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A Reactivation of Ocular Toxoplasmosis during Pregnancy

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A Reactivation of Ocular Toxoplasmosis during Pregnancy

Abstract

Background: T*oxoplasma gondii* is a parasite estimated to affect over 500 million people worldwide. The feline is the definitive host for the parasite and infection may be acquired or congenital via maternal transmission. Humans may acquire the infection by ingestion of raw or undercooked meats and vegetables, contaminated water, or exposure to infected cat feces. The infection is often benign, self-limiting, and asymptomatic for humans, but potentially life threatening to infants or the immunocompromised patient.

Case Report: A 22 year-old Caucasian female, pregnant at 12 weeks gestation, presented to the optometry service with acute symptoms of hazy vision and a new gray stationary blind-spot in the inferior field of vision of the right eye. Clinical picture led to diagnosis of reactivated ocular toxoplasmosis.

Conclusion: Ocular toxoplasmosis primarily affects the retina, producing a retinochoroiditis with resultant scarring and potential blindness. Treatment with a combination of antibiotics and steroid may be required. Allergy history and current pregnancy were important factors to consider when determining treatment of our patient.

Keywords

Toxoplasma gondii, ocular toxoplasmosis, retinochoroiditis, uveitis

INTRODUCTION

Toxoplasmosis gondii is an intracellular parasite that affects over 36 million people in the United States and is the second leading cause of death from foodborne illness.[1-3] It affects approximately one third of people worldwide, with the highest prevalence in South America and Africa.[1,2,4,5] Infection rates vary greatly, with high concentrations in certain regions or cultures based on climate, food preparation, hygiene, cat population, and general healthcare. Using the feline as the host, the parasite can be either acquired or congenitally transmitted.

Acquired toxoplasmosis may occur by ingestion of raw or undercooked meats and vegetables, unpasteurized milk, or water contaminated with *Toxoplasma* oocytes. The infection may also be acquired via exposure to an infected feline, its feces, contaminated litter box or soil. Less common, is the transmission during organ transplant or blood transfusion. The acquired form of the infection in healthy individuals often goes undetected, with flu-like symptoms being the most common presentation. In the immunocompromised, the course may be more life-threatening due to the risk of encephalitis, pneumonia, or myocarditis.[1,6-8]

Congenital toxoplasmosis occurs when the primary infection of a woman is acquired just before or during pregnancy with transplacental transmission during gestation. The prevalence of congenital infection has been reported as high as 1 in 10,000 live births in the United States.[7,9,10] The incidence of congenital transmission increases with each trimester and may be as high as 80% in the third trimester.[11] However, the manifestations tend to be more severe the earlier in pregnancy the infection is acquired by the mother.[6,9,11-13] Sequelae can range from subclinical manifestations to perinatal death, with most complications presenting months to years after delivery.[9,14] The characteristic triad of congenital toxoplasmosis is hydrocephalus, cerebral calcifications, and retinochoroiditis.[9,11]

Ocular toxoplasmosis occurs in over 80% of congenital *Toxoplasma* infection, but only 1% of patients with the acquired infection.[7] However, serologic testing suggests more cases may be attributed to the acquired form than originally believed.[4,7,13] Ocular toxoplasmosis is often diagnosed based on characteristic retinal findings. Involvement of the macula or optic nerve may result in permanent damage and visual impairment. Treatment is aimed at preserving macular and optic nerve function.

Case Report

A 22 year-old Caucasian female presented to the optometry service with acute symptoms of hazy vision and a new gray stationary blind-spot in the inferior field of vision of the right eye. She also was experiencing mild light sensitivity, but no pain, flashes of light, or new floaters. Symptoms began approximately 3 days prior and had been persistent. She denied a history of ocular trauma or surgery. The patient had a history of ocular toxoplasmosis in the right eye at age 10 with recurrence at age 16, resulting in chorioretinal scars adjacent to the optic nerve. She was treated for the initial episode with clindamycin and oral prednisone at which time she experienced a significant anaphylactic reaction to clindamycin. The patient was 12 weeks pregnant when she presented for the most recent visit. Medical history was negative for diabetes, hypertension, and HIV/AIDS. She was on no medications and had a drug allergy to clindamycin.

The patient's uncorrected visual acuities with a Snellen chart measured 20/40 OD and 20/20 OS. Her visual acuity improved to 20/25-1 OD with pinhole testing. Amsler grid testing was abnormal in the right eye with a relative scotoma inferior to fixation. Her pupils were equal, round, reactive to light, and no afferent pupillary defect was noted in either eye. The slit lamp examination of the anterior segment showed multiple, fine keratic precipitates of the right cornea while the left cornea was clear. The anterior chamber of the right eye revealed grade 2 cells while the left eye was clear and quiet. The intraocular pressures were 15 mm Hg and 14 mm Hg in the right and left eyes, respectively, as measured by Goldmann applanation tonometry. A dilated fundus examination showed grade 3 cells throughout the anterior and posterior vitreous of the right eye only. The nerves appeared healthy with a cup-to-disc ratio of 0.15 and the retinal vessels showed normal course and caliber in both eyes. The right fundus was slightly difficult to assess due to the haze from the overlying vitritis. Two chorioretinal scars approximately 0.75DD and 0.50DD in size were noted within the superior temporal arcade adjacent to the right optic nerve. A third small chorioretinal scar was found along the superior temporal arcade of the right eye and adjacent to an elevated, white "fluffy" lesion with surrounding retinal edema nearly 1DD in size. The macula of the right eye exhibited an epiretinal membrane with traction toward the old chorioretinal scars, likely secondary to the contracting forces of the scar tissue (Figure 1). The peripheral retina was flat and intact 360 degrees in both eyes.

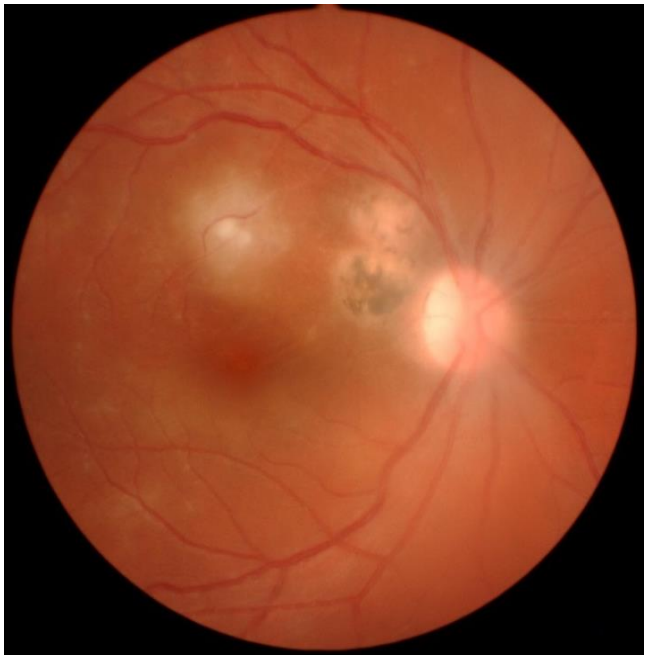

Figure 1. Fundus of the right eye at initial presentation exhibiting chorioretinal scars adjacent to the optic nerve, an epiretinal membrane with macular involvement, and an active toxoplasmosis lesion along the superior temporal arcade with an overlying vitritis.

The patient's history of ocular toxoplasmosis and classic clinical presentation led to the diagnosis of reactivated ocular toxoplasmosis during pregnancy. The patient was instructed to begin sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily. Due to the inflammatory spillover, prednisolone acetate 1% suspension every hour and scopolamine twice daily were prescribed for the anterior chamber reaction in the right eye. The patient was educated on the importance of adherence with the medical regimen and risk of vision loss. She was also instructed to monitor vision with an Amsler grid daily and call immediately if any changes occurred. The patient was to return to the clinic in 2 days for follow-up and consideration to begin oral prednisone.

The patient returned to the clinic 3 days later, having followed the medication regimen as prescribed. The hazy vision and stationary gray blind-spot in the inferior visual field of the right eye were stable. Her visual acuities remained correctable to 20/25-1 OD and 20/20 OS. The relative scotoma inferior to fixation was still present on the Amsler grid, but seemed less dark to the patient. Her right pupil was pharmacologically dilated and no afferent pupillary defect was noted in either eye on reverse testing. The anterior segment evaluation of the right eye was unchanged, with fine keratic precipitates of the cornea and grade 2 cells in the anterior chamber.

Grade 3 cells were present throughout the right vitreous. The chorioretinal scars along the superior temporal arcade and the epiretinal membrane in the right eye were stable. No changes were noted in the elevated white "fluffy" lesion adjacent to the small chorioretinal scar. The patient was instructed to continue sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily, prednisolone acetate 1% every hour and scopolamine twice daily in the affected eye. She was to continue daily monitoring of an Amsler grid and return to the clinic in 4 days.

One week after the initial visit the patient noted a subjective improvement in the vision of her right eye. She stated the stationary blind-spot inferiorly in that eye was smaller, less dark, and now described as a small brown spot. Her uncorrected distance visual acuities were 20/25-1 OD without improvement with pinhole testing and 20/20 OS. The relative scotoma inferiorly in the right eye with the Amsler grid appeared smaller and less dense. The affected corneal keratic precipitates had resolved and the anterior chamber reaction was improved with trace cells noted. The dilated fundus exam revealed grade 2 vitritis in the right eye. The old chorioretinal scars and epiretinal membrane were stable. The elevated white "fluffy" lesion in the right eye appeared slightly smaller with less surrounding retinal edema (Figure 2). The patient was instructed to continue sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily, scopolamine twice daily, and reduce prednisolone acetate 1% suspension to every 2 hours in the affected eye. She was to continue daily monitoring of an Amsler grid and return to the clinic in 1 week.

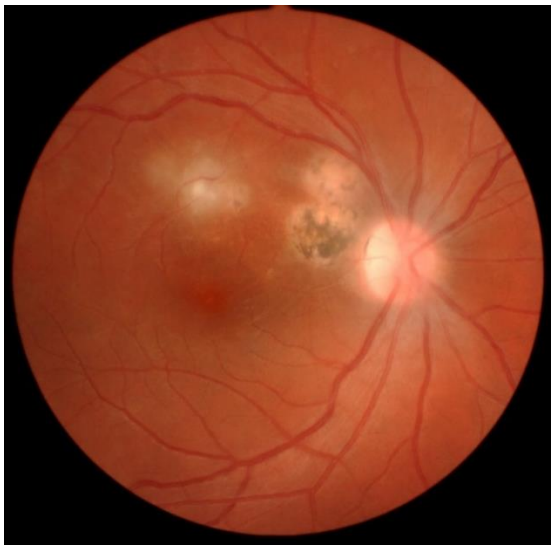

Figure 2. Fundus of the right eye 1 week after initiation of antibacterial therapy. Slight improvement is noted in the active toxoplasmosis lesion and overlying vitritis.

At 2 weeks, clinical and subjective findings remained relatively stable. The prednisolone acetate 1% suspension was reduced to 4 times per day, otherwise the medication regimen was continued. The patient noted further subjective visual improvement in the right eye at the 3-week follow-up examination. She stated her vision was no longer hazy and the inferior relative scotoma with the Amsler grid was still present, but "faded." Her best corrected visual acuities were 20/25+1 OD and 20/20 OS. The vision in her right eye was likely reduced secondary to the longstanding epiretinal membrane. The right eye anterior chamber reaction was resolved. The dilated fundus examination showed marked improvement of the posterior segment inflammation in the right eye. The vitreous haze was minimal with trace cells in the posterior chamber. The active lesion in the right eye was still elevated, but smaller with minimal surrounding retinal edema (Figure 3). The patient was instructed to continue sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily, taper prednisolone acetate 1% suspension as directed (three times per day for 1 week, then twice daily for 1 week, and once daily for 1 week), and discontinue scopolamine. She was instructed to monitor an Amsler grid daily and return to the clinic in 2 weeks.

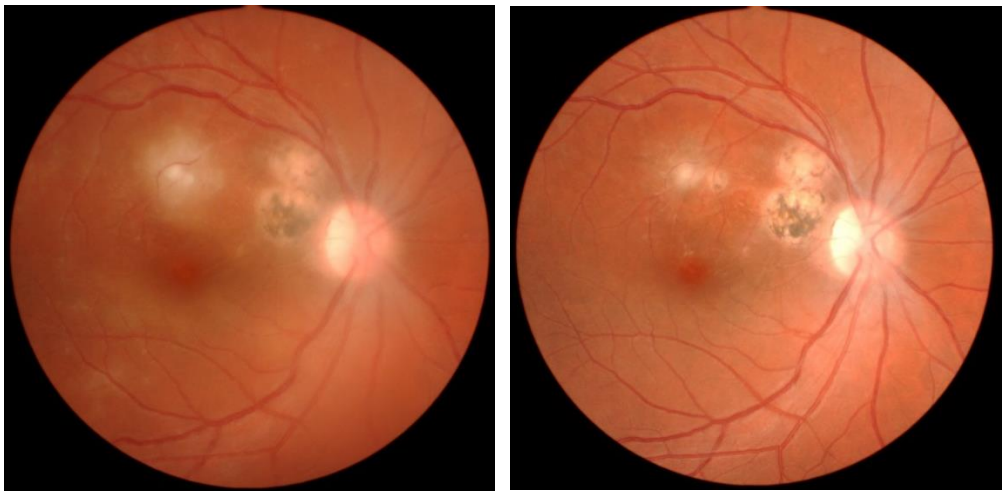

Figure 3. Fundus of the right eye comparing appearance at initial presentation (left) to appearance after 21 days of antibiotic therapy (right). Marked improvement in retinal lesion, overlying vititris, and patient symptoms were noted.

The patient returned to the clinic 2 weeks later (5 weeks after the initial visit). She was taking sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily and prednisolone acetate 1% suspension twice daily in the right eye with good adherence. She stated vision was "back to normal." The inferior scotoma of the right eye was stable. The visual acuities remained 20/25+1 with +0.25 sphere OD and 20/20 uncorrected OS. The anterior chamber was clear and quiet in each eye.

The dilated fundus examination in her right eye showed a resolution of the vitritis. The active toxoplasmosis lesion in the affected eye was dull white with minimal elevation and no surrounding edema. The patient was instructed to continue sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily for 1 week and then discontinue usage. She was to finish the prednisolone acetate 1% suspension taper with once daily dosing for 1 week and then discontinue usage. Education was provided to the patient regarding resolution of ocular findings and future signs, symptoms, and risk factors for recurrence of ocular toxoplasmosis. She was to return to the clinic in 4 months for follow-up.

DISCUSSION

Toxoplasmosis is a parasitic infection that affects over 2.5 billion people in the world.[1,4,5] It has been estimated that half the United States population are seropositive for *Toxoplasma* antibodies by the fourth decade. However, data suggests the prevalence has been on the decline, with approximately 14% seropositivity amongst individuals by 40 years of age.[2,15] *Toxoplasma gondii* accounts for the most cases of infectious posterior uveitis and may result in visual impairment.[8,16.17]

In ocular toxoplasmosis, active tachyzoites enter retinal cells causing a focal necrotizing retinochoroiditis resulting in an elevated, white "fluffy" lesion of the inner retinal layers with surrounding edema. The release of inflammatory cells and *Toxoplasma* antigens into the vitreous yield an overlying vitritis in virtually all cases.[4,6-8,10,12,13,17,18] Ocular toxoplasmosis is first noted between 15 and 35 years of age in 60% of cases and occurs bilaterally in 22 to 40% of all cases.[7-19] When transmitted congenitally, it is more often bilateral (85%) and has a higher predilection for the macula (58%).[19] Reactivation of the ocular infection occurs in 79% of cases within 5 years, with an average of 3 recurrences. It is most likely to reactivate within the first year of an active retinal infection.[4,7,18,19] The retinochoroiditis often recurs adjacent to inactive, pigmented scars and is believed to be due to the rupture of retinal cysts lying dormant near the location of prior infection.

Active retinochoroiditis from ocular toxoplasmosis causes symptoms in 90% of cases.[7] Symptoms may include floaters, photopsia, metamorphopsia, reduced vision, or visual field loss. Secondary complications occur in 33% of patients including anterior segment inflammation, cataract, secondary glaucoma, retinal vasculitis, choroidal neovascularization, retinochoroid vascular anastomoses (ciliary retinal shunt vessels), neuroretinitis, retinal detachment, and papillitis with secondary optic atrophy.[4,7,16] Severity of symptoms and visual impairment are

directly related to macular or optic nerve involvement and degree of vitritis. The long-term prognosis for nearly 25% of patients with ocular toxoplasmosis is best corrected visual acuity worse than 20/200 in at least one eye.[19]

Ocular toxoplasmosis is often diagnosed based on the characteristic focal necrotizing retinochoroiditis with overlying vitritis, or "headlight in the fog" appearance.[4,13] The differential diagnosis for ocular toxoplasmosis includes ocular histoplasmosis, sarcoidosis, tuberculosis, syphilis, ocular toxocariasis, fungal infection, cytomegalovirus, and a focal retinoblastoma in infants. The classic appearance, the presence of adjacent, inactive chorioretinal scars, and the prior history of ocular toxoplasmosis enabled the diagnosis of reactivated ocular toxoplasmosis to be made with confidence in this case. When the etiology is less clear, serological or molecular testing may be used to aid in diagnosis.

Toxoplasmosis acquired by an immunocompetent individual is often self-limiting and rarely requires treatment. Treatment is required for an acquired infection in the immunocompromised patient, pregnant women with suspected or confirmed primary *Toxoplasma gondii* infection, and any case of congenital toxoplasmosis regardless of symptoms.[11] Active retinochoroiditis is typically another indication for treatment, as demonstrated in our patient. Providers may elect not to treat small, peripheral retinal lesions that are at low risk for visual complications and may resolve without intervention. However, treatment is required when active lesions are threatening the macula, papillomacular bundle or optic nerve, grade 3 or greater vitritis, infection lasting longer than 1 month, reduced vision, lesions greater than 1DD in size, or threat of a retinal detachment.[7,13,16,18] The goal of treatment for ocular toxoplasmosis is primarily to preserve the integrity and function of the macula and optic nerve.

In our case, the immunocompetent patient was 12 weeks pregnant with a reactivation of a chronic ocular toxoplasmosis infection with risk to her vision. Pregnant women who acquire the infection prior to pregnancy are not at risk for transmission to the fetus or future offspring.
The mother develops permanent immunity through antibodies to the primary infection, and therefore protects the unborn child.[7,9,11,13,14,20] Although there have been some documented cases of reactivation of a chronic infection transmitted to the fetus, this is quite rare. This most often happens in a female that is immunocompromised from conditions such as organ transplant therapies or acquired immunodeficiency syndrome.[9,11,14] It was important to consider a treatment regimen that was effective and safe for both mother and unborn child.

The classic triple therapy for toxoplasmosis is pyrimethamine, sulfadiazine, and oral prednisone. The regimen consists of a loading dose of 75 to 100 mg of pyrimethamine daily for two days, followed by 25 to 50 mg daily and a 2-gram loading dose of sulfadiazine, followed by 1 gram every six hours as well as 5 mg of folinic acid daily for four to six weeks. Oral prednisone 20 to 80 mg daily may be started the second to third day of therapy and tapered over two to six weeks. However, treatment regimens may vary due to limited clinical studies and significant side effects of the medications.[16,17,21] Pyrimethamine is contraindicated in the first 18 weeks of pregnancy due to the risk of teratogenic effects on the fetus. It may cause bone marrow suppression due to folate antagonism, requiring close monitoring of blood counts and co-administration of folinic acid. Sulfadiazine requires high fluid intake to prevent renal crystallization and some individuals may experience a severe allergic reaction to this sulfa medication. Use of oral corticosteroids is controversial, and many questions remain unanswered such as the additive benefit versus anti-parasitic treatment alone, dosage, when to initiate the treatment regimen, and duration of treatment.[16,22] Further research is required to determine their benefit in cases of toxoplasmosis.

Alternative medications for ocular toxoplasmosis noted in the literature include clindamycin, spiramycin, sulfamethoxazole/trimethoprim, azithromycin, minocycline, clarithromycin, and atovaquone. Clindamycin has shown to be an effective treatment either as monotherapy or combined with the classic triple therapy.[7,23] A small randomized clinical trial suggested intravitreal injection of clindamycin and dexamethasone may also be an acceptable alternative to triple oral therapy for ocular toxoplasmosis.[4,23,24] The injection therapy showed good efficacy and may be more convenient and provide better drug availability while providing less medication side effects, adherence complications, hematologic monitoring, and potentially fewer follow-up visits.[4,23] It may be a good alternative when oral medications are contraindicated or do not provide an adequate response.[24]

Treatment regimen during pregnancy is dependent on when the *Toxoplasma* infection was acquired. Spiramycin, not commercially available in the United States, is recommended for pregnant women with primary infection before 18 weeks gestation to decrease the risk of *Toxoplasma gondii* transmission to the fetus.[9,11,14,16,18] Medication may be switched to triple therapy to treat fetal infection confirmed by a positive polymerase chain reaction of amniotic fluid or acute maternal infection only after 18 weeks, due to the teratogenic risk of pyrimethamine.[9,11,14] New findings suggest spiramycin combined with sulfamethoxazole/trimethoprim may have superior efficacy to spiramycin alone in preventing fetal transmission.[25] This combination was also found to be at least as

effective as pyrimethamine/sulfadiazine, proving a good alternative to classic therapy, especially during pregnancy.[25]

In our case, the patient had a reactivation of her chronic infection and was not immunocompromised. Therefore, no risk of transmitting the *Toxoplasma* infection to the fetus was present. Treatment was still required due to her symptomatic reactivation and threat to vision. Because of the pyrimethamine contraindication during pregnancy, previous allergic response to clindamycin, and lack of spiramycin availability in the United States, the alternative treatment of sulfamethoxazole/trimethoprim 800/160 mg by mouth twice daily for 6 weeks was initiated. Sulfamethoxazole/trimethoprim alone was shown to be an effective alternative to the classic triple therapy in a randomized clinical trial and uncontrolled case series.[5,26,27] Another study suggested recurrences of retinochoroiditis were reduced with intermittent, long-term dosing of sulfamethoxazole/trimethoprim.[7,28] It is first line treatment in many low income countries due to availability and low cost when compared to pyrimethamine.[5] Prednisolone acetate 1% and scopolamine were added to treat the secondary anterior chamber reaction and tapered appropriately. Oral corticosteroids were not added as the patient's clinical course continued to improve with antibiotic treatment alone.

Prevention is the key to reducing the prevalence of infection from *Toxoplasma gondii*. Preventative measures include adequately cooking meat, washing fruits and vegetables, and avoiding unpasteurized milk. Contaminated water has been an increasingly recognized source of infection. Thorough hand washing should occur after contact with raw meats/vegetables, cats, litter boxes, and contaminated soils. Litter boxes should be cleaned daily to prevent sporulation. Pregnant women who are seronegative for *Toxoplasma* antibodies should avoid contact with cats, litter boxes, or potentially contaminated soil and other surfaces during pregnancy. Sand boxes should be covered when not being used. Transmission during blood transfusions or organ transplantations are rare, however, seropositive donors should be avoided.

CONCLUSION

Toxoplasmosis is a common parasitic infection throughout the world and continues to be a life-threatening condition in the infant or immunocompromised individual. Ocular toxoplasmosis is the leading cause of retinochoroiditis and has the potential to cause irreversible ocular damage and visual impairment. There continues to be a lack of consensus on treatment, and further research is required to determine a safe and effective treatment regimen. Utilizing preventative measures remains critical to reducing future transmission of *Toxoplasma gondii.*

In our case, the patient was in her first trimester of pregnancy and therefore careful consideration needed to be made regarding the risk of congenital transmission and safe treatment options. The patient responded well to an alternative antibiotic therapy without the need for oral corticosteroids and she continued to have a healthy pregnancy.

REFERENCES

1. Toxoplasmosis. Centers for Disease Control and Prevention; January 10, 2013. Accessed September 20, 2020. https://www.cdc.gov/parasites/toxoplasmosis.
2. Furtado JM, Smith JR, Belfort R, Gattey D, Winthrop KL. Toxoplasmosis: a global threat. *J Glob Infect Dis.* 2011;3(3):281-284. doi: 10.4103/0974-777X.83536
3. Aguirre AA, Longcore T, Barbieri M, et al. The one health approach to toxoplasmosis: epidemiology, control, and prevention strategies. *Ecohealth.* 2019;16(2):378-390. doi: 10.1007/s10393-019-01405-7
4. Park, YH, Nam HW. Clinical features and treatment of ocular toxoplasmosis. *Korean J Parasitol.* 2013;51(4):393-399. doi: 10.3347/kjp.2013.51.4.393
5. Konstantinovic N, Guegan H, Stajner T, Belaz S, Robert-Gangneux F. Treatment of toxoplasmosis: current options and future perspectives. *Food Waterborne Parasitol.* 2019;15:e00036. doi: 10.1016/j.fawpar.2019.e00036
6. Saadatnia G, Golkar M. A review on human toxoplasmosis. *Scand J Infect Dis.* 2012;44(11):805-814. doi: 10.3109/00365548.2012.693197
7. Jabs DA, Nguyen QD. Ocular toxoplasmosis. In: *Retina.* Schachat AP, ed. 4th ed. Mosby; 2006;2:1583-1595.
8. Soheilian M, Ramezani A, Soheilian R. How to diagnose and treat ocular toxoplasmosis. *Rev Ophthalmol. February 15,* 2011. Accessed June 4, 2020. https://www.reviewofophthalmology.com/article/how-to-diagnose-treat-ocular-toxoplasmosis
9. Hampton MM. Congenital toxoplasmosis: a review. *Neonatal Netw.* 2015;34(5):274-278. doi: 10.1891/0730-0832.34.5.274
10. Ausiello, D, Goldman L. *Cecil Textbook of Medicine*. 22nd ed. Saunders; 2004:2088-2092.
11. Milewska-Bobula B, Lipka B, Golab E, et al. Recommended management of toxoplasmosis *gondii* infection in pregnant women and their children. *Przegl Epidemiol.* 2015;69:291-298, 403-410.
12. Liesegang TJ, Skuta GL, Cantor LB, eds. *Basic and Clinical Science Course. Section 9*. American Academy of Ophthalmology. 2007;277-280.

13. Rothova A. Ocular involvement in toxoplasmosis. *Br J Ophthalmol.* 1993;77(6):371-377. doi: 10.1136/bjo.77.6.371
14. Montoya JG, Remington JS. Management of toxoplasma gondii infection during pregnancy. *Clin Infect Dis.* 2008;47(4):554-566. doi: 10.1086/590149
15. McAuley J. Congenital toxoplasmosis. *J Pediatric Infect Dis Soc.* 2014;3(1):S30-S35. doi: 10.1093/jpids/piu077
16. Lima GSC, Saraiva PGC, Saraiva FP. Current therapy of acquired ocular toxoplasmosis: a review. *J Ocul Pharmacol Ther.* 2015;31(9):511-517. doi: 10.1089/jop.2015.0059
17. Guex-Crosier Y. Update on the treatment of ocular toxoplasmosis. *Int J Med Sci.* 2009;6(3):140-142. doi: 10.7150/ijms.6.140
18. 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. doi: 10.1016/j.preteyeres.2013.12.005
19. Bosch-Driessen LE, Berendschot TTJM, Ongkosuwito JV, Rothova A. Ocular toxoplasmosis: clinical features and prognosis of 154 patients. *Ophthalmology.* 2002;109(5):869-878. doi:10.1016/s0161-6420(02)00990-9
20. Nussenblatt RD, Belfort R Jr. Ocular toxoplasmosis: an old disease revisited. *JAMA* 1994;271(4):304-307. doi:10.1001/jama.1994.03510280066035
21. Stanford MR, See SE, Jones LV, Gilbert RE. Antibiotics for toxoplasmic retinochoroiditis: an evidence-based systematic review. *Ophthalmol* 2003;110:926-931; quiz 31-2. doi: 10.1016/S0161-6420(03)00083-6. doi: 10.1016/s0161-6420(02)00990-9
22. Jasper S, Vedula SS, John SS, Horo S, Sepah YJ, Nguyen QD. Corticosteroids as adjuvant therapy for ocular toxoplasmosis. *Cochrane Database Syst Rev.* 2013;4(4). doi: 10.1002/14651858.CD007417.pub2
23. Soheilian M, Ramezani A, Azimzadeh A, et al. Randomized trial of intravitreal clindamycin and dexamethasone versus pyrimethamine, sulfadiazine, and prednisolone in treatment of ocular toxoplasmosis. *Ophthalmology.* 2011;118(1):134-141. doi: 10.1016/j.ophtha.2010.04.020
24. Lasave AF, Diaz-Llopis M, Muccioli C, Belfort Jr R, Arevalo JF. Intravitreal clindamycin and dexamethasone for zone 1 toxoplasmic choroiditis at twenty-four months. *Ophthalmology.* 2010;117(9):1831-1838. doi: 10.1016/j.ophtha.2010.01.028
25. Valentini P, Buonsenso D, Barone G, et al. Spiramycin/cotrimoxazole versus pyrimethamine/sulfonamide and spiramycin alone for the treatment of toxoplasmosis in pregnancy. *J Perinatol.* 2015;35(2):90-94. doi: 10.1038/jp.2014.161

26. Opremcak, EM, Scales DK, Sharpe, MR. Trimethoprim-sulfamethoxazole therapy for ocular toxoplasmosis. *Ophthalmology*. 1992;99(6):920-925. doi: 10.1016/s0161-6420(92)31873-1
27. Soheilian M, Sadoughi MM, Ghajarnia M, et al. Prospective randomized trial of trimethoprim/sulfamethoxazole versus pyrimethamine and sulfadiazine in the treatment of ocular toxoplasmosis. *ophthalmology*. 2005;112 (11):1876-1882. doi: 10.1016/j.ophtha.2005.05.025
28. Silveira C, Belfort R Jr., Muccioli C, et al. The effect of long-term intermittent trimethoprim/sulfamethoxazole treatment on recurrences of toxoplasmic retinochoroiditis. *Am J Ophthalmol.* 2002;134(1):41-46. doi: 10.1016/s0002-9394(02)01527-1