5-2014

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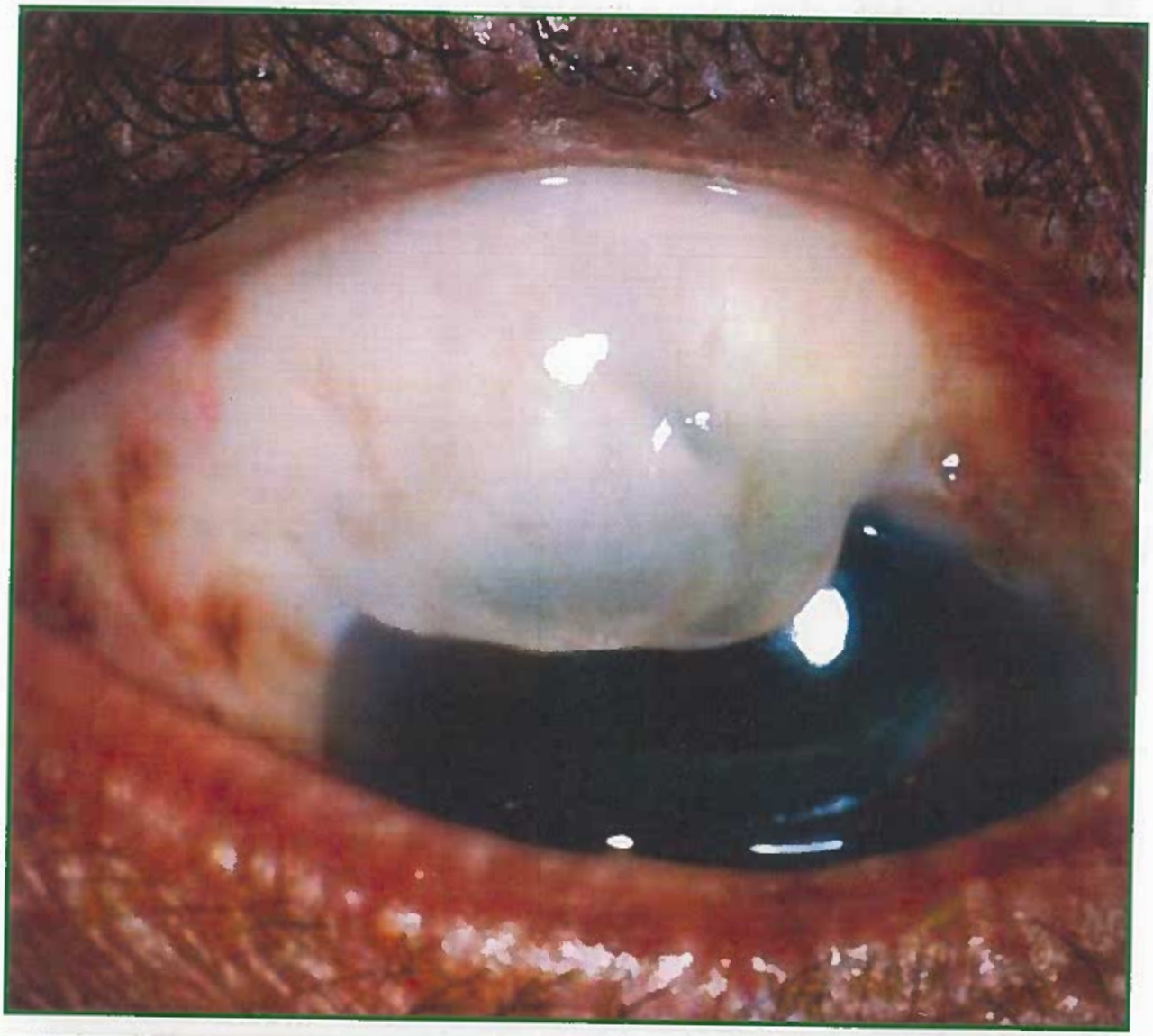
Recommended Citation

Holdeman, N. R., Burnham, S., Cruz, R. A., & Tang, R. A. (2014). Toxoplasmosis gondii: An Atypical Presentation of Optic Neuritis. Clinical and Surgical Ophthalmology, 32(2), 40–45. https://doi.org/10.1167/13.15.75

CSO Clinical Surgical & Ophthalmology

VOLUME 32, NUMBER 2, 2014



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Nicky R. Holdeman, OD, MD; Steven Burnham, BSc; R. Alejandro Cruz, MD; Rosa A. Tang, MD, MPH, MBA

Abstract

***Toxoplasma gondii* is a parasite whose natural host is the cat. Ocular toxoplasmosis can be categorized into two forms of infections: congenital, where an infant is infected in utero; and acquired, where an individual is typically infected by ingesting food contaminated with *T. gondii* oocytes. Although acquired infections are uncommon in the United States, toxoplasmosis should remain in the differential diagnosis of an infectious optic neuritis.**

The typical manifestation of toxoplasmosis is a retinochoroiditis, with a "headlight in the fog" appearance, due to dense inflammation of the vitreous; consequently, the diagnosis is often made clinically. This case describes a healthy 36-year-old Hispanic male who had an atypical presentation of ocular toxoplasmosis, with minimal vitritis and papillomacular involvement; thus serology was necessary for a definitive diagnosis. Treatment led to a rapid improvement in vision and ultimately a good prognosis.

Introduction

Toxoplasma gondii is an obligate intracellular protozoan parasite. Nearly one third of humanity has been exposed to this organism; however, only 1% to 3% will develop ocular manifestations.[1-3] Despite the relatively low rate of ocular involvement, *T. gondii* is one of the leading causes of posterior uveitis and is the leading cause of infectious retinochoroiditis worldwide.[1,2] The natural host of *T. gondii* is the feline family. Via fecal matter, cats release oocysts into the environment, which can remain viable for extended periods. Humans typically acquire infection by ingesting the oocysts found in contaminated soil, fruits, vegetables and undercooked meats or through congenital transmission in utero.[4] The oocysts develop into tachyzoites, the primary infectious form of *T. gondii*, which cause acute tissue destruction and inflammation. Tachyzoites then transform into bradyzoites, which form protective cysts and may remain dormant until a precipitating event causes reactivation.[3]

Case Study

A 36-year-old, healthy Hispanic male presented to a local optometrist with complaints of an acute onset of constant, blurred vision and "black specks" in the left eye that started earlier that morning. Prior to this event, the patient had never experienced any vision abnormalities. His family ocular and medical history was unremarkable. He was not using any medications and had no known drug or environmental allergies. The patient was a police officer who had never smoked and consumed alcohol only occasionally. He denied any sexually transmitted diseases.

Unaided acuities were 6/4.5- (20/15-) in the right eye and 6/6- (20/20-) in the left; refraction yielded a low simple hyperopia in both eyes. Gross inspection and slit lamp examination were unremarkable, with no cells detected in the anterior chamber or in the vitreous in either eye. Ophthalmoscopy revealed no abnormalities in the right eye but disclosed optic nerve edema in the left eye. Humphrey visual field, (HVF) 24-2 SITA Fast of the right eye was normal, but did show a generalized depression, with an enlarged blind spot in the left eye (Fig. 1).

Following the examination, further discussion revealed a history of cold sores, with a recent labial infection. The patient also reported that he had experienced flu-like symptoms, with a low-grade fever, which had persisted for approximately two months. In addition, he noted that his daughter and his stepdaughter both had cats, but he denied changing the litter or having any close contact with either pet. Lastly, he acknowledged that he enjoyed hunting and

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Disclosures: Dr. R. Alejandro Cruz reports no disclosures. S. Burnham reports no disclosures. Dr. Rosa Tang serves as principal investigator for NORDIC Pseudotumor Cerebri Clinical Trial and receives research support by NFI, NIH, Roosevelt Hospital NY, NORDIC, Biogen, Teva, Bayer, Eisai. Dr. Tang receives honoraria from serving on the advisory committee membership of Amprya, Teva and Merck. Dr. Tang receives honoraria as a member of the speaker's bureau for Biogen, Serona, Bayer, and Teva. Dr. Nicky R Holdeman is a medical consultant for Bausch & Lomb Pharmaceuticals and the Cooper Institute in Dallas, Texas. Dr. Holdeman receives research support from Allergan Pharmaceutical and SARCode Bioscience, Inc.

This article has been peer-reviewed.

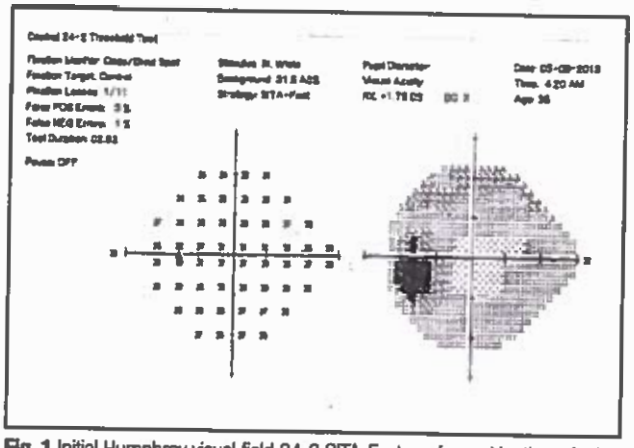

Fig. 1 Initial Humphrey visual field 24-2 SITA-Fast, performed by the referring optometrist, showed an overall depression and enlarged blind spot in the left eye. The right visual field was unremarkable and was not included.

had recently handled deer meat. The patient was referred to his primary care physician (PCP), with a recommendation to obtain an MRI of the brain and orbits.

An MRI, with and without contrast, was performed as well as a CBC, CRP, ESR, thyroid panel, lipid profile and hepatic function testing. The MRI of the brain and orbits was unremarkable and clinical pathology revealed no abnormalities. Over the course of the following week, the patient's symptoms gradually worsened but there were no significant changes noted upon examination.

A referral was then made to a neuro-ophthalmologist, who noted a 0.6 log unit afferent pupillary defect (APD), 1+ vitreal cells, and 4+ optic nerve edema in the left eye; examination of the right eye was unremarkable (Fig. 2). A visually evoked potential showed normal implicit times and amplitudes in both eyes. A multifocal electroretinogram (mfERG) was normal in the right eye but there was a reduced response in the inferior temporal field in the left eye (Fig. 3). Optical coherence tomography (OCT) of the right eye was normal but the left eye had significant subretinal fluid in the superior papillomacular bundle (Fig. 4). Intravenous fluorescein angiography (IVFA) showed no abnormalities in the right eye, but disclosed diffuse leakage of the left optic disc, with no vascular or macular irregularities (Fig. 5). With evidence of an inflammatory process, a chest X-ray, PPD, ACE levels, RPR, FTA-ABS, HIV testing, Bartonella antibodies, and Toxoplasma antibodies were requested. The patient was prescribed oral azithromycin while awaiting the results of the ancillary tests.

Twelve days after the initial presentation, the patient requested to be seen emergently due to a sudden change in vision. His BCVAs remained 6/6 (20/20) in the right eye, but had declined to 6/60 (20/200), with eccentric

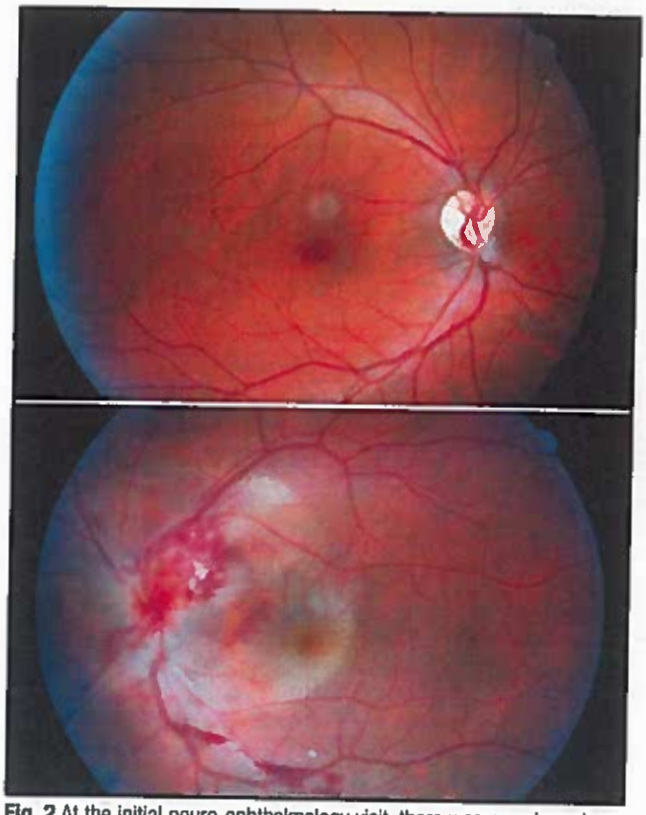

Fig. 2 At the initial neuro-ophthalmology visit, there was massive edema of the left optic nerve, with peri-papillary and pre-retinal hemorrhages, as well as venous engorgement and a large area of serous fluid superotemporally suggestive of neuroretinitis. The right eye was unremarkable.

fixation, in the left. The APD in the left eye had progressed to 0.9 log units and color perception by HRR plates was decreased in the left eye. Amsler grid showed a defect in the temporal half of the left eye and a HVF 24-2 SITA Fast disclosed a generalized, relative, deep scotoma centered on the blind spot in the left eye (Fig. 6). The visual field of the right eye had low test reliability, but showed no significant defects. A repeat OCT demonstrated persistent subretinal fluid in the papillomacular bundle of the left eye, while the right eye remained unremarkable (Fig. 7).

The patient was admitted to the hospital for observation. Soon thereafter, testing revealed *T. gondii* IgG and IgM antibodies, indicating a recently acquired toxoplasmosis infection. The patient was given a five-day course of pyrimethamine, sulfadiazine, leucovorin calcium, methylprednisolone succinate, valacyclovir, and pantoprazole. The patient was referred to the Center for Disease Control for evaluation of long-term antibiotic treatment.

The patient was last seen for a scheduled follow-up evaluation four months after the initial onset. Best-corrected visual acuities were now 6/6 (20/20) in both

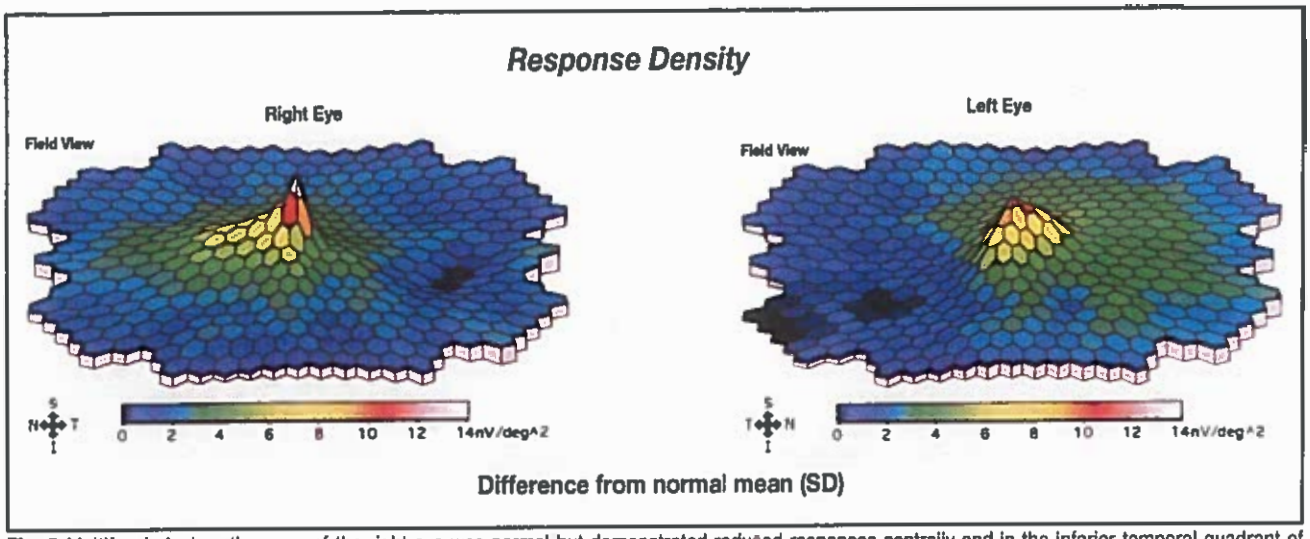

Fig. 3 Multifocal electroretinogram of the right eye was normal but demonstrated reduced responses centrally and in the inferior-temporal quadrant of the left eye.

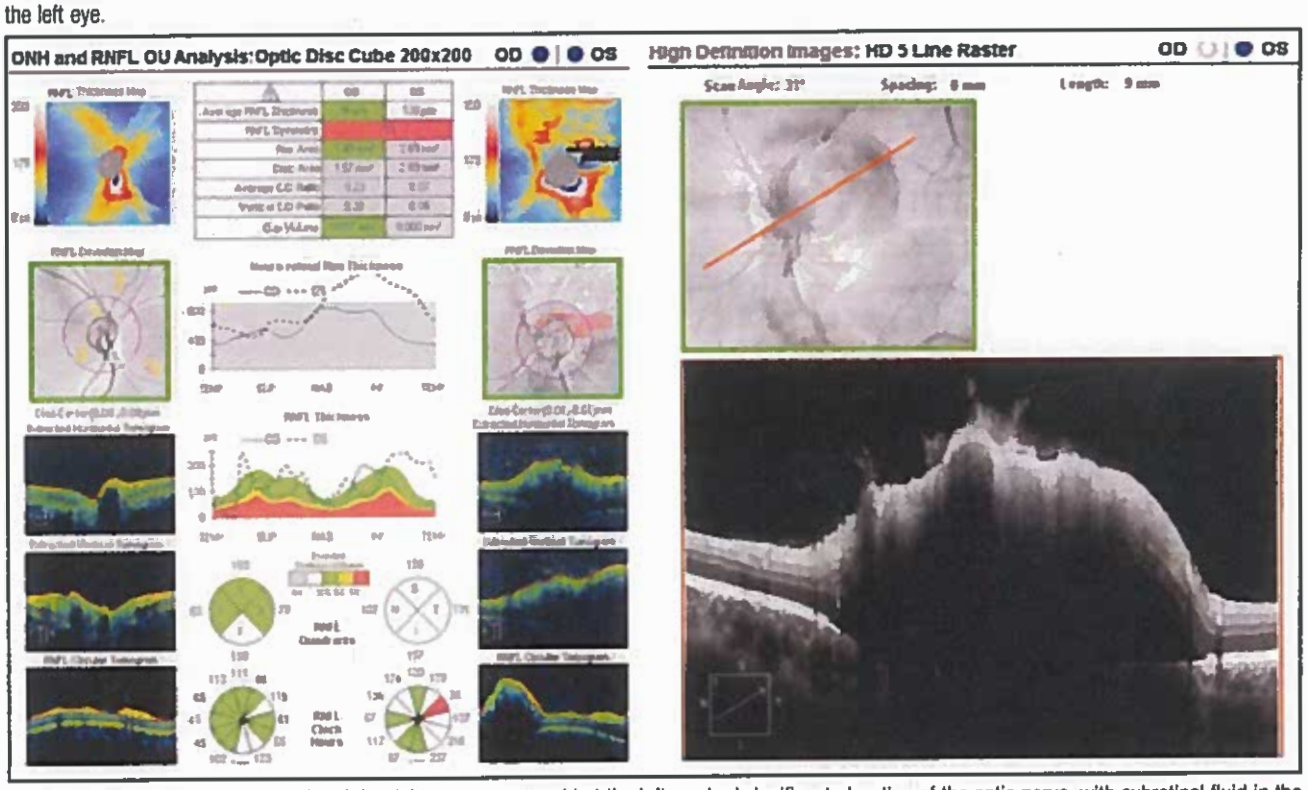

Fig. 4 Optical coherence tomography of the right eye was normal but the left eye had significant elevation of the optic nerve, with subretinal fluid in the superior papillomacular bundle.

eyes. There was significant reduction in the optic nerve edema of the left eye, resolution of the pre-retinal and retinal hemorrhages, with mild residual retinal scarring (Figs. 8, 9). Humphrey visual fields demonstrated improvement in the left eye compared to prior testing (Fig. 10). Initial findings of what may have progressed to a necrotic and non-resolving neuro-retinitis secondary to a *T. gondii* infection were almost entirely resolved.

Discussion

Although acquired *T. gondii* is rare in the United States, it is still a potential cause of infectious optic neuritis, as demonstrated by this case. Clinicians often diagnose ocular toxoplasmosis based on the signs of active retinochoroidal lesions, vitreous inflammation, and a "headlight in the fog" appearance, all of which are commonly found in immunocompetent patients.[1,5,6] However, this healthy male had

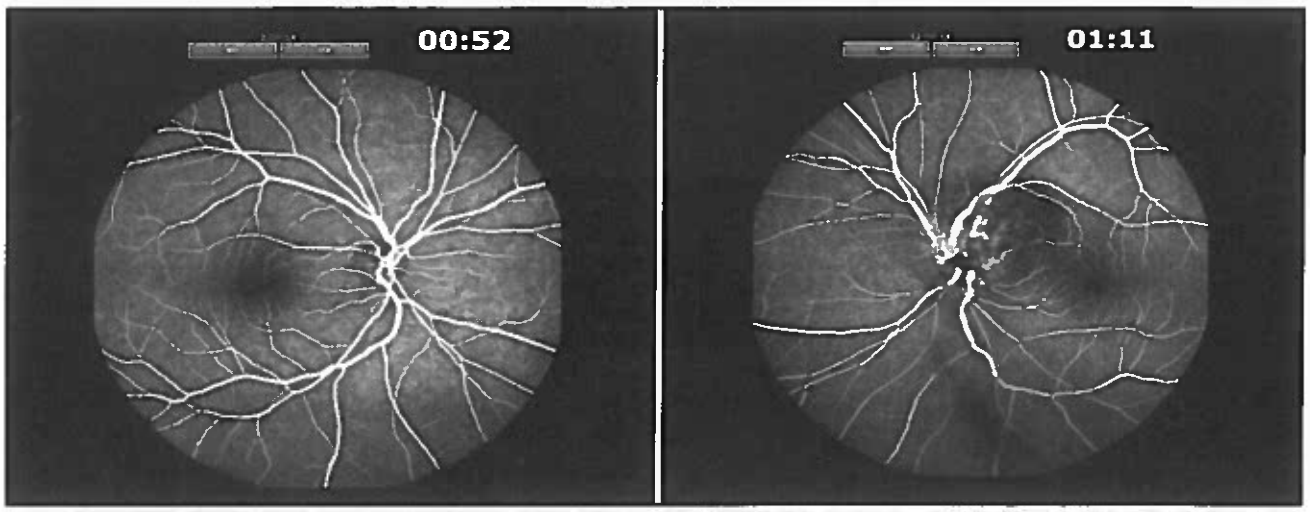

Fig. 5 Intravenous fluorescein angiography showed no abnormalities in the right eye, but disclosed diffuse leakage of the left optic disc, with no vascular or macular irregularities.

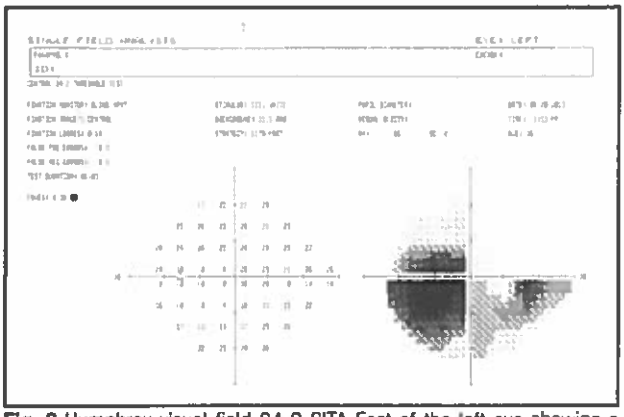

Fig. 6 Humphrey visual field 24-2 SITA Fast of the left eye showing a deep, arcuate defect surrounding the left blind spot and encroaching central vision

minimal vitritis, with optic nerve involvement, which is an unusual presentation for toxoplasmosis.[5] Despite lack of significant vitreous inflammation, there is not necessarily reason to suspect that every patient is immunocompromised. It has been reported that deep retinal lesions (i.e., punctate outer retinal toxoplasmosis) are often associated with less vitreous inflammation, as in this case.[5] This atypical manifestation required the exclusion of other infectious entities that can produce an optic neuritis, such as toxocariasis, cat scratch disease, tuberculosis, sarcoidosis, Lyme disease, syphilis, herpes, or cytomegalovirus.[6,7] Serology is supportive and the presence of IgM antibodies, detected by IFA and ELISA testing, indicates the presence of a recent infection. However, these tests are not diagnostic in every situation, as 20% to 70% of the general population can show positive titers.[8] It may be necessary to confirm difficult or atypical cases with paracentesis of the anterior chamber, using polymerase chain reaction, to detect *T. gondii* DNA in the aqueous.[1,8]

Indications for treatment vary considerably between practitioners,[9] despite the fact that more than 94% of patients with ocular toxoplasmosis will have permanent visual defects, per automated perimetry.[10] Many clinicians opt to monitor a peripheral lesion in an immunocompetent individual with good acuities, as the infections are typically self limiting[1,9] However, reduced acuities, associated with lesions threatening major vessels, the optic nerve, and/or perifoveal areas, are indicators for treatment, as was seen in this case.[1,8] Treatment of vision threatening toxoplasmosis typically includes some combination of antimicrobial and anti-parasitic agents, although their efficacy has not been proven in clinical trials.[11] Choices often involve a multidrug approach including pyrimethamine, with some combination of azithromycin, sulfadiazine, clindamycin, or sulfamethoxazole/trimethoprim. Patients treated with pyrimethamine should also receive folinic acid (leucovorin calcium) to minimize bone marrow suppression.[1,7,11,12] The use of oral prednisone, with concurrent antimicrobial treatment, may be beneficial in immunocompetent patients, especially when there is optic nerve and/or macular involvement.[1,7] However, one must consider that systemic therapy is expensive and can have significant side effects. A viable and potentially safer option for patients who cannot tolerate systemic therapy, is a combination of clindamycin and dexamethasone given as an intravitreal injection.[1,13] Longer-term treatment of ocular toxoplasmosis is aimed at reducing the severity and frequency of recurrences. Use of intermittent trimethoprim/sulfamethoxazole for several months has been shown to reduce the rate of recurrence.[1,14] Management of choroidal neovascularization includes photodynamic therapy or anti-VEGF agents (intravitreal bevacizumab or ranibizumab).[1,15-17]

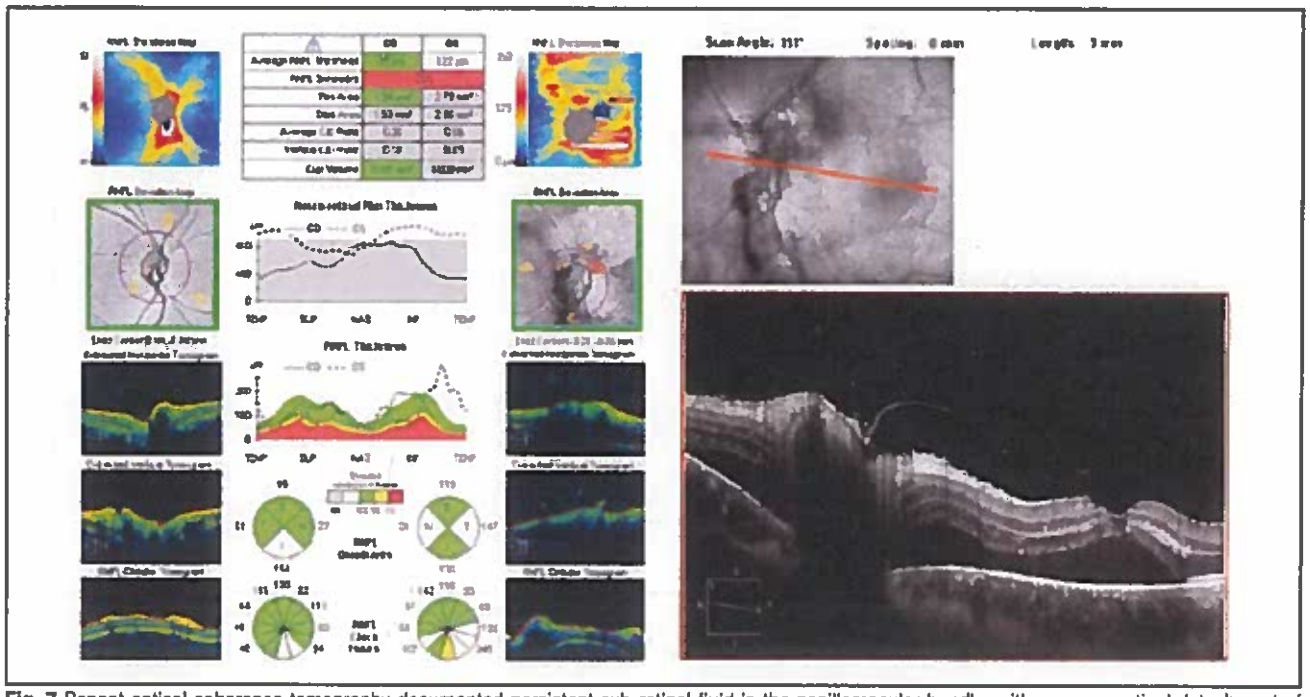

Fig. 7 Repeat optical coherence tomography documented persistent sub-retinal fluid in the papillomacular bundle, with a serous retinal detachment of the left eye, while the right eye remained within normal limits.

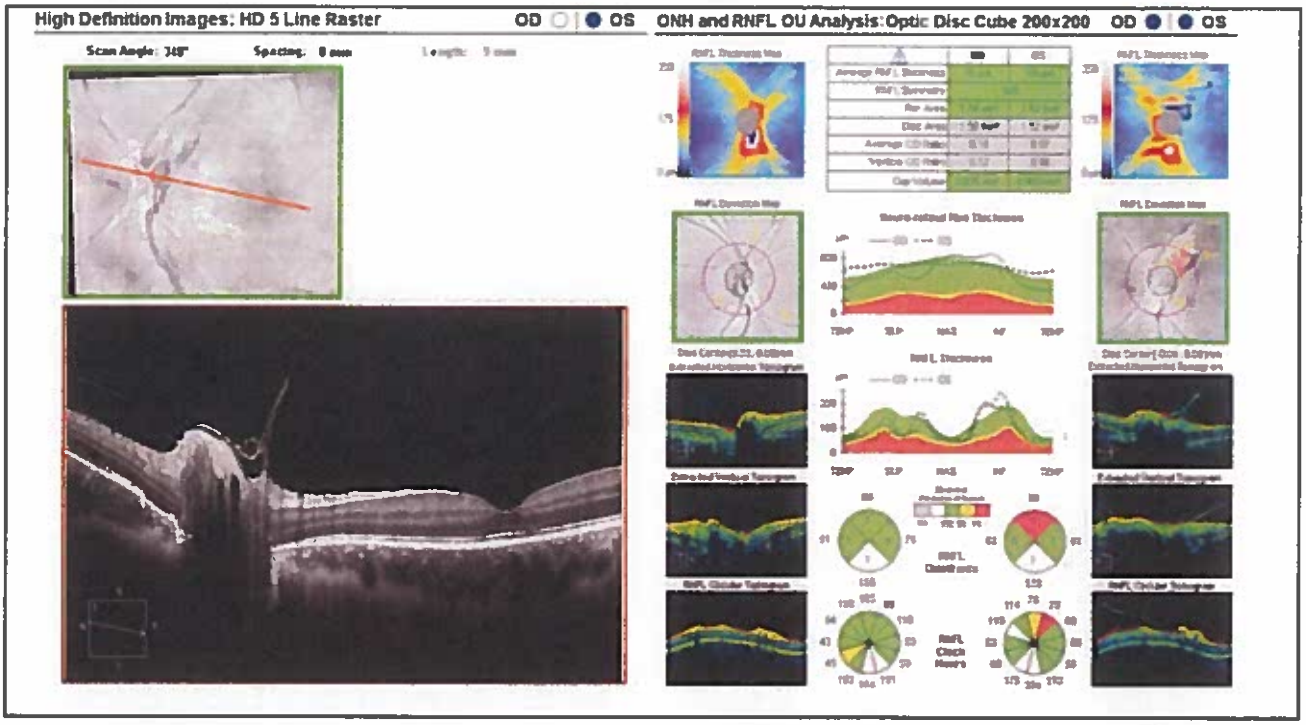

Fig. 8 Several weeks following treatment, OCT showed significant reduction of optic nerve edema, mild retinal scarring, and gradual dissipation of serous fluid in the left eye.

The ocular complications associated with toxoplasmosis include risk of recurrence, visual field defects, retinal detachment, sub-retinal neovascular membranes, cataracts, cystoid macular edema, papillitis, glaucoma, and chronic posterior uveitis.[1,7] Since this patient had a newly acquired lesion, with optic nerve and macular involvement, frequent progress exams were indicated to properly manage potential complications. Fortunately,

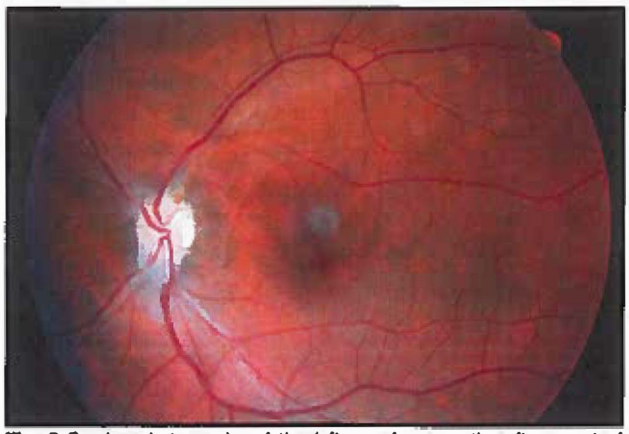

Fig. 9 Fundus photography of the left eye, four months after onset of symptoms, showed resolution of optic nerve edema, fading of pre-retinal and retinal hemorrhages and mild residual retinal scarring.

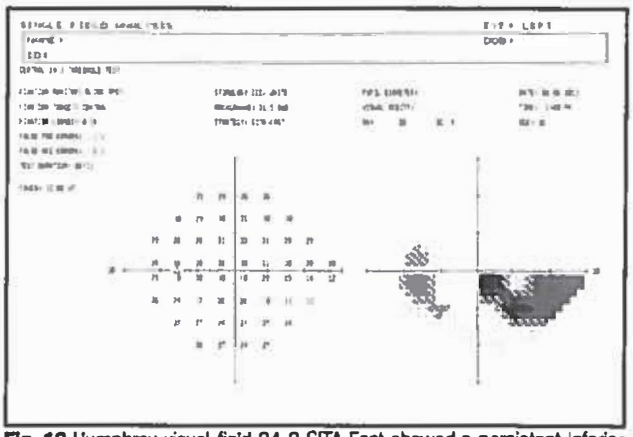

Fig. 10 Humphrey visual field 24-2 SITA Fast showed a persistent inferior arcuate defect in the left eye, but was somewhat improved compared to prior tests.

early diagnosis and intervention led to a good visual prognosis.

Conclusion

Although acquired ocular toxoplasmosis is uncommon in the United States, infection via contaminated food or water does occur.[16-19] Consequently, clinicians should consider toxoplasmosis in cases of atypical optic neuritis and use appropriate tests to assist in the diagnosis and management. ❑

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