Uncommon progression of toxoplasmic papillitis: patient perception and case report

Papilite por toxoplasmose ocular com evolução incomum: percepção do paciente e relato de caso

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ABSTRACT

Ocular toxoplasmosis frequently presents as necrotizing retinochoroiditis and, less often, as peripapillary chorioretinitis and/or papillitis. The progression from papillitis to peripapillary retinochoroiditis has been rarely described. We report the case of a 52-year-old patient living in southern Brazil, who developed papillitis in the right eye and was treated with systemic corticosteroids (prednisone 0.6 mg/kg/day and pulse therapy with methylprednisolone 15 mg/kg/day, for 3 days). After 14 days, the patient developed peripapillary retinochoroiditis with vitritis and decreased visual acuity (20/60), and was immediately initiated on the classic oral treatment for toxoplasmosis, consisting of pyrimethamine (50 mg/day), sulfadiazine (4 g/day), folinic acid (15 mg every 3 days) and prednisone (0.6 mg/kg/day). The visual acuity of the right eye normalized after treatment (20/20), which lasted approximately 70 days, but scotomas were detected on visual field examination, especially in the lower nasal quadrant. Although two studies mentioned this presentation, our report emphasizes the possible manifestation of ocular toxoplasmosis as papillitis in the initial phase, with progression to peripapillary retinochoroiditis and permanent visual field defects, which justifies early treatment for toxoplasmosis in suspected cases, especially in endemic regions.

RESUMO

A toxoplasmose ocular manifesta-se com maior frequência por um quadro de retinocoroidite necrotizante e, com menor frequência, por coriorretinite justapapilar e/ou papilite. A evolução de papilite para retinocoroidite justapapilar raramente foi descrita. Apresenta-se o relato de caso de uma paciente de 52 anos, habitante da Região Sul do Brasil, que iniciou com quadro de papilite em olho direito, sendo tratada com corticoides sistêmicos (prednisona 0,6/mg/kg ao dia e pulsoterapia com metilprednisolona 15mg/kg ao dia, por 3 dias), mas, após 14 dias, evoluiu para retinocoroidite justapapilar, com vitreíte e diminuição de acuidade visual (20/60), sendo imediatamente instituído o tratamento via oral clássico para toxoplasmose, com pirimetamina (50 mg ao dia), sulfadiazina (4 g ao dia) e ácido folínico (15 mg a cada 3 dias), e mantida a prednisona (0.6 mg/kg/dia). A acuidade visual do olho direito normalizou após o tratamento (20/20), que durou em torno de 70 dias, porém desenvolveu escotomas ao exame de campo visual, sobretudo de quadrante nasal inferior. Embora tenham sido encontrados dois trabalhos que mencionam essa forma de apresentação, o presente relato destaca-se por enfatizar a possibilidade de manifestação da toxoplasmose ocular por meio de papilite na fase inicial, que evolui com retinocoroidite justapapilar, causando defeito permanente de campo visual, justificando que se avalie a instituição de tratamento precoce para toxoplasmose dos casos suspeitos, sobretudo em região endêmica.

INTRODUCTION

The seroprevalence of toxoplasmosis varies in the population, according to studies that found positivity rates of 7.4% in Mexico, 23% to 84% in Brazil, 23.9% to 46% in Africa, 28% in North America, 33% in New Zealand, 37% in Chile and 47% in Europe.[1] Although existing data are still scarce, it is estimated ocular toxoplasmosis rates in the population are 0.45% in North America, 0.5% in Australia, 6% in Colombia and 17.7% in the most endemic region of Brazil (the city of Erechim, Rio Grande do Sul).[1]

Ocular toxoplasmosis presents in several forms, but necrotizing retinochoroiditis is the most common manifestation.[2] Optic nerve involvement occured in a minority of cases, and its incidence may vary according to the region where the study was conducted.[3-5] However, there is no uniform terminology for papillary alteration, and its various designations, including papilledema (resulting from intracranial hypertension), papillitis, papillopathy, papilloretinitis, neuroretinitis, and optic disc edema, may hinder comparisons.[6]

Regarding etiology, viral, bacterial, fungal and parasitic infections, including toxoplasmosis, can trigger the onset of optic disc edema.[6] However, papillitis must be differentiated from other etiologies, such as ischemic anterior optic neuropathy, intraorbital compression, and central nervous system lesions and infections.[7]

Papillitis alone due to toxoplasmosis is an uncommon finding; it was found in 5.9% of patients in a study conducted in southern Brazil,[3] 2.9% in a study in Congo[5] and 2% in a study in Japan.[4] In comparison, peripapillary retinochoroiditis showed a high frequency in southern Brazil, reaching 35.3% of 926 patients with ocular toxoplasmosis.[3] However, in other countries, the frequency was lower, as found in New Zealand, with 19% among 16 patients;[8] in Congo, with 14.3% among 35 patients;[5] in Turkey, with 10.16% of 118 patients;[9] in South Korea, with 8.7% of 46 patients;[10] and in Japan, with 5% among 189 patients.[4]

The present report differs from others by presenting a case of ocular toxoplasmosis starting as pure papillitis and later progressing to peripapillary retinochoroiditis, a manifestation that was not detected in the initial exams. This form of progression was described in two recent studies conducted in New Zealand[8] and Iran.[11] However, those studies only mentioned its occurrence, and did not emphasize the importance of early recognition, especially in toxoplasmosis-endemic regions.

A signed written informed consent for publication of clinical details and clinical images was obtained from the patient. The project was posted on the *Plataforma Brasil*, submitted for analysis by the Research Ethics Committee of the *Universidade do Oeste de Santa Catarina* (Unoesc), and was approved under number 4.430.804.

CASE REPORT

A 52-year-old white female patient was seen on December 19, 2019, for complaints of blurred vision and a sensation of brightness in her right eye (RE) that started 7 days before. She had been taking oral prednisone 40 mg per day for 3 days. She denied previous episodes in this eye and reported the left eye (LE) had always presented decreased visual acuity. The visual acuity was 20/20 RE and 20/40 LE.

On fundus examination, papilledema on the RE and a normal LE were observed. Tonometry was 19 mmHg RE and 12 mmHg LE. Retinography and angiography (Topcon 50DX retinograph, United States) and optical coherence tomography (Heidelberg CT, Germany) were performed on the same day and showed papilledema in the RE and a normal LE (Figure 1).

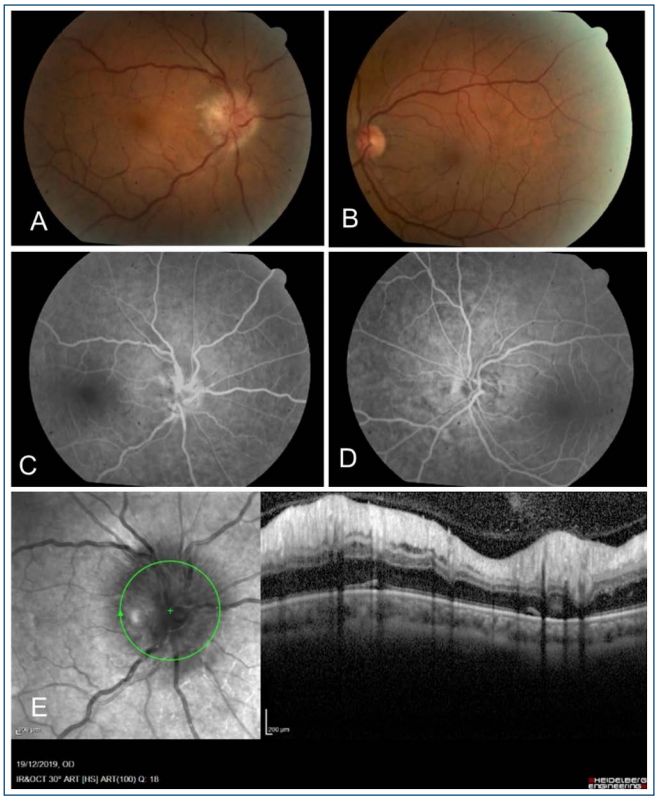

Figure 1. Exams performed on December 19, 2019. (A) Right eye retinography showing papilledema. (B) Left eye retinography showing normal papilla. (C) Right eye angiography showing hyperfluorescence with contrast leakage, confirming papilledema. (D) Left eye angiography showing normal papillary fluorescence. (E) Right eye papillary optical coherence tomography showing a diffuse increase in peripapillary retinal thickness.

On the following day, the patient underwent cranial computed tomography, which showed no abnormalities. On the sixth day, she started pulse therapy with methylprednisolone 15 mg/kg per day, for three days.

On the 11th day, visual acuity was 20/50 RE and 20/40 LE. Vitreous turbidity and peripapillary retinochoroiditis were observed in the RE (Figure 2). Laboratory tests requested on December 21, 2019, showed immunoglobulin M (IgM) 0.34 IU/mL and immunoglobulin G (IgG) above 200 IU/mL for toxoplasmosis; tests for HIV 1 and 2 and syphilis were negative; other tests, such as blood count, urea, creatinine, blood glucose, urinalysis, thyroid-stimulating hormone, glutamic pyruvic transaminase, glutamic oxaloacetic transaminase, hepatitis B antibody testing, hepatitis C antibody testing, and Chagas' disease test were normal. The patient was treated for toxoplasmosis with pyrimethamine (50 mg per day), sulfadiazine (4 g per day), prednisone (0.6 mg/kg per day) and folinic acid (15 mg every 3 days).

On the 13th day, the patient presented visual acuity of 20/60 and intraocular pressure (IOP) of 31 mmHg in the RE. Eye drops of dorzolamide 20 mg/mL + timolol maleate 5 mg/mL 12/12 hours, only in the RE, were added. On the 25th day, the patient presented with arterial hypertension and was treated with 25 mg captopril sublingual. On the 30th day, she was seen at the emergency room for acute renal colic attributed to the use of sulfadiazine, which was discontinued for one week. On the 33rd day, visual acuity was 20/30 RE, and IOP in the RE was 13 mmHg. On the 44th day, visual acuity was 20/20 RE, and arterial sheathing was observed; the decision was made to maintain treatment for another 15 days.

After 5 months, visual acuity was 20/20(-1) RE and 20/40 LE. The 24-2 visual field test performed with a Solaris campimeter (Eyetec, São Paulo, Brazil, 2019) showed scotomas throughout the lower nasal quadrant of the RE, some in the inferior temporal quadrant, and a normal LE, indicating slight worsening compared with the examination performed after 12 months of follow-up (Figure 2). The timeline is shown in Table 1.

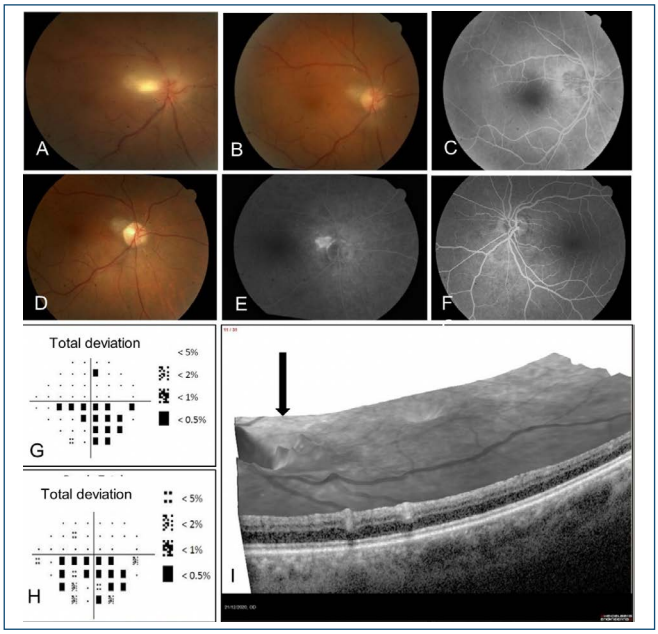

Figure 2. (A) Right eye retinography on January 9, 2020, showing a peripapillary retinochoroiditis lesion and diffuse papilledema. (B) Right eye retinography on February 13, 2020, showing a healing peripapillary retinochoroiditis lesion and improvement of papilledema. (C) Right eye angiography on February 13, 2020, showing an area of peripapillary hypofluorescence (blockage) and discrete contrast leakage, showing a healing papillary retinochoroiditis lesion. (D) Right eye retinography on December 21, 2020, showing a peripapillary scar. (E) Right eye angiography on December 21, 2020, with a hyperfluorescent area with no peripapillary contrast leakage (fibrous scarring tissue). (F) Normal left eye angiography. (G) Visual field of the right eye on May 25, 2020, with scotomas in the lower nasal quadrant. (H) Visual field of the right eye on December 14, 2020 with scotomas in the lower nasal quadrant and lower temporal quadrant. (I) Optical coherence tomography of the right eye on December 21, 2020, showing peripapillary scar.

Table 1. Timeline of disease progression, examinations and treatments performed

Timeline	Initial consultation and follow-up	Procedures and results	Medications used
Day 1	Visual acuity: 20/20 RE and 20/40 LE. Tonometry: 19 mmHg RE and 12 mmHg LE	Retinography, angiography and optical coherence tomography showing papilledema in the RE	Oral prednisone 0.6 mg/kg/day
Day 2	Complementary examination performed	Normal cranial computed tomography	Systemic corticosteroids were maintained
Day 6	Patient referred for pulse therapy	Hospitalization	Intravenous methylprednisolone 15 mg/kg/day for 3 days
Day 11	Visual acuity: 20/50 RE and 20/40 LE	IgM 0.34 and IgG above 200 for toxoplasmosis HIV, syphilis, and other tests: normal Fundoscopy: vitreous turbidity and peripapillary retinochoroiditis in the RE	Pyrimethamine (50 mg/day), sulfadiazine 4 g/day and folinic acid 15 mg every 3 days were added
Day 13	Visual acuity: 20/60 RE and 20/40 LE IOP: 31 mmHg RE and 12 mmHg LE	Fundoscopy: same as previous picture	Eye drops of dorzolamide + timolol maleate 12/12 hours were added
Day 21	Revision of retinography results	Fundoscopy: peripapillary retinochoroiditis in the RE	Continuation of treatment
Day 23	Hypertension crisis	Patient referred to the emergency department	One 25 mg captopril tablet (emergency sublingual use)
Day 30	Renal colic crisis	Patient referred to the emergency department	Discontinued sulfadiazine for 1 week
Day 33	Revision: visual acuity 20/30 RE	Decreased vitreous turbidity	Continuation of treatment
Day 44	Revision: visual acuity 20/20 RE	Retinography: peripapillary scarring and arterial sheathing	Continuation of treatment for another 15 days
5 months	Revision: visual acuity 20/20(-1) RE	Visual field exam: scotomas in the nasal and temporal quadrants of the RE	No treatment
12 months	Revision: visual acuity 20/20 RE	Visual field exam: scotomas in the lower visual hemifield of the RE Imaging exams: peripapillary scarring in the RE	No treatment

RE: right eye; LE: left eye; IgM: immunoglobulin M; IgG: immunoglobulin G; IOP: intraocular pressure.

In an interview, the patient reported she had experienced a constant feeling of heaviness in the stomach caused by medications, which improved after the end of treatment. She recalled the episode of hypertension and renal colic during treatment. Her blood pressure is now normal; she is not taking medication and no longer has renal colic.

Regarding the scotoma in the RE (Figure 2), the patient reported it does not interfere with near vision and that she can perform her work activities; it does cause confusion with distance vision, although the patient can drive with little difficulty.

DISCUSSION

Retinochoroiditis is a condition that affects the retina and the underlying choroid, and is considered the typical presentation of ocular toxoplasmosis; however, it can also manifest as less common conditions, such as papillitis, neuroretinitis, and scleritis.[2]

The initial manifestation of the present case was pure unilateral papillitis, which was confirmed by retinography, angiography and optical coherence tomography, but the condition progressed to peripapillary retinochoroiditis after treatment with systemic corticosteroids. Induction with steroids was considered, but it seemed more likely that the peripapillary lesion was present, but not initially detectable on imaging.

Two descriptions similar to the present case were found in the literature. In Iran, a patient with ocular toxoplasmosis whose initial presentation was papilledema with a macular star, which later progressed to a peripapillary lesion, and her visual acuity increased from 0.1 to 0.9 after specific treatment for toxoplasmosis.[11]

The patient in this report did not present with a macular star but had significant vascular sheathing 44 days after the start of treatment, which partially regressed after the end of treatment. In New Zealand, similar to our case, two patients who first presented with ocular toxoplasmosis in the form of papillitis alone developed peripapillary retinochoroiditis after two weeks.[8]

Unilateral papillitis with superior infiltrates but with no subsequent development of retinochoroiditis was observed in a patient with old chorioretinal scars, who was diagnosed as toxoplasmosis due to positive IgG and ruling out of bacterial, viral, and vascular diseases. Specific treatment of toxoplasmosis was initiated, with good progression of visual acuity and normalization of the visual field.[12]

Peripapillary toxoplasmosis is less common than the involvement of other retinal sites and ranges from 35.3% in southern Brazil[3] to 5% in Japan.[4] In the Democratic Republic of Congo, one patient presented with peripapillary retinochoroiditis with no vitritis, due to toxoplasmosis in the LE. The initial visual acuity was counting fingers, but there was a favorable response to treatment for toxoplasmosis, with a final visual acuity of 20/20 after 8 months, although the patient developed papillary pallor and impairment of the upper visual hemifield.[13]

In the present case, visual acuity also recovered (20/20), but on the visual field exam performed in the 5th month, a defect was observed; it was especially evident in the lower nasal quadrant due to the superior temporal location of the peripapillary scar. The visual field defect remained the same in the lower nasal quadrant, but showed a slight increase in the lower temporal quadrant one year after onset of the disease.

Papillitis due to toxoplasmosis may present bilaterally, as described in the report of a patient who presented with an active upper peripapillary lesion in only one eye (LE), but whose visual acuity normalized after specific treatment.[7] However, bilateral papillitis with no retinochoroiditis occurred in a patient with positive IgG and IgM for toxoplasmosis, and good results were obtained from treatment with pyrimethamine, sulfadiazine and folinic acid without the use of corticosteroids.[14]

The adverse effects of treatment for ocular toxoplasmosis are significant, and the patient presented with nausea, hypertension, abdominal pain, malaise, and renal colic. In one study, the classic treatment for ocular toxoplasmosis – corticoids, pyrimethamine, sulfadiazine and folinic acid – triggered adverse effects in 85% of 147 patients, and 10% dropped out of treatment.[15] In a review of 31 studies on treatment for toxoplasmosis involving 2,795 patients who used pyrimethamine, mostly with sulfadiazine or sulfadoxine, almost all patients required discontinuation or change of treatment because of adverse effects.[16]

The patient presented with renal colic, the cause of which was not investigated, and the classic treatment was temporarily replaced by trimethoprim/sulfamethoxazole. Sulfadiazine can cause kidney stones through crystallization or metabolic mechanisms.[17] The hypertensive crisis of the patient was associated with both the emotional disorder caused by the effects of the disease, and the physiological effects of treatment, such as sodium retention caused by prolonged use of corticosteroids. The number of complications associated with the classical treatment has driven the proposal of alternative methods; replacing the classic

treatment with trimethoprim and sulfamethoxazole is considered by some researchers to offer acceptable or similar results,[18,19] while others note the evidence to support this alternative is weak.[20]

Although there was damage to the visual field, the patient reported the defect interfered minimally with near vision, and she was able to continue with her work activities; however, it sometimes interfered with her distance vision, causing confusion. The cause of deficiency in the LE (20/40 visual acuity) was not determined.

The main lesson taken from the present case study is that ocular toxoplasmosis may have an initial presentation of pure papillitis, especially in regions endemic for the disease, and early specific treatment is necessary to prevent damage to the retina.

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