Papillitis and Neuroretinitis as Atypical Presentations of Ocular Toxoplasmosis

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Brief report

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Abstract

We report three cases of optic nerve toxoplasmisis, an unusual form of ocular toxoplasmosis. In one patient the optic nerve involvement occurred in an eye with a toxoplasmic chorioretinal scar and choroidal neovessels in the supramacular area, subretinal fibrosis, and pigment epitheium detachment. The other two patients had papilledema without healed or active chorioretinal lesions, but both had retinal hemorrhage and macular involvement. The diagnosis was based on clinical examination and elavated serum toxoplama antibodies. Optical coherence tomography helped uncover the structural chorioretinal changes. All three patients were treated with a combination of oral antitoxoplasmic drugs, oral prednisone, and intravitreal injection of bevacizumab. Visual acuity improved in all of them. Optic nerve involvement in ocular toxoplasmosis must be considered when papilledema occurs both in isolation and in the presence of an active or scarred chorioretinal lesion.

Introduction

Toxoplasmosis, caused by the protozoan Toxoplasma gondii (T. gondii), can affect several organs including the eye. Ocular toxoplasmosis (OT) may result from both congenital and acquired infection after birth.[1] Approximately 20% of infected people develop OT, which is the leading cause of posterior infectious uveitis in immunocompetent people [1, 2]. OT in the form of retinochoroiditis can account for up to 85% of all infectious causes of posterior uveitis.[2] Its hallmark sign is a focal necrotizing retinitis associated or not with vitritis and anterior uveitis. Regardless of wthether it is teated or not, retinal necrosis heals by leaving a pigmented retinochoroidal scar. Toxoplasma-induced retinal choroiditis can also manifest itself as mulitiple gray-white punctate lesions deep in the retina [3, 4]. Optic nerve toxoplasmosis is a less common presentation and is believed to occur in 5.3–16.5% of all OT.[5] Involvement of the optic nerve typically occurs next to or far from an active retinochoroiditis lesion. It can also present without an active or scarred lesion as papillitis or neuroretinitis [5]. It is usually accompanied by vitritis and sometimes by anterior uveits, but some other times there is neither vitritis nor anterior uveitis [6]. Posterior segment complications of OT include, among others, cystoid macular edema, retinal detachment, retinal artery or vein occlusion, vasculitis, and subretinal and choroidal neovascularization (CNV) [7–9]. CNV is a rare and late complication of toxoplasmic chorioretinitis. We report herein three cases of optic nerve toxoplasmosis presenting as papillitis and neuroretinitis with some of the above complications.

Case Description

Case #1

A 56-year old woman with uneremarkable past medical, ophthalmological, and family history presented complaining of blurred vision in the right eye that started two months earlier. Her visual acuity was limited to counting fingers in the right and 1.0 in the left eye. The anterior segment was free of inflammation signs both eyes. There were no signs of vitritis either. Intraocular pressure (IOP) was 16 mmHg in both

eyes. Fundus examination revealed papilledema covering the upper half of the optic disc, a chorioretinal scar, and fibrotic lesion near the macula in the right eye (Fig. 1). The left eye appeared normal. Optical cohérence tomography (OCT) of the right eye showed an elevated optic disc, thickening of peripapillary retinal fiber layer (RNFL) in the superior, inferior and nasal sectors, pigment epithelium detachment (PED), small pockets of intraretinal fluid, and subretinal fibrosis in the macula area (Fig. 1). OCT examination of the left eye showed no macular or optic disc abnormalities. The average central retinal thickness was 361 µm in the right and 193 µm in left eye. The average peripapillary RNFL thickness was 172 µm and 121 µm in the right and left eye, respectively. Laboratory tests showed normal white blood cell (WBC) count (3.79 $10^3/mm^3$) and red blood cell (RBC) count (3.93.$10^6/mm^3$). Hemoglobin (Hb) level was normal (11.8%) and hematocrit too (35.4%). Erythrocyte sedimentation rate (ESR) at the first hour was accelerated (43 mm), and the WBC differential count was predominantly lymphocytic (neutrophils: 35% lymphocytes: 55%, eosinophils: 3%, monocytes: 7%). Serum toxoplasmosis antibody titers were 77 IU/ml for IgM and 0.01 IU/ml for IgG. The diagnosis of toxoplasma-related pure papillitis with pre-existing CNV was made and the patient was treated with a combination of oral antiparasitic drugs (association pyrimetamin, sulfadiazine, rovamycin), folic acid, oral prednisone, and intravitreal injection of 0.05 ml of bevacizumab (Avastin, Roche, Basel, Switzerland). She received a total of 3 intravitreal injections, one per month and parasitic drugs for 4 weeks. A month later, visual acuity in the right eye increased to 0.5, fundus photography showed no change relative to baseline, and OCT scan revealed persistence of the optic disc elevation (Fig. 1) and complete resorption of the intraretinal fluid (Fig. 1). The patient was advised to pursue with another round of antiparasitic drugs.

Case #2

A 59-year-old female patient presented with intermittent redness in both eyes, more pronounced in the left eye for the last 2 months. She also had pain, blurred vision and myodesopsia in her left eye. Her medical history was marked by similar episodes during the last two years. She also reported suffering for rheumatism. Best corrected visual acuity was 9/10 in the right and 5/10 in the left eye. Anterior segment and fundus examinations of the right eye were unremarkable. The left eye showed keratic precipitates, 1 + anterior chamber cells and 2 + anterior vitreous cells. Fundus examination of the right eye was normal whereas the left eye had papilledema with exudates and hemorrhage in the papillomacular bundle. Peripalillary and macular OCT scans were normal in the right eye, but showed an epiretinal membrane, macular edema, and intraretinal exudates. Average peripapillary RNFL thickness was greater in the left (234 µm) than the right eye (138 µm), with the increase in thickness affecting more the superior and nasal quadrants. Laboratory testing showed normal WBC count (7.6 x $10^3/mm^3$), normal Hb level (15 g/dl) and WBC differential count (neutrophils: 59%, lymphocytes: 36%, monocytes: 5%). ESR was within normal range (17 mm/hr). Toxoplasmosis antibodies titers were 192 IU/ml for IgG and 0.04 IU/ml for IgM. She was diagnosed with toxoplasma neuropapillitis. She was started on oral antitoxoplasmosis drugs (sulfadiazine, pyrimetamin, and rovamycin), oral folic acid, and oral as well as eye drops corticosteroids. After 5 weeks of follow-up, visual acuity was 7/10 in the left eye, and both keratitic and vitreous cells were no longer present. Papilledema decreased substantially, retinal hemorrhage completely

resorbed, but exsudates remained unchanged. She unfortunately suffered adverse reactions more likely to sulfadiazine, and the parasitic drugs were discontinued. However, she continued to be treated with corticosteroids orally and through periocular injections.

Case #3

This was a 62-year-old woman whose main complaints were pain and redness of left eye for the last 48 hours preceding her presentation. She had a history of insomnia and peripheral spondylarthritis for which she was under care. Her best corrected visual acuity was 10/10 in both eyes. Anterior segment examination showed conjonctival hyperhemia with perikeratic circle, keratic precipitates and posterior synechiae from 6 to 10 o'clock in the right and at 9 o'clock in the left eye, with diffuse iris atrophy in both eyes. IOP was 15 mm Hg in the right and 13 mm Hg in left eye. Fundus examination was normal in both eyes. Laboratory workup showed normal WBC count (5300/mm^3), normal WBC differential count (neutrophils: 66%, lymphocytes: 32%, monocytes: 2%), serum C-reactive protein within normal level (6 ml/l), and accelerated ESR (50 mm/hr). The patient was diagnosed with bilateral chronic anterior uveitis and treated with oral prednisone and atropine eye drops. Symptoms and signs progressively improved. She returned a month later with tearing and mild lagophthalmos in her right eye. She reported being diagnosed with right side facial palsy four days before her presentation, for which she was prescribed prednisolone and vitamins pills. Visual acuity was 0.6 and 0.8 in right and left eye, respectively. Anterior and posterior segment examinations were unremarkable. IOP was 16 mmHg in both eyes. She continued with the same treatment. One year after her first presentation to our office, she returned again, complaining of blurred vision in both eyes and impression of visual field amputation in the left eye. Visual acuity was 0.9 in right and 0.5 in the left eye. Anterior segment examination showed mutton fat keratic precipitates in both eyes but more pronounced in the left. Pupils were regular with slugish reactivity to lighgt, there were pigments on the anterior lens capsule and signs of vitritis with 2 + cells in the left eye. Fundus examination was normal in right eye whereas the left eye had papilledema with superotemporal justapapillary hemorrhage resembling a branch retinal vein occlusion (Fig. 2). OCT scans revealed posterior vitreous detachment in both eyes with papilledema in left eye (Fig. 2) and small retrofoveal retinal detachment in the right eye. WBC was normal (6700/mm^3), WBC differential count was abnormal (neutrophils: 40%, lymphocytes: 60%), and ESR was accelerated (60 mm/hr). Serum toxoplasmosis antibody titers were 275 IU/ml for IgG and 0.2 IU/ml for IgM. She was treated for neuropapillitis with the combination sulfadiazine, pyrimetamin, and rovamycin. She also received folic acid and oral prednisone. A month later, she was symptomless. Visual acuity improved to 1.0 in the right and 0.6 in the left eye. There were no keratic precipitates and vitreous cells. IOP was 12 mmHg and 11 mmHg in right and left eye, respectively. Fundus examination was normal in right eye, and showed partial resorption of both papilledema and retinal hemorrhage in the left eye (Fig. 2). OCT imaging showed retinal reattachment in right eye, and decreased papilledema and retinal hemorrhage. At the 2-month follow-up visit, she complained again of redness and blurred vision in left eye, which started after she stopped all medications due to side effects. Visual acuity decreased to 0.8 in right eye but remained stable in the left eye. There were keratic precipitates in both eyes, but more pronounced in left eye.

Ophthalmoscopic assessment was normal in the right eye and showed substantial papilledema decrease and retinal hemorrhage in the left eye. On OCT was unremarkable in the right eye. In the left eye it confirmed the significant decrease of papilledema, but revealed an important macula edema (Fig. 2). Antiparasitic drugs were reinstated along with oral and topical corticosteroids.

Discussion

The clinical presentation of toxoplasmosis in our three patients covers two types of optic nerve involvement, namely pure papillitis and neuroretinitis. Although these types have been described previously, they occur infrequently. The particularity of the cases presented herein resides in the other signs accompanying this papillary involvement. In addition to papiledema, the first patient had CNV in the same area as the chorioretinal scar. CNV complicating ocular toxoplasmosis has been described previoulsy, with its prevalence ranging between 2% and 19%. CNV has previously been observed in association with healed toxoplasma chorioretinal lesions [10], as observed in the first patient. It can also rarely occur during the active phase of a chorioreritinis [11, 12]. In our patient, the combination of a past history of toxoplasma chorioretinitis evidenced by the scar in conjunction with CNV, a recent 2-month history of blurred vision, and papilledema is consistent with inflammation reactivation. Management options for CNV in healed toxoplasma chrorioretinitis include observation, laser photocoagulation, photodynamic therapy, corticosteroids and intravitreal injection of anti-vascular endothelial growth factor (VEGF) agents [13]. Because the optic nerve involvement was active and coexisted with a healed chorioretinal with CNV, the patient was treated with a combination of anti-VEGF and antiparasitic drugs, with favorable outcome. Functional improvement following bevacizumab intravitreal injection for CNV in toxoplasmosis has been reported in the literature [13]. The combination was meant for the antiparasitic drugs to prevent inflammation reactivation that can be induced by the intravitreal anti-VEGF agent used to treat CNV while, at the same time, acting on the parasite [13, 14].

The last two patients had neuroretinitis without chorioretinal scars in the context of chronic anterior uveitis. Both had retinal hemorrhage and the third patient had exudative retinal detachment in addition. In fact, optic nerve involvement in OT may present in various forms, namely contiguous to a juxtapapillary chorioretinitis, neuroretinitis, pure papillitis, distant to an active chorioretinitis lesion, and various combinations of these.[15] When optic nerve is affected without any chorioretinal scar or active lesion, asserting the diagnosis OT-related papillitis based on clinical ground alone can be challenging, but serologic tests may provide evidence of exposure to the parasite [15]. In these two patients serum IgG and/or IgM toxoplasma antibodies were elevated, allowing to suspect toxoplamosis as the cause of the disc swelling. Based on the clinical and OCT findings, patient #1 had pure papillitis whereas patients #2 and #3 had neuroretinitis.

In all three patients visual acuity improved after treatment, but to different extents likely due to the difference in macular involvement. Indeed, the increase in visual acuity after treatment is known to differ among the different types of papillitis, with the difference being driven more by macular than optic nerve involvement [15]. This is supported for instance by observations from previous studies that improvement

in visual acuity is often greater in pure papillitis than in papillitis with concurrent chorioretinal lesions [6, 15]. For others, the pre-treatment visual acuity reduction is often lower in pure papillitis than papillitis with macular involvement [6]. Thus, the pre- and post-treatment visual acuity mostly depend on whether the macula is involved or not rather than involvement of the optic nerve.

To conclude, papillary toxoplasmosis is an infrequent presentation of OT. Clinicians should be aware of this entity and be alerted in the presence of papilledema. The diagnosis is easier clinically when papilledema is associated with an active or a scarred chorioretinitis lesion. In isolated optic nerve involvement, serologic tests can help guide the diagnosis.

Abbreviations

OT
ocular toxoplasmosis
CNV
choroidal neovasculaization
IOP
intraocular pressure
OCT
optical coherence tomography
RNFL
retinal nerve fiber layer
PED
pigment epithelium detachment
WBC
white blood cells
RBC
red blood cells
ESR
erythrocyte sedimentation rate
VEGF
anti-vascular endothelial growth factor

Declarations

Authors' contribution

NNK compiled the cases. NNK and JCM searched and reviewed the literature. NNK drafted the manuscript. All authors contributed critically reviewed and discussed the manuscript, and approved the final version.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

All procedures performed in accordance with the ethical standards of University of Kinshasa School of Public Health and with the Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent was obtained ws obtained from all participants.

Consent for publication

Consent is not required as the information is anonymized and the submission does not include images that may identify the people involved.

Competing interests

The authors declare that they have no competing interests.

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Figures

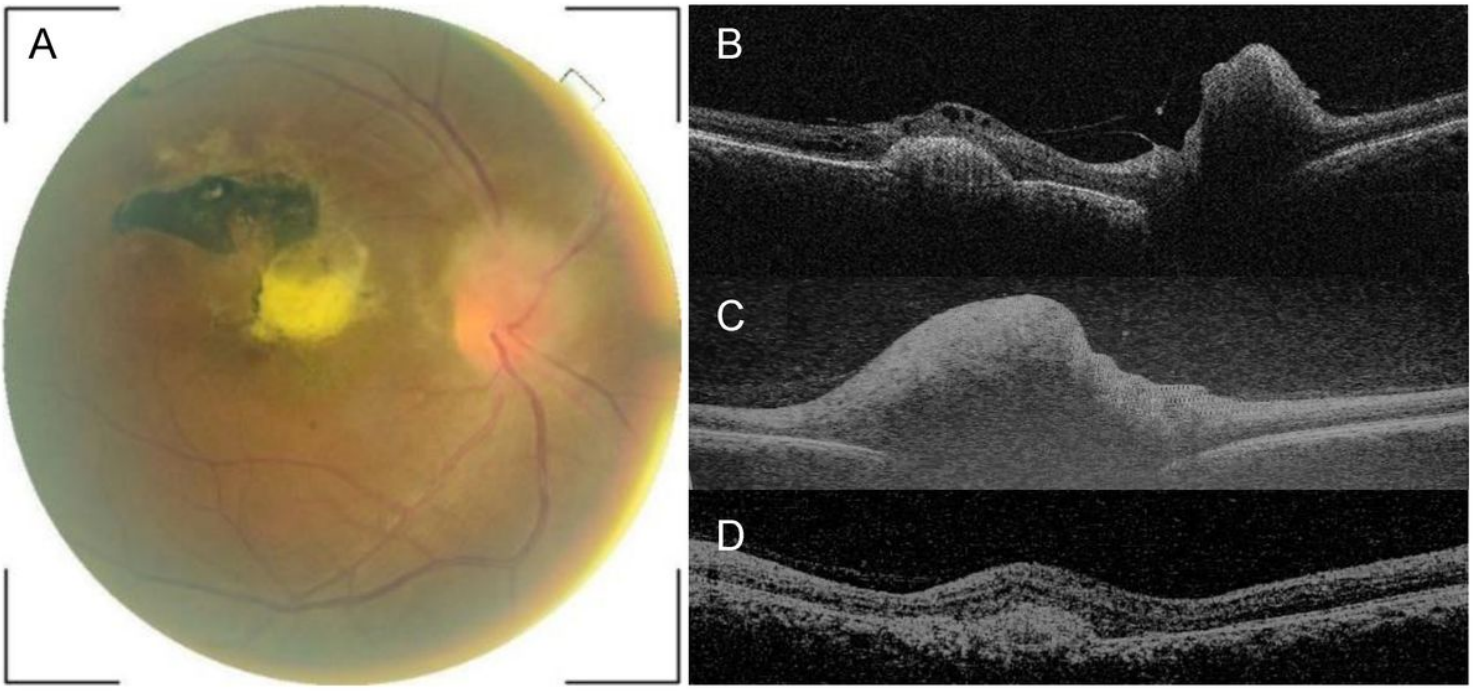

Figure 1

Baseline righ eye fundus fundus photo of patient #1 showing papilledema in the superior part of optic disc and chorioretinal scar and fibrosis near the macula (1A). Baseline OCT (1B) shows optic disc elevation, pigment epithelium detachment with a few pockets of intraretinal liquid and subretinal fibrotic tissue in the macula area. After treatment, there was no apparent change on fundus photograph whereas OCT scans shows persistence of the disc elevation (1C) and resorption of the intraretinal liquid (1D).

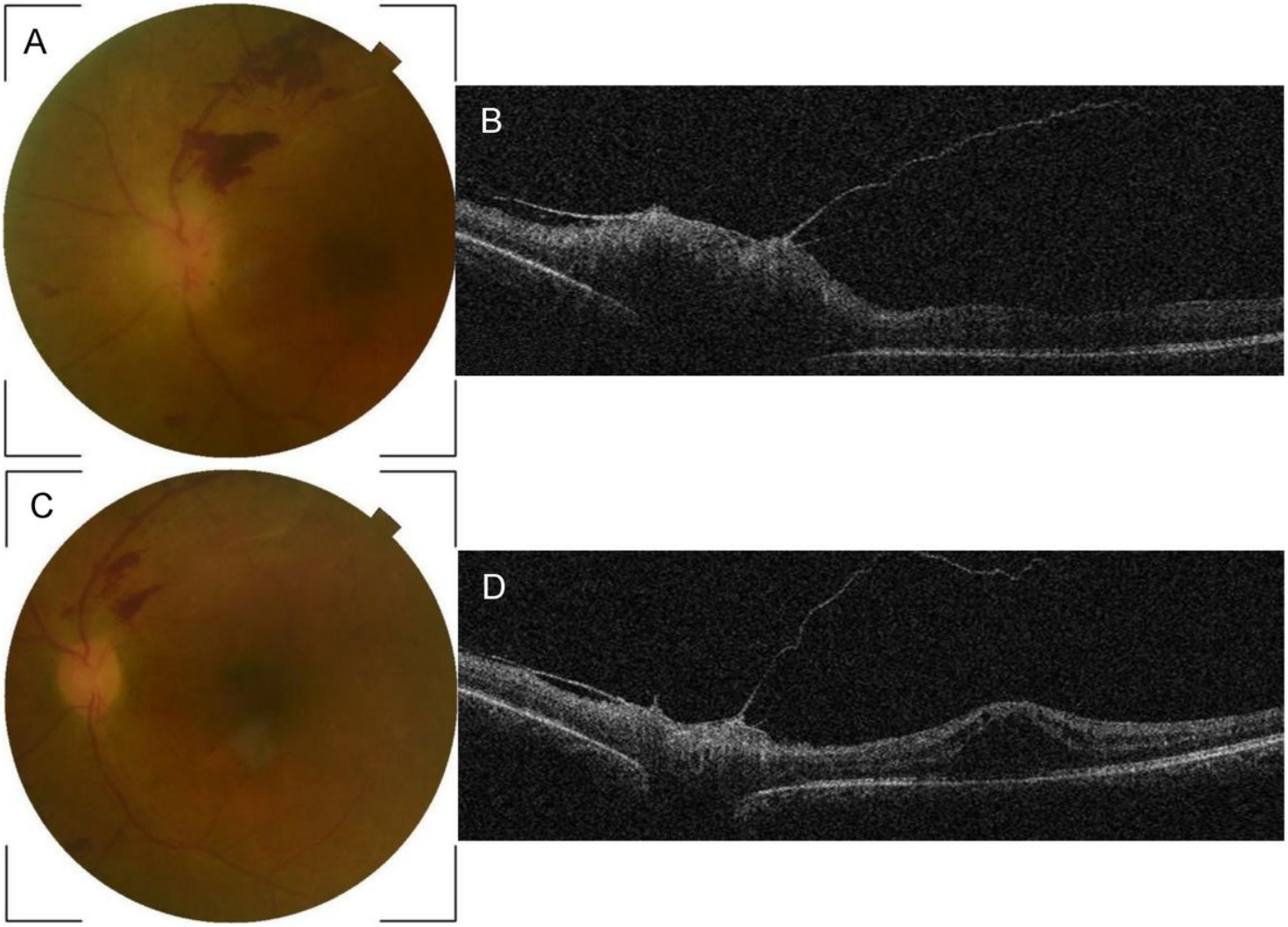

Figure 2

Baseline fundus photo (2A) of the left eye of patient #3 displaying papilledema with retinal hemorrhage along the superotemporal retinal vein. OCT scan shows elevation of the optic disc, an epiretinal membrane, posterior vitreous detachment (PVD), and slight thickening of the macula (Figure 2B). Post-treatment imaging depicts almost complete resorption of the papilledema (2C), substantial resorption of the retinal hemorrhage (2C), significant reduction in optic dsc elevation (2D), PVD, and an macular serous detachment (2D).