

Rare Manifestation of Acute Blindness in Ocular Toxoplasmosis: A Case Report

Manifestación raras de ceguera aguda en toxoplasmosis ocular:
reporte de un caso

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SUMMARY

Introduction: Toxoplasmosis is one of the most common zoonoses worldwide. Clinical manifestations of ocular toxoplasmosis are highly specific. Atypical manifestations are not uncommon and are not always recognized as specific to ocular toxoplasmosis. Here, we present a rare manifestation of acute blindness in ocular toxoplasmosis in an immunocompetent patient.

Case Illustration: A 48-year-old female presented with a 1-week history of sudden blurry vision of the left eye. The patient denied any details about the redness or pain in the eye or the eye injury. Headache, fever, and abdominal pain were reported as the other symptoms. She has contact with the cat. The ophthalmological examination revealed abnormal visual acuity not improved by the pinhole and abnormal posterior segment. Anti-toxoplasma Immunoglobulin antibodies in serum were detected using a Chemiluminescence Microparticle Immunoassay (CMIA), which revealed positive. The diagnosis of neuro retinitis toxoplasmosis

was established. The patient started treatment with clindamycin, pyrimethamine, and methylprednisolone. After 25 days of treatment, the patient had clinical improvement which is normal visual acuity, Ishihara color testing, and posterior segment.

Conclusion: Blurry vision can occur in ocular toxoplasmosis. Identification and adequate treatment can reduce the risk of permanent visual impairment, recurrence, severity, and duration of acute symptoms.

Keywords: Blindness, toxoplasmosis, ocular, immunocompetent.

RESUMEN

Introducción: La toxoplasmosis es una de las zoonosis más comunes a nivel mundial. Las manifestaciones clínicas de la toxoplasmosis ocular son muy específicas. Las manifestaciones atípicas no son infrecuentes y no siempre se reconocen como específicas de la toxoplasmosis ocular. Aquí presentamos una rara manifestación de ceguera aguda en la toxoplasmosis ocular en pacientes inmunocompetentes.

Ejemplo de caso: Una mujer de 48 años de edad se presentó con una historia de 1 semana de visión

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borrosa repentina en el ojo izquierdo. La paciente negó cualquier detalle sobre el enrojecimiento o el dolor en el ojo o la lesión en el ojo. El dolor de cabeza, la fiebre y el dolor abdominal se informaron como los otros síntomas. Ella tiene contacto con un gato. El examen oftalmológico reveló agudeza visual anormal no mejorada por estenopeico y segmento posterior anormal. Se detectaron anticuerpos de inmunoglobulina anti-toxoplasma en suero mediante un inmunoensayo de micropartículas de quimioluminiscencia (CMIA), que resultó positivo. Se estableció el diagnóstico de neurorretinitis toxoplásmica. El paciente inició tratamiento con clindamicina, pirimetamina y metilprednisolona. Después de 25 días de tratamiento, el paciente tuvo una mejoría clínica como es agudeza visual, prueba de color de Ishihara y segmento posterior normales.

Conclusión: *La visión borrosa puede ocurrir en la toxoplasmosis ocular. La identificación y el tratamiento adecuado pueden reducir el riesgo de discapacidad visual permanente, recurrencia, gravedad y duración de los síntomas agudos.*

Palabras clave: *Ceguera, toxoplasmosis, ocular, inmunocompetente.*

INTRODUCTION

One of the most prevalent zoonoses in the world is toxoplasmosis. In adults, the seroprevalence of antibodies to *Toxoplasma gondii* ranges from 22.5% to more than 80.0% (1). Our poor understanding of the pathophysiology of ocular toxoplasmosis is reflected by our inability to unequivocally confirm a clinical diagnosis based on laboratory tests. Although the clinical manifestations of the disease are usually very specific, atypical manifestations are not uncommon, and these are not always recognized as specific for ocular toxoplasmosis even by experienced ophthalmologists. This situation raises questions about the sensitivity and specificity of clinical diagnosis, which, in the absence of sufficiently sensitive laboratory tests for this disease, are still considered the gold standard (2).

The diagnosis of ocular toxoplasmosis can be helped by the results of serological tests although this is not in itself conclusive. Patients with ocular toxoplasmosis are always positive for *Toxoplasma*-specific Immunoglobulin G (IgG), but also infected individuals who show

no signs of ocular involvement. Therefore, the detection of *Toxoplasma*-specific IgG has a low diagnostic value (3). In some patients, *Toxoplasma*-specific IgM can be detected in the serum, which may indicate a recently acquired infection. However, in the case of acute infection, an equivocal or positive result has no diagnostic value. If serological data confirm the presence of a recently acquired infection, then the alternative of a reactivated latent state can be excluded. The absence of specific antibodies provides strong evidence for the origin of toxoplasmosis in ocular disease. The parasite itself has been detected in the peripheral blood of both patients with ocular toxoplasmosis and controls (4).

Ocular toxoplasmosis rarely results in blindness in immunocompetent patients and is usually asymptomatic. However, blindness can still occur. Appropriate identification and treatment can reduce morbidity in ocular toxoplasmosis patients. This case illustrates the rarity of the presentation of acute blindness in an ocular toxoplasmosis immunocompetent patient.

CASE ILLUSTRATION

A 48-year-old female came with a main complaint of a sudden blurred left eye in the middle pointing to the upper left like being covered by fog since 1 week ago. The patient reported only seeing the bottom of the eye with the left eye. Headache at the back of the head appeared intermittent since 1 week ago. Previously, the patient had a fever and abdominal pain 2 weeks ago for 3 days. The patient had no complaints of double vision, pain when glancing, fever, weakness, shortness of breath, joint pain, red face, nausea, vomiting, or diarrhea to exclude the presence of autoimmune disease. The patient has no history of trauma, diabetes mellitus, hypertension, stroke, autoimmune disease, cancer, and HIV. The patient frequently contacts her cat, which she pets at home.

Ophthalmological examination found visual acuity of 5/5 on the right eye and 5/20 but not improved by pinhole on the left eye, intraocular pressure of the right and the left eye were 19.3 and 19.5 mmHg, Ishihara color test of the right and the left eye were 14/14 and 1/14, the field of view (confrontation test) can count fingers

in all quadrants, ocular motility can be in any direction without pain, the tangent screen of the left eye found central scotoma, anterior segment examination was normal with a negative relative afferent pupillary defect on the right eye, posterior segment examination on the right eye was normal but the posterior segment on the left eye found superior and inferior nasal blurred optic nerve head margin, hyperemia, peripapillary hemorrhage, retina hemorrhage, peri-macular, and star-shaped exudate with negative macular reflects and still positive fundus reflects (Figure 1).



Figure 1. Posterior segment examination on the left eye before treatment. Fundoscopy showed a) hyperemic and blurred optic nerve head in the superior and inferior nasal border and b) star-shaped exudate with negative macular reflections.

Routinely laboratory examination was found. The patient was tested for antibodies with an Abbot Alinity tool[®] using a chemiluminescence microparticle immunoassay (CMIA) reagent. Toxoplasma and Cytomegalovirus (CMV) antibody was reactive (Table 1). Acquired immunosuppression was excluded. Serology for HIV was non-reactive. A head magnetic resonance imaging (MRI) was normal. The patient's assessment was neuro retinitis toxoplasmosis on the left eye with therapy initiated were clindamycin 300 mg orally every 8 hours, pyrimethamine 25 mg orally every 8 hours, methylprednisolone 62.5 mg IV bolus every 6 hours.

Table 1. Laboratory testing

Test	Result	Reference range
IgM-Toxoplasma	4.039	reactive >2.6
IgG-Toxoplasma	1.821	reactive >8
IgM-anti-CMV	2.73	reactive > 4.2
IgG-anti-CMV	3	reactive > 2

Outcome and follow-up

Four days later, the patient was re-evaluated and presented an improvement in her vision. The methylprednisolone dose was lowered to 62.5 mg intravenous bolus every 12 hours. On the seventh day of treatment, the patient's eyes have a significant improvement and the methylprednisolone dose was changed to 62.5 mg IV bolus every 24 hours. Patients were discharged on day 7 with the therapy of methylprednisolone 16 mg orally every 8 hours, clindamycin 300 mg orally every 8 hours, Pyrimethamine 25 mg orally every 8 hours, and maintained for 6 weeks. In outpatient follow-up, the patient's eyes have a significant improvement. Ophthalmology examination found improvement in visual acuity (10/20), and Ishihara color testing (5/14). However, posterior segment examination still found blurred superior and inferior nasal optic nerve head margin, hyperemic, and peripapillary hemorrhage in the left eye. On the twenty-fifth day of treatment, a significant improvement with normal visual acuity, Ishihara color testing, and posterior segment (Figure 2).

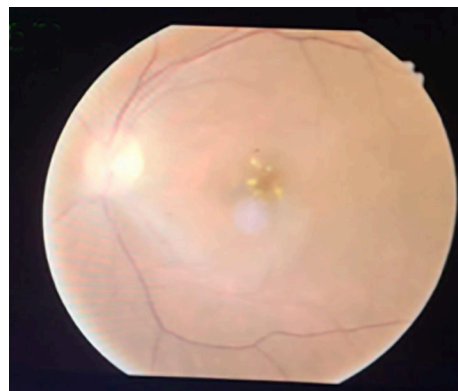


Figure 2. Follow-up of posterior segment examination on the left eye after treatment. Fundoscopy showed improvement, the exudate was decreased.

DISCUSSION

A common side effect of immunodeficiency conditions, such as those brought on by cancer, steroid and cytotoxic medication therapy, and AIDS, is disseminated toxoplasmosis. Ocular toxoplasmosis (OT) does not need immune suppression to occur. It is thought to represent either a reactivation of congenital infection or a postnatally acquired infection by a parasite (5). In immunocompetent patients, typical OT often presents with white focal retinitis and overlying vitreous inflammation (also known as the headlight in the fog sign) (6). Toxoplasma-associated chorioretinitis is usually a self-limiting infection and generally resolves spontaneously within 4-8 weeks (5). The most common cause of posterior uveitis is OT and is the result of acquired or congenital infection by the parasite *Toxoplasma gondii* with sources of infection are food and water contaminated with oocysts from cat feces or meat contaminated with tissue cysts. Congenitally acquired OT results from vertical transmission from mother to child, and may be evident at birth or later. Postnatally acquired OT becomes apparent when symptoms associated with active retinocortical lesions appear (7).

The prevalence of toxoplasma is estimated that 25 %-30 % of the world's population is infected (8). In immunocompetent patients in Brazil, the prevalence of OT ranges from 6 to 18 percent (9). In a prior study, 24 % of individuals with OT experienced legal blindness (10). More virulent *Toxoplasma* strains cause more frequent and more severe forms of OT in immunocompetent patients in tropical regions, especially in South America. Additionally, it has been demonstrated that IL17 inhibits parasite control while enhancing pathology in the eye (11). Most patients present with uveitis secondary to ocular toxoplasmosis in their second to fourth decades of life (12). The advanced age of the patient at the first manifestation has an impact on the risk of recurrence as well. The relative risk for individuals aged 40 years was significantly increased and may be related to reduced immune defenses in the aging host (13).

The most common manifestation of ocular toxoplasmosis is *Toxoplasma retinochoroiditis* (TR) which is usually a unilateral, unifocal

retinocortical lesion associated with vitritis. Granulomatous anterior chamber inflammation is common, and retinal vasculitis (usually arteriolitis) occurs in about one-third of patients. Vision loss may be permanent due to macular scar formation or optic atrophy (14). Optic nerve involvement is less common but can cause severe visual field defects as well as loss of color vision. Scotoma is directly related to the size and location of the retinochoroidal scar during the inactive parasite stage. The classic ocular manifestations of toxoplasmosis are a fine white nidus, focal necrotizing retinitis, or contiguous retinochoroiditis with a variable pigmented chorioretinal scar. Often active lesions are obscured by severe vitritis resulting in the classic 'headlights in the fog' sign (15). In this case, it is in line with that we found visual acuity and the Ishihara color test is abnormal on the left eye, tangent screen found central scotoma and posterior segment examination on the left eye found superior and inferior nasal blurred optic nerve head margin, hyperemia, peripapillary hemorrhage, retina hemorrhage, peri-macular, and star-shaped exudate with negative macular reflects and still positive fundus reflects.

Serological testing is often the first step in diagnosis using IgG and IgM antibodies. IgM antibodies appear immediately after acute infection, increasing from 5 days to several weeks and reaching a maximum after 1 to 2 months, and decreasing more rapidly than IgG reaching a maximum in 1 month. If both IgG and IgM are negative, this indicates the absence of infection or a very recent acute infection. If the test shows positive IgG and negative IgM, this indicates a long-standing infection (infection more than 1 year ago). If both IgG and IgM are positive, this indicates a recent infection or a false positive test result. If an acute infection is suspected, retesting is recommended in 2 to 3 weeks. A 4-fold increase in IgG antibody titer between tests indicates recent infection (16). In this case, we found reactive IgM-Toxoplasma.

Even though the absence of IgG antibodies almost excludes the probability of ocular illness, false-negative results can occasionally be seen. In those with typical fundus characteristics but negative IgG test results, it is crucial to integrate several serological test systems. There may also be several unusual clinical signs and symptoms

of freshly acquired ocular toxoplasmosis (e.g., large active lesions without a scar). In many situations, determining the disease's cause requires laboratory validation. Setting a precise clinical diagnosis can be difficult because other conditions that can cause uveitis, including toxocariasis, multifocal choroiditis, punctate inner choroidopathy, acute posterior multifocal placoid pigment epitheliopathy, histoplasmosis, acute retinal necrosis syndrome (caused by the herpes simplex virus and varicella-zoster virus), tuberculosis, sarcoidosis, serpiginous choroiditis, syphilis, endophthalmitis, and ocular lymphoma may present with some clinical features of toxoplasma retinochoroiditis. In these circumstances, more laboratory testing is necessary to find additional potential infections (17).

Failure to respond to antiviral therapy leads clinicians to diagnose ocular toxoplasmosis (18,19). Treatment is recommended for lesions within the vascular arcade, adjacent to the optic disc, or larger than 2 optic disc diameters to reduce the possibility of visual loss (20). Antibiotics and corticosteroids have been the mainstay of pharmacologic therapy. Treatment is given to reduce the risk of permanent visual impairment (aiming to reduce the size of the retinochoroidal scar), the risk of recurrence, and the severity and duration of acute symptoms. Antibiotics are usually given for 6 to 8 weeks. Steroids are also sometimes used to decrease the severity of intraocular inflammation symptoms (21-23). Indications for corticosteroid use include severe vitreous inflammation, decreased vision, the proximity of the lesion to the fovea or optic disc, and large active lesion size. The preferred drug for oral corticosteroids is prednisone at a dose of 0.5-1.0 mg/kg/day (20,24). The combination of pyrimethamine and sulfadiazine has synergistic effects at different steps of nucleic acid synthesis in *T. gondii*, and corticosteroids have remained the classic 'triple drug therapy' (23). A study showed patients treated with triple-drug therapy showed a greater reduction in retinal lesion size compared with patients receiving other treatment regimens or no treatment (25). Clindamycin concentrates on the ocular tissue and penetrates the cyst wall of the tissue, often added to classic triple therapy as part of 'fourfold therapy' (20). Long-term

intermittent treatment in immunocompetent patients decreased the recurrence of the disease from 24 to 7 % during a 20-month follow-up period (26). In this case, patients had resolution of active retinochoroiditis and improved vision with clindamycin, pyrimethamine, and methylprednisolone therapy.

Toxoplasmic chorioretinitis does not need immunocompromising to occur. Since ocular toxoplasmosis is a potentially blinding disease, preventive measures should be taken to avoid it. Proper washing of hands and strict food hygiene is important. In this case, a serological examination is performed to confirm the diagnosis so that the patient can be given the right therapy.

CONCLUSION

Ocular toxoplasmosis can cause blurry vision and potentially trigger permanent blindness. Recurrence, intensity, and duration of acute symptoms can all be decreased with early detection and appropriate treatment. Clindamycin, pyrimethamine, and methylprednisolone can be treatment options.

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Conflicts of interest

All of the authors declare no conflict of interest-

REFERENCES

1. Maenz M, Schlüter D, Liesenfeld O, Schares G, Gross U, Pleyer U. Ocular toxoplasmosis past, present and new aspects of an old disease. *Prog Retin Eye Res.* 2014;39:77-106.
2. Stanford MR, See SE, Jones LV, Gilbert RE. Antibiotics for toxoplasmic retinochoroiditis: An evidence-based systematic review. *Ophthalmology.* 2003;110(5):926-932.

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3. Chapman DJ, Ashburn D, Ogston SA, Ho-Yen DO. The relationship between ocular toxoplasmosis and levels of specific toxoplasma antibodies. *Epidemiol Infect.* 1999;122(2):299-303.
4. Bou G, Figueroa MS, Martí-Belda P, Navas E, Guerrero A. Value of PCR for Detection of *Toxoplasma gondii* in Aqueous Humor and Blood Samples from Immunocompetent Patients with Ocular Toxoplasmosis. *J Clin Microbiol.* 1999;37(11):3465.
5. Holland GN, Lewis KG. An update on current practices in the management of ocular toxoplasmosis. *Am J Ophthalmol.* 2002;134(1):102-114.
6. Chang CH, Hung JH, Hsu SM. Ocular toxoplasmosis in a patient with acquired immunodeficiency syndrome. *Lancet Infect Dis.* 2023;23(1):130.
7. Feliciano-Alfonso JE, Vargas-Villanueva A, Marín MA, Triviño L, Carvajal N, Moreno M, et al. Antibiotic treatment for ocular toxoplasmosis: A systematic review and meta-analysis: Study protocol. *Syst Rev.* 2019;8(1).
8. Sholehen A, Pralampito F, Galih A, Ghaus A, Airina A, Purnami N. The role of family intervention in early detection of congenital deafness: A case study. *J Comm Med Public Health Res.* 2020;1(2):97-104.
9. Dubey JP, Lago EG, Gennari SM, Su C, Jones L. Toxoplasmosis in humans and animals in Brazil: High prevalence, high burden of disease, and epidemiology. *Parasitology.* 2012;139:1375-1424.
10. Kim M, Choi SY, Won JY, Park YH. Patterns of ocular toxoplasmosis presenting at a tertiary eye care center in Korean patients. *Medicine.* 2018;97:15.
11. Greigert V, Bittich-Fahmi F, Pfaff AW. Pathophysiology of ocular toxoplasmosis: Facts and open question. *PLoS Negl Trop Dis.* 2020;14(12).
12. Dodds EM, Holland GN, Stanford MR, Yu F, Siu WO, Shah KH, et al. Intraocular Inflammation Associated with Ocular Toxoplasmosis: Relationships at Initial Examination. *Am J Ophthalmol.* 2008;146(6).
13. Holland GN, Crespi CM, ten Dam-van Loon N, Charonis AC, Yu F, Bosch-Driessen LH, et al. Analysis of recurrence patterns associated with toxoplasmic retinochoroiditis. *Am J Ophthalmol.* 2008;145(6).
14. Harrell M, Carvounis PE. Current treatment of *Toxoplasma retinochoroiditis*: An evidence-based review. *J Ophthalmol.* 2014;2014.
15. Park YH, Nam HW. Clinical features and treatment of ocular toxoplasmosis. *Korean J Parasitol.* 2013;51(4):393-399.
16. Paquet C, Yudin MH. No. 285-Toxoplasmosis in Pregnancy: Prevention, Screening, and Treatment. *J Obstet Gynaecol Can.* 2018;40(8):e687-693.
17. Kalogeropoulos D, Sakkas H, Mohammed B, et al. Ocular toxoplasmosis: A review of the current diagnostic and therapeutic approaches. *Int Ophthalmol.* 2022;42(1):295-321.
18. Butler NJ, Furtado JM, Winthrop KL, Smith JR. Ocular toxoplasmosis II: Clinical features, pathology, and management. *Clin Exp Ophthalmol.* 2013;41(1):95-108.
19. Wibawani R, Soeprijanto B, Ferriastuti W, Triyono EA. Head Computed Tomography Images of HIV/AIDS Patients with Suspected Cerebral Toxoplasmosis in Dr. Soetomo General Hospital Surabaya. *Biomolecular and Health Sci J.* 2019;2(1):21-26.
20. Pradhan E, Bhandari S, Gilbert RE, Stanford M. Antibiotics versus no treatment for *Toxoplasma retinochoroiditis*. *Cochrane Database Syst Rev.* 2016;2016(5).
21. Eyles DE, Coleman N. Antibiotics in the treatment of toxoplasmosis. *Am J Trop Med Hyg.* 1953;2(1):64-69.
22. Nurdianto AR, Aryati A, Suryokusumo MG, Mufasirin M. Effect of hyperbaric oxygen therapy to IFN γ and TNF α expression in pregnant *Rattus norvegicus* infected with Tachyzoite of *Toxoplasma gondii*. *Bali Medical J.* 2019;8(1):94.
23. Nurdianto AR, Aryati, Suryokusumo MG, Mufasirin M, Suwanti LT, Sardjono TW, et al. Hyperbaric oxygen downregulates ICAM-1 expression in artery spiralis of pregnant *Rattus norvegicus* infected by Tachyzoite from *Toxoplasma gondii*. *Eurasia J Biosci.* 2020;14:1757-1762.
24. Yuliawati I, Nasronudin N. Pathogenesis, diagnostic and management of toxoplasmosis. *Indonesian J Trop Infect Dis.* 2015;5(4):100-105.
25. Rothova A, Meenken C, Buitenhuis HJ, Brinkman CJ, Baarsma GS, Boen-Tan TN, et al. Therapy for ocular toxoplasmosis. *Am J Ophthalmol.* 1993;115(4):517-523.
26. Silveira C, Belfort R, Muccioli C, Holland GN, Victora CG, Horta BL, et al. The effect of long-term intermittent trimethoprim/sulfamethoxazole treatment on recurrences of toxoplasmic retinochoroiditis. *Am J Ophthalmol.* 2002;134(1):41-46.