be started as early as possible, especially in the active period. This case demonstrated the typical findings of ocular toxoplasmosis, which is focal necrotizing chorioretinitis appearing as a whitish fluffy lesion with vitritis. The typical toxoplasmic lesion is usually near or at the border of an old pigmented and/or atrophic scar (satellite lesions) and seen at the posterior pole of the fundus.^{3,6} An active retinochoroidal lesion usually heals within 1-4 months in healthy patients and is replaced with a sharp demarcated atrophic scar with a pigmented border, which resolves from the periphery to the centre.⁷ Few patients may develop foci of inflammation within or adjacent to the optic nerve head. It is commonly associated with vitritis, ranging from mild to severe vitritis. Severe vitritis gives a “headlight in the fog” appearance, a bright white reflex seen when one shines the light of the indirect ophthalmoscope into the back of the eye.⁶

SD-OCT examination in this patient documented a hyper-reflectivity on the retinal layer and disorganized retinal structure as well as thickened



Figure 3. Four weeks after treatment, the toxoplasmic lesion was smaller in size and vitreous opacity was decreased

choroid under the active lesion. These findings are in line with the literature, which states disruption, thickening, and hyperactivity of the neurosensory retina with photoreceptors interruption and elevation of retinal pigment epithelial layers are the typical findings in toxoplasmic retinochoroiditis lesions. The acute phase also shows thickening and hypo-reactivity of the choroid beneath the lesion.^{8,9} The old and inactive scar is seen with a demarcated and thinning border on funduscopy examination. SD-OCT picture shows disorganized neurosensory retina, deprivation of photoreceptors, and retina pigment epithelial layer atrophy. Normal choroid structure beneath inactive scar lesion is barely identified.⁸

The diagnosis of ocular toxoplasmosis is clinical, based on the medical history and clinical findings on slit-lamp or funduscopy examination that is consistent with *Toxoplasma gondii* infection of the retina. Various serology tests that are helpful for diagnosing include the Sabin-Feldman dye test, indirect fluorescent antibody test, immunosorbent agglutination assay, and ELISA.¹⁰ *Toxoplasma gondii* antibody titers in ocular fluid or polymerase chain reaction (PCR) of aqueous or vitreous fluid are other latest tools to confirm the disease.¹¹ Sabin-Feldman dye test uses *Toxoplasma gondii* tachyzoites to detect IgG antibodies and the classic gold standard for serology testing, but it is not frequently used due to the risk of laboratory-acquired infection.³ ELISA is more commonly used as it can simultaneously test larger samples, and the results are objective. It measures IgG and IgM

antibody levels in the serum or ocular fluid. Serum IgM and IgG antibodies develop within 1-2 weeks after infection and become undetectable after 6-9 months for IgM antibodies while IgG antibodies last throughout life with varying titers.³ Positive results of the antibody titers with significant multiplications of 4 times or conversion from negative to a positive result of IgG antibody titers within 2-3 weeks may confirm the diagnosis.³ Our patient IgG antibodies serum titer against *T. gondii* was found to be elevated, which confirmed the diagnosis.

The aims of the treatment are to reduce the risk of permanent visual impairment by reducing the size of the scar, the risk of recurrence, and the severity and duration of the symptoms. The current suggested treatment options act against the tachyzoite form of *Toxoplasma gondii*; thus, the elimination of bradyzoite (cysts) form is not accomplished. Hence, these treatments are effective in the acute phase while they still carry risks of reactivation from chronic/past infection.¹¹ Although there is no consensus regarding the best treatment for ocular toxoplasmosis, classic “triple-drug therapy” of pyrimethamine (loading dose 50-100 mg; therapeutic dose 25-50 mg/day), sulfadiazine (therapeutic dose 4x1 g/day), and corticosteroids have been the most commonly used drugs combination.¹¹⁻¹³ Corticosteroids are used to suppress inflammation and minimize chorioretinal damage.³ Hence, these classic drugs combination is a good choice for sight-threatening lesion. Pyrimethamine may cause myelosuppression (leukopenia and/or thrombocytopenia), so folic acid 5-10 mg/day is added, and a blood test is done every 2 weeks during the treatment period. Skin rash, gastrointestinal disorders, kidney stones, and Steven-Johnson syndrome are the side effects of the sulfa component in the regiment. Sulfa can be replaced with oral Clindamycin 300 mg, 4 times daily, Azithromycin 500 mg/day, or Atovaquone 750 mg, 2-4 times daily.¹¹⁻¹³

Our patient was treated with Trimethoprim-Sulfamethoxazole instead of using a combination of sulfadiazine/pyrimethamine, which is the classical and standard regiments for ocular toxoplasmosis. As stated in the literature, a combination of trimethoprim-sulfamethoxazole (160 mg/800 mg, 2x/day) is also safe as the substitution of pyrimethamine-sulfadiazine in treating ocular toxoplasmosis.³ A combination of trimethoprim-sulfamethoxazole was shown recently to have similar efficacy to classical therapy in a randomized clinical trial. As sulfamethoxazole has some adverse effects in bone marrow, it is contraindicated in pregnancy, babies under 2 months old, severe renal/

hepatic failure, serious hematological disorders, and individuals who are sensitive to trimethoprim and sulfamethoxazole.¹⁴ These regimens are also recommended for prophylaxis against *Toxoplasma* infection, especially for patients who have severe or frequent recurrences, lesions adjacent to the fovea, or any critical position that increases the risk of vision loss.¹⁰ Alternatively, intravitreal injection of Clindamycin and dexamethasone are acceptable as Clindamycin is non-toxic to the retina, can cross the ocular barrier, and penetrates cells well.³ Clindamycin 1,5 grams injection has a half-life of 5-6 days and is given every 1-2 weeks. The intravitreal injection may increase patient convenience, better systemic side effects, greater drug availability, and fewer follow-up visits and blood work-up.

Systemic corticosteroids (0,25-0,75 mg/kg, not more than 60 mg/day) can be started 48 hours after starting anti-parasitic drugs in immunocompromised patients. Main indications are severe vitreous inflammation, decreased vision, the proximity of lesions to the fovea or optic disk, and the large size of the active lesion. The preferred oral corticosteroid is prednisone at a dose of 0,5-1,0 mg/kg/day. Topical corticosteroids are also used by ophthalmologists, with the main indications include ocular pain, redness, photophobia, moderate to severe anterior chamber inflammation, and elevated intraocular pressure.¹¹

Complications from ocular toxoplasmosis include chronic iridocyclitis, cataract, secondary glaucoma, band keratopathy, cystoid macular edema, retinal detachment, and optic nerve atrophy. Choroidal neovascularization has also been reported as one of the complication.¹⁵

Ocular toxoplasmosis is usually recurrent due to reactivation of the parasite, which is difficult to be eradicated completely with the current treatment options. Studies reported a 5-year recurrence rate was 79%, and some patients had multiple recurrences.¹⁶ The visual outcome after the treatment is also based on the location of the lesion and complications afterward. A lesion located near the macula will cause more severe visual impairment.

CONCLUSION

On top of the classic treatment for ocular toxoplasmosis, Trimethoprim-Sulfamethoxazole regimens as the alternative option for active ocular toxoplasmosis also shows significant improvement with less adverse effect. Moreover, the standard treatment is expensive, might have major adverse effects, and could not be readily available in some countries. As presented in this case report, the regiments resulted in a good outcome with

significant improvement.

Being a potentially blinding disease, ocular toxoplasmosis preventive measures should be taken, such as proper handwashing and satisfactory food hygiene. Newer treatment options need to be effective in preventing and treating the disease with lower doses of drugs, better patient compliance, cost reduction, and fewer adverse effects. Moreover, prophylaxis to the disease needs to be advised, especially for immunocompromised and recurring patients.

CONFLICT OF INTERESTS

There is no competing interest regarding the manuscript.

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AUTHOR CONTRIBUTION

Priscilla Dwianggita is responsible for the study from the conceptual framework.

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