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Case Report

A Case Report of Ocular Toxoplasmosis Associated with Chagas Disease and Literature Review

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A CASE REPORT OF OCULAR TOXOPLASMOSIS ASSOCIATED WITH CHAGAS DISEASE AND LITERATURE REVIEW

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Abstract

Introduction: Ocular toxoplasmosis (OT) is one of the most frequent clinical manifestations of toxoplasmosis infection. Likewise, another relatively common chronic parasitic condition in Colombia is Chagas disease (CD). At present, there is little information about patients living with CD and other chronic parasitic conditions such as toxoplasmosis; therefore, this report aims to present a case of OC in a patient with chronic CD. Clinical case: A patient recently diagnosed with CD, chronic phase with cardiac involvement, consulted for decreased visual acuity accompanied by placoid chorioretinitis in the macula with an active retinitis zone adjacent to the placoid chorioretinitis. 2+ vitreous cells were present with a headlight in the fog sign. Anterior chamber cells were 1+. As serology (IgM, IgG) for toxoplasmosis was positive, OT was diagnosed. With this diagnosis, treatment was started with trimethoprim-sulfamethoxazole, clindamycin, and prednisone, after which the lesion resolved, leaving an atrophic scar. Visual acuity improved. During 24 months of follow-up, no recurrences were observed. The patient continued clinical follow-up for CD. Conclusion: The clinical features of this patient appear to be similar to those without this coinfection. It also shows several commonly encountered features of OC and the resolution of symptoms using a relatively standard therapy.
Keywords: ocular toxoplasmosis, Toxoplasma gondii, American trypanosomiasis, Trypanosoma cruzi.

Reporte de un caso de toxoplasmosis ocular asociado a enfermedad de Chagas y revisión de la literatura

Resumen

Introducción: la toxoplasmosis ocular (TO) es una de las manifestaciones clínicas más frecuentes de la infección por toxoplasmosis. Así mismo, en Colombia, otra afección parasitaria crónica relativamente frecuente es la enfermedad de Chagas (EC). Actualmente, existe poca información sobre pacientes que conviven con la EC y otras afecciones parasitarias crónicas como la toxoplasmosis; por lo tanto, el objetivo de este reporte es presentar un caso de TO en un paciente con EC crónica. Caso clínico: paciente con diagnóstico reciente de EC, fase crónica cardíaca, consultó por disminución de agudeza visual acompañada de placa de coriorretinitis en área macular con zona de retinitis activa adyacente a la placa de coriorretinitis. Se observaron células

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vítreas 2+ con signo del faro en la niebla. Las células de la cámara anterior eran 1+. Como la serología (IgM, IgG) para toxoplasmosis era positiva se diagnosticó TO. Con este diagnóstico se inició tratamiento con trimetoprim-sulfametoxazol, clindamicina y prednisona, tras lo cual la lesión se resolvió, dejando una cicatriz atrófica. Se observó una mejoría de la agudeza visual. Durante 24 meses de seguimiento, no se observaron recidivas. El paciente continuó en seguimiento clínico por EC. Conclusiones: Las características clínicas de estos pacientes parecen ser similares a las de los pacientes sin esta coinfección y muestra varias características encontradas comúnmente en la TO, así como la resolución de los síntomas con una terapia relativamente común.

Palabras clave: toxoplasmosis ocular, *Toxoplasma gondii,* tripanosomiasis americana, *Trypanosoma cruzi*.

Introduction

Ocular toxoplasmosis (OT) is one of the most common clinical manifestations of toxoplasmosis. This infection is caused by the apicomplexan parasite *Toxoplasma gondii* (1). The seroprevalence in the whole population is high; some studies estimate it at 30-60 % of the total global population (1-4).

This infection is more common in tropical and subtropical regions and has a higher seroprevalence than in more temperate areas (1). In general, infection usually follows the oral route, mainly by consuming raw or undercooked meat infected with cysts, although epidemics have been attributed to contamination of water resources with oocysts (1).

The high prevalence appears to be due to the parasite's high success and effectiveness, attributed to its molecular mechanisms of invasion, motility, immune evasion, and infective behavior. These include a broad host range (such as birds and warm-blooded aquatic inhabitants) and large-scale production of primary oocysts from feline hosts (1).

One of the regions with the highest seroprevalence is Latin America. Seroprevalence estimates range from 33 % to 98 % depending on the year, sociodemographic characteristics, and country (1, 3, 5-7). In Colombia, seroprevalence studies report that 46 % of positive antibodies are present in specific populations (2).

The modes of transmission of toxoplasmosis include poorly cooked meat or contact with raw meat (8, 9), water contaminated with cat feces (10), and congenital transmission (11). Vegetables and fruits have been suggested as sources of infection, but no one has been able to prove such an epidemiological link (12). It is important to say that owning a cat is not a risk factor for acquiring *T. gondii* infection (although owning three or more cats seems to have a relationship) (1).

For the diagnosis of this infection, a thorough clinical history is crucial. After this, one commonly used method is serology, which assesses the presence of IgM and IgG antibodies. Other diagnostic procedures usually involve polymerase chain reaction (PCR), additional serological methods (IgM and IgG avidity tests), immunohistochemical identification, in vitro culture, and animal inoculation (13, 14). All of these tests require specialized equipment and training. For treatment, pyrimethamine, trimethoprim-sulfamethoxazole, clindamycin, sulfadiazine, azithromycin, and atovaquone, among others, can be used (13, 14). The classic therapy is usually pyrimethamine (25–50 mg *per os* daily in one or two doses), sulfadiazine (1 g four times a day *per os*), and a systemic corticosteroid, generally prednisone (14). The first two can affect different steps in synthesizing tetrahydrofolate and have proven to be adequate therapies for this condition (14). On the other hand, trimethoprim-sulfamethoxazole appears to prevent recurrence if taken for extended periods (14).

Ciencia y Tecnología para la Salud Visual y Ocular
Science and Technology in Ocular Health and Vision

One of the characteristics of this infection is the ability of the parasite to disseminate throughout the tissues (1). During this dissemination, especially during acute infection, the retina is one of the most affected areas. Data from Brazil and Colombia suggests that OT is relatively common in South America. In this regard, in Colombia, some studies indicate an incidence of 3 per 100,000 inhabitants per year (4); other studies estimate this incidence at 42 per 1,000 cases of toxoplasmosis (15), and toxoplasmosis was deemed to be the culprit of 40 % of the cases of uveitis (16). This means that the burden related to OT is considerable: in relatively low-incidence settings, it was calculated that 2,400 DALYs are lost due to toxoplasmosis (1).

This loss of DALYs can be more significant if combined with other chronic diseases, mainly parasitic. One such case is the chronic form of Chagas disease (CD). Although DALYs have decreased in certain regions, the burden is still high in specific populations (17). Having said that, although it is not extensively characterized, CD has been associated with peripheric and central nervous system alterations, as well as with retinal and optic nerve alterations (18, 19), an aspect that could deepen visual problems in the general population and those who also live with toxoplasmosis. In Colombia, for instance, there are at least 4.8 million individuals at risk of acquiring CD, and approximately almost half a million are currently infected (20). Unfortunately, the number of screening tests is low compared to the at-risk population (21). Also, not all the public health laboratories have the installed capacity to perform the tests; even more, not all the laboratories can perform all three possible tests (Immunofluorescence Assay, Hemagglutination Assay, or ELISA) (22). Finally, even when the number of patients affected by toxoplasmosis is considerable and even when the prevalence of CD is relatively high, due to the lack of surveillance capability for this clinical condition, there is not much information about patients living with CD and other chronic parasitic conditions such as toxoplasmosis (23). No relationship, epidemiological or otherwise, has been readily established. Due to this, a case of OT in a patient with chronic CD is presented.

METHODS

Search strategies

Literature searches were conducted in the following databases: PubMed, Scopus, SciELO, Redalyc, Lilacs, and Google Scholar. The search strategy combined four search terms related to the impact of spider bites on human health: 1) Chagas disease, 2) ocular toxoplasmosis, 3) *Toxoplasma gondii*, 4) *Trypanosoma cruzi*, 5) American trypanosomiasis, 6) toxoplasmosis, 7) uveitis, 8) retinitis, and 9) chorioretinitis. The search included all publications until March 28, 2023, without a date threshold.

Study selection and data extraction

The studies were eligible for inclusion if they reported cases or series of OT in patients with CD and included at least one patient. We defined studies as a case report if they described a single case and as a series of cases if they described more than one patient. Studies not published in English, French, Spanish, or Portuguese were excluded. Two reviewers independently screened the search results for inclusion and then extracted all data using a standardized data extraction form. The discrepancies were resolved through discussion until a consensus was reached. Information was extracted about the first author, country, year of publication, number of patients, sex, clinical manifestations, treatment, report characteristics, and outcome.

Results

Ciencia y Tecnología para la Salud Visual y Ocular
Science and Technology in Ocular Health and Vision

The literature search yielded 87 studies (Figure 1). Of these, 12 duplicates were excluded. On screening titles and abstracts for relevance, 63 studies were excluded, totaling eight full-text articles that were assessed. None of these met the inclusion criteria. Just one prevalence study with no disclosure of signs of symptoms reported one of such occurrences but did not specify symptomatology (23).

Ciencia y Tecnología para la Salud Visual y Ocular
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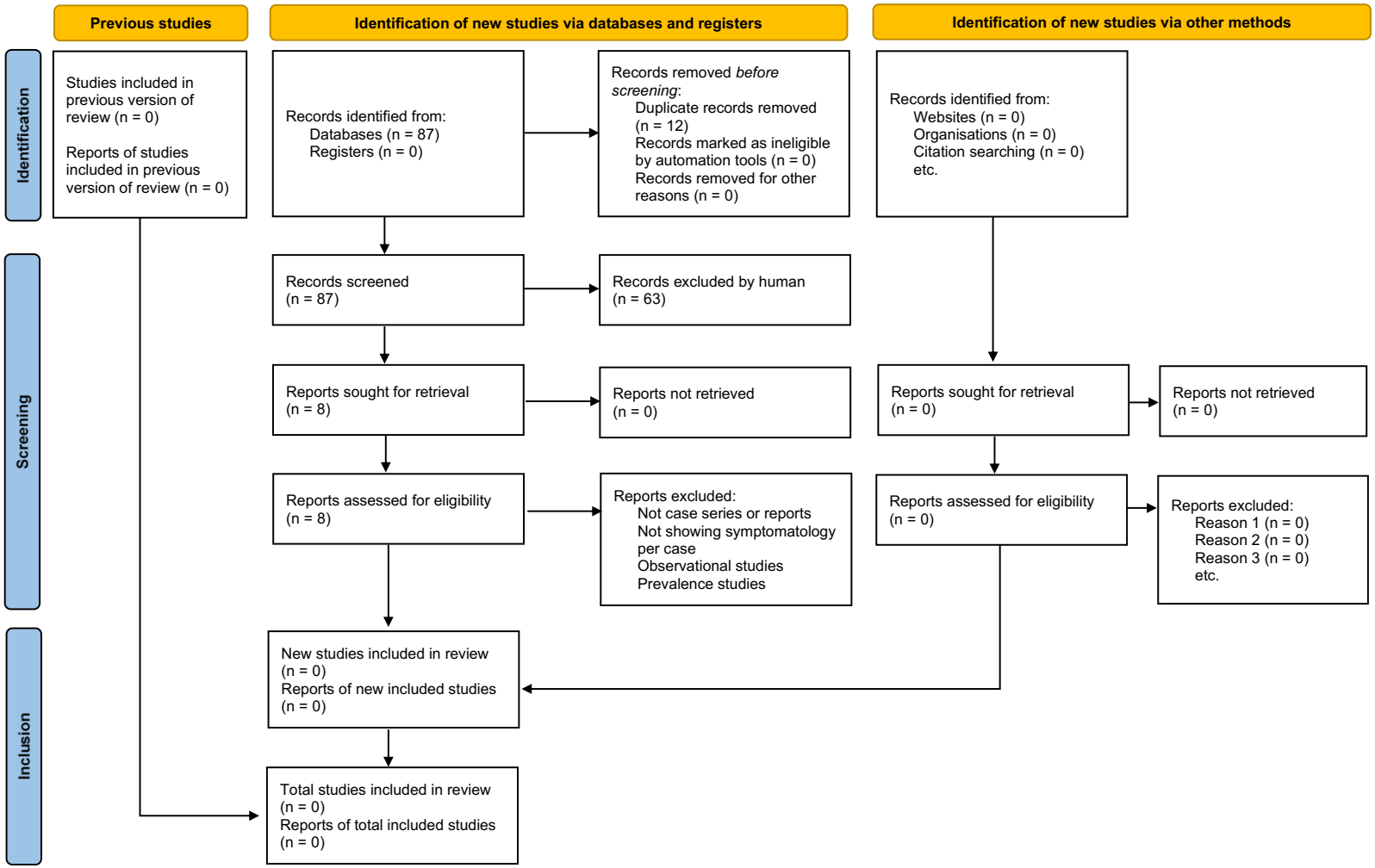
Figure 1. PRISMA 2020 flow diagram for updated systematic reviews, including searches of databases, registers, and other sources



Source: Based on (24).

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Ciencia y Tecnología para la
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Case report

A 28-year-old male patient from Tolima, recently diagnosed with CD, chronic phase with cardiac involvement, consults for two weeks of decreased vision in the right eye, accompanied by ocular pain, unilateral red eye, myodesopsias, lacrimation, headache, palpitations, and dyspnea. He did not present with fever, nausea, or vomiting and mentioned no ocular trauma. No central nervous system infestation was suspected. He reported a history of living with dogs and cats since childhood and is in frequent contact with the dirt and feces of his pets. He states that he cooks his meat thoroughly. Other aspects of his medical history are shown in Table 1.

Table 1. Medical history

Pathologies:	Chronic form of Chagas disease with cardiac involvement
Allergies:	No
Gynecological:	Not applicable
Hospitalizations:	No
Surgeries:	No
Pacemaker:	**NO**
Medications:	Metoprolol 50 mg every 12 hours *per os*
Family health:	Mother with type 1 diabetes mellitus. Father with hypertension. Brother with Chagas disease
Other:	No

Source: Authors' elaboration.

On physical examination, the patient weighed 73 kg, was 169 cm tall, had a blood pressure of 116/78, was tachycardic with 108 beats per minute, and had a respiratory rate of 20. Pectus excavatum was noticeable. No fever was related or documented; the temperature was 36.1 °C. Ophthalmologic examination showed visual acuity in the right eye of 0.4 without correction and in the left of 1.0 without correction. Tarsal papillae hyperemia was also observed in both eyes.

During ophthalmoscopy, findings were made in the right eye; the left eye was normal. In this regard, the left eye ophthalmoscopy was normal, with no evident signs of retinitis or chorioretinitis, and no anterior chamber or vitreous cells were detected. Left intraocular pressure was normal. No cicatricial lesions were evident upon examination.

Meanwhile, the right eye ophthalmoscopy showed placoid chorioretinitis with a pigmented center of approximately three-disc diameters in the macular area and an active retinitis zone adjacent to the placoid chorioretinitis, with a headlight in the fog sign. Vitritis was present with 2+ vitreal vitreous cells, and no epiretinal membranes were detected. No keratic precipitates were found, and anterior chamber cells were 1+. Intraocular pressure on examination was normal. No punctate lesions, areas of necrosis, retinal detachment, arteritis, phlebitis, iridocyclitis, papillitis, scleritis, or optic neuritis were detected. The clinical findings were incompatible with Kyrieleis arteritis.

The rest of the physical examination showed vasoconstriction (cold and moist skin), tachycardia, and NYHA II/IV dyspnea. The blood count showed mild leukocytosis without eosinophilia. The serology results for toxocara, cysticercus, VDRL, HIV, and CMV were negative. IgG and IgM ELISA results for *T.*

Ciencia y Tecnología para la Salud Visual y Ocular
Science and Technology in Ocular Health and Vision

gondii were positive (Table 2). Due to the clinical findings, the serology results, and the ophthalmoscopy signs, the clinical picture was deemed secondary to OT.

Table 2. Medical Exams

Exam – Chronology	Results
Trypanosoma cruzi - Serology - November 15, 2018	Reactive recombinant antigens Total antigens positive
Electrocardiogram – December 12, 2018	Frequent ventricular extrasystoles
Electrocardiogram – January 4, 2019	Sinus bradycardia
Echocardiogram – February 7, 2019	Left ventricular cavity of normal diameter for the body surface; end-diastolic volume: 92 ml; preserved systolic function and ejection fraction of 48 %; wall thickness in the normal range RV: Average size and function LA: Slightly dilated with an area of 20 cm^2 (average: 16 cm^2) RA: Slightly dilated with an area of 17.5 cm^2 Septum intact, no endocavitary thrombus Aortic and mitral valves with slight leaflet redundancy and minimal regurgitant jets Pulmonary and tricuspid valves with slight leaflet redundancy and minimal regurgitant jets No signs of pulmonary hypertension The patient was bradycardic during the procedure
Chest X-ray – February 25, 2019	Prominent heart in AP projection due to pectus excavatum as an anatomical variant without real cardiomegaly. Vascular structures of usual appearance. Rest of exam: normal
24-hour Holter – March 6, 2019	Sinus rhythm with a minimum rate of 40 beats/minute, maximum of 115; average: 68. Frequent polymorphic ventricular extrasystoles with a coupling period greater than 1, some interpolated, others with compensatory pauses, in intermittent duplets and three beats of non-sustained ventricular tachycardia. Idioventricular rhythm with a heart rate of 54 beats/minute; occasionally conducted atrial extrasystoles. Normal conduction. No significant changes in the ST segment. QTC interval: 361 ms
VDRL - April 10, 2019	Negative
VIH - April 10, 2019	Negative
CMV – April 10, 2019	Negative
Hemogram - April 10, 2019	Leukocytes: 11,100/µL Differential: neutrophils: 57 %%; lymphocytes: 30 %; basophils: 1 %; eosinophils: 3 %; monocytes: 8 % Hb: 14.8 g/dl HCT: 48.1 % RBC: 5.22 M/µL Platelets: 184,000/µl
Toxoplasmosis serology - April 12, 2019	IgG positive IgM positive
Toxocariasis serology - April 16, 2019	Negative
Cisticercosis serology - April 16, 2019	Negative

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Hemogram - May 23, 2019	Leukocytes: 6,600/ul Differential: neutrophils: 54 %%; lymphocytes: 34 %; basophils: 2 %; eosinophils: 1 %; monocytes: 9 % Hb: 15.3 g/dl HCT: 49.6 % RBC: 5.52 M/µl Platelets: 211,000/µl

Source: Authors' elaboration.

For treatment, trimethoprim-sulfamethoxazole (160/800 mg) every 12 hours and clindamycin (300 mg) every 6 hours for four weeks were initiated. Forty-eight hours after the antibiotics were started, oral prednisone was added to the regimen in decreasing doses. After four weeks of treatment, the lesion was resolved entirely, leaving an atrophic scar. There was an improvement in visual acuity. During 24 months of follow-up, no recurrences were observed. The patient continued clinical follow-up for CD.

Discussion

This case describes an acute episode of OT in a patient with CD. Although this coinfection is described infrequently in the literature, it seems comparable to patients not infected with T. cruzi. The clinical manifestation of the aforementioned ocular involvement occurred over the age of 40, one of the age groups in which this disease is most frequently observed (11), and the serological levels and evolution are consistent with those reported and observed in other investigations (14). In this regard, being coinfected with CD did not complicate this patient's clinical picture, even when CD can have neurological and optical manifestations (18, 19). This relationship must be further studied.

Interestingly, despite being coinfected, it did not differ from the typical manifestation of the disease, which is usually unilateral (14). In addition, the development of the lesion and the eventual scar were identical to those described in the literature (14). The minor sign of "headlight in the fog" was another puzzling discovery, suggesting that vitritis, however mild, was present (25).

Additionally, this patient displayed altered vision and floaters, two of the most typical clinical complaints recorded (14). Although this patient's immunologic status indicated recovery (24), treatment was started to promote quality of life and prevent potential complications (14), which this patient did not experience.

This case seems relatively minor compared with other reported cases of OT (26, 27). It did not exhibit any complications like those reported in previous studies about immunocompromised individuals (28). Luckily for the patient, severe symptoms were not observed (14).

Even though it could be inferred from this evidence that these individuals behave no differently from those with no CD, there is unfortunately little information or monitoring on this kind of coinfected individual in the scientific literature. Additionally, although a recurrence is feasible given the patient's advanced age, it is unlikely to occur (13, 14). It would have been intriguing to examine alterations in the retina using advanced methods like optical coherence tomography angiography. Still, there was limited availability of this equipment in the environment where this case was evaluated (29).

However, even if oral contamination from undercooked meat in his home or outdoors cannot be ruled out, the source of illness for this patient is unknown; his continuing interaction with cats may be a significant source. Given that his earlier serological status is unclear, the same can be said for reactivation from a congenital infection (30). Therefore, a series of measures can and should be taken

to prevent infection, including removing cats from farms that produce meat, immunizing cats to prevent the release of oocysts, controlling rodent populations, cooking meat to a minimum of 67 °C to kill oocysts, injecting meat with 2 % sodium chloride or 1.4 % sodium/potassium and keeping it at 4 °C for at least 8 hours to kill viable cysts, hand washing, utensil washing, and water treatment with adequate filters of 1 micron in diameter, among others (1).

In conclusion, this case shows OT in a patient living with CD. The clinical characteristics of this patient appear to be similar to those of patients without this coinfection, and the report shows several common attributes of OT. The limitations of this case include the lack of more advanced diagnostic tools and the lack of a report from an ophthalmologist or optometrist. The strengths include assessing several parasitic infections and the patient's follow-up for 24 months.

References

1. Furtado JM, Winthrop KL, Butler NJ, Smith JR. Ocular toxoplasmosis I: parasitology, epidemiology and public health. Clin Exp Ophthalmol. 2013;41(1):82-94. DOI: https://doi.org/10.1111/j.1442-9071.2012.02821.x
2. Rosso F, Les JT, Agudelo A, Villalobos C, Chaves JA, Tunubala GA, et al. Prevalence of infection with Toxoplasma gondii among pregnant women in Cali, Colombia, South America. Am J Trop Med Hyg. 2008;78(3):504-8. DOI: https://doi.org/10.4269/ajtmh.2008.78.504
3. Cañón-Franco WA, López-Orozco N, Gómez-Marín JE, Dubey JP. An overview of seventy years of research (1944–2014) on toxoplasmosis in Colombia, South America. Parasit Vectors. 2014;7(1):427. DOI: https://doi.org/10.1186/1756-3305-7-427
4. de-la-Torre A, López-Castillo C, Gómez-Marín J. Incidence and clinical characteristics in a Colombian cohort of ocular toxoplasmosis. Eye. 2009;23(5):1090-3. doi:10.1038/eye.2008.219
5. Nussenblatt RB, Belfort R. Ocular toxoplasmosis: an old disease revisited. Jama. 1994;271(4):304-7. DOI: https://doi.org/10.1001/jama.1994.03510280066035
6. Silveira C, Belfort Jr R, Muccioli C, Abreu MT, Martins MC, Victora C, et al. A follow-up study of Toxoplasma gondii infection in southern Brazil. Am J Ophthalmol. 2001;131(3):351-4. DOI: https://doi.org/10.1016/S0002-9394(00)00830-8
7. Sobral CA, Amendoeira MRR, Teva A, Patel BN, Klein CH. Seroprevalence of infection with Toxoplasma gondii in indigenous Brazilian populations. Am J Trop Med Hyg. 2005;72(1):37-41. DOI: https://doi.org/10.4269/ajtmh.2005.72.37
8. Dubey J, Jones J. Toxoplasma gondii infection in humans and animals in the United States. Int J Parasitol. 2008;38(11):1257-78. DOI: https://doi.org/10.1016/j.ijpara.2008.03.007
9. Kijlstra A, Jongert E. Control of the risk of human toxoplasmosis transmitted by meat. Int J Parasitol. 2008;38(12):1359-70. DOI: https://doi.org/10.1016/j.ijpara.2008.06.002
10. Bowie WR, King AS, Werker DH, Isaac-Renton JL, Bell A, Eng SB, et al. Outbreak of toxoplasmosis associated with municipal drinking water. Lancet. 1997;350(9072):173-7. DOI: https://doi.org/10.1016/S0140-6736(96)11105-3

11. Holland GN. Ocular toxoplasmosis: a global reassessment:. Part I: epidemiology and course of disease. Am J Ophthalmol. 2003;136(6):973-88. DOI: https://doi.org/10.1016/j.ajo.2003.09.040
12. Kniel KE, Lindsay DS, Sumner SS, Hackney CR, Pierson MD, Dubey J. Examination of attachment and survival of Toxoplasma gondii oocysts on raspberries and blueberries. J Parasitol. 2002;88(4):790-3. DOI: https://doi.org/10.1645/0022-3395(2002)088[0790:EOAASO]2.0.CO;2
13. Kalogeropoulos D, Sakkas H, Mohammed B, Vartholomatos G, Malamos K, Sreekantam S, et al. Ocular toxoplasmosis: a review of the current diagnostic and therapeutic approaches. Int Ophthalmol. 2022;42(1):295-321. DOI: https://doi.org/10.1007/s10792-021-01994-9
14. Butler NJ, Furtado JM, Winthrop KL, Smith JR. Ocular toxoplasmosis II: clinical features, pathology and management. Clin Exp Ophthalmol. 2013;41(1):95-108. DOI: https://doi.org/10.1111/j.1442-9071.2012.02838.x
15. Cifuentes-González C, Zapata-Bravo E, Sierra-Cote MC, Boada-Robayo L, Vargas-Largo ÁP, Reyes-Guanes J, et al. Colombian Ocular Infectious Epidemiology Study (COIES): Ocular Toxoplasmosis Incidence and Sociodemographic Characterization, 2015-2019. Int J Infect Dis. 2022;117:349-55. DOI: https://doi.org/10.1016/j.ijid.2022.02.028
16. De-la-Torre A, López-Castillo CA, Rueda JC, Mantilla RD, Gómez-Marín JE, Anaya JM. Clinical patterns of uveitis in two ophthalmology centres in Bogota, Colombia. Clin Exp Ophthalmol. 2009;37(5):458-66. DOI: https://doi.org/10.1111/j.1442-9071.2009.02082.x
17. Martins-Melo FR, Carneiro M, Ribeiro ALP, Bezerra JMT, Werneck GL. Burden of Chagas disease in Brazil, 1990–2016: findings from the Global Burden of Disease Study 2016. Int J Parasitol. 2019;49(3-4):301-10. DOI: https://doi.org/10.1016/j.ijpara.2018.11.008
18. Villas-Bôas FdS, Ramiro AC, Martins TdSM, Sousa WMd, Noya-Rabelo MM, Prata JA, et al. Association between Chagas disease and changes in the optic nerve and retinal nerve fiber layer. Arq Bras Oftalmol. 2019;82:183-8. DOI: https://doi.org/10.5935/0004-2749.20190036
19. Wackermann PV, Fernandes RMF, Elias Jr J, Dos Santos AC, Marques Jr W, Barreira AA. Involvement of the central nervous system in the chronic form of Chagas' disease. J Neurol Sci. 2008;269(1-2):152-7. DOI: https://doi.org/10.1016/j.jns.2008.01.006
20. WHO. Chagas disease in Latin America: an epidemiological update based on 2010 estimates. Weekly Epidemiol Rec. 2015:33–44.
21. INS. Boletin Epidemiológico Semanal. 2016.
22. Olivera MJ, Porras Villamil JF, Toquica Gahona CC, Rodríguez Hernández JM. Barriers to Diagnosis Access for Chagas Disease in Colombia. J Parasitol Res. 2018;2018:14. DOI: https://doi.org/10.1155/2018/4940796

23. Mendoza Millán DL, Quintero Rodríguez A, Alarcón de Noya B, Díaz Bello Z, Mauriello L, Colmenares C, et al. Toxoplasmosis y Enfermedad de Chagas: seroprevalencia y factores de riesgo en embarazadas del HUC. Bol Venez Infectol. 2020:29-36.
24. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. DOI: https://doi.org/10.1136/bmj.n71
25. Holland G, O'Connor G, Belfort R, Remington J, Pepose J. Ocular infection and immunity. St Louis: Mosby. 1996:1088-128.
26. Seers T, Myneni J, Chaudhry NL, Ugarte M. Bilateral ocular toxoplasmosis in a returning traveller: age and route of infection as potential risk factors. BMJ Case Rep. 2021;14(1). DOI: https://doi.org/10.1136/bcr-2020-237068
27. Matias M, Gomes A, Marques T, Fonseca AC. Ocular toxoplasmosis: a very rare presentation in an immunocompetent patient. BMJ Case Rep. 2014;2014. DOI: https://doi.org/10.1136/bcr-2014-205846
28. Yoo TW, Mlikotic A, Cornford ME, Beck CK. Concurrent cerebral American trypanosomiasis and toxoplasmosis in a patient with AIDS. Clin Infect Dis. 2004;39(4):e30-4. DOI: https://doi.org/10.1086/422456
29. Park JH, Lee S-Y, Lee EK. Morphological characteristics of ocular toxoplasmosis and its regression pattern on swept-source optical coherence tomography angiography: a case report. BMC Ophthalmol. 2019;19(1):199. DOI: https://doi.org/10.1186/s12886-019-1209-8
30. Perkins E. Ocular toxoplasmosis. Br J Ophthalmol. 1973;57(1):1. DOI: https://doi.org/10.1136/bjo.57.1.1