Case Reports in Ophthalmology

Case Rep Ophthalmol 2023;14:369–375
DOI: 10.1159/000528787
Received: April 28, 2022
Accepted: November 7, 2022
Published online: August 16, 2023

Case Report

Monitoring Delayed Toxoplasmosis-Related Branch Retinal Artery Occlusion Using Widefield en face Optical Coherence Tomography and Multimodal Imaging

Prashanth Iyer Noy Ashkenazy Jeremy Liu Diana Laura
Marilyn Ann Marquez Thomas Albini

Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA

Keywords

Toxoplasmosis · Chorioretinitis · Retinal artery occlusion · Paracentral acute middle maculopathy · Swept-source optical coherence tomography

Abstract

Ocular toxoplasmosis has a known, rare association with acute retinal artery occlusion (RAO). We describe a 21-year-old male who presented with acute focal toxoplasmosis chorioretinitis in the right eye treated with intravitreal clindamycin, intravitreal dexamethasone, and adjunct oral therapy for vision-threatening retinitis with subsequent quiescence. Nine months from his initial presentation, the patient presented with a branch RAO adjacent to an inactive retinal scar in the right eye. Widefield en face structural swept-source optical coherence tomography (SS-OCT) centered on the middle retina showed paracentral acute middle maculopathy (PAMM) in an arteriolar distribution. The patient was started on 81 mg of aspirin daily. Six months later, the en face structural SS-OCT and corresponding B-scans showed resolution of PAMM. Along with a review of the literature on toxoplasmosis-related RAOs, we present the first case of delayed-onset RAO in ocular toxoplasmosis.

Correspondence to:
Thomas Albini, talbini@med.miami.edu

Case Rep Ophthalmol 2023;14:369–375
DOI: 10.1159/000528787

Introduction

Ocular toxoplasmosis, the most common cause of infectious posterior uveitis, presents with vitritis and focal yellow lesions of necrosis in the retina. Toxoplasmosis has been associated with rarer vascular manifestations occurring during the acute phase of the disease, including retinal artery occlusions (RAOs), vein occlusions, perivasculitis, and choroidal vascular occlusions [1, 2]. Multimodal imaging, specifically swept-source optical coherence tomography (SS-OCT; PLEX Elite 9000, Carl Zeiss Meditec, Dublin, CA), can offer an advantage over traditional imaging techniques because of its widefield capabilities. We herein present a unique case of toxoplasmosis chorioretinitis, identified to have a delayed-onset branched retinal artery occlusion (BRAO) using multimodal imaging and 12 × 12 mm SS-OCT.

Case Report

A 21-year-old Brazilian male with a history of amblyopia in the left eye presented to the retina clinic with acute decreased vision and floaters in the right eye (OD) for 1 week. Visual acuity was 20/200 in OD and 20/70 in the left eye (OS). Intraocular pressure was 31 mm Hg in OD and 14 mm Hg in OS. Anterior segment examination revealed 3+ cells and diffuse keratic precipitates in OD; OS was normal. Fundus examination OD demonstrated vitreous haze and a superior yellow lesion (Fig. 1a). Fluorescein angiography (Optos®, UK) in OD revealed leakage in the superior macula (Fig. 1b). Optical coherence tomography (OCT) (Heidelberg Spectralis, Heidelberg Engineering, Germany) of OD through the macular lesion revealed inner retinal hyperreflectivity and edema suggestive of retinal necrosis (Fig. 1c, d). Fundus examination of OS revealed a central macular scar. Serum laboratory analysis was positive for toxoplasmosis IgG.

A clinical diagnosis was made of acute focal toxoplasmosis chorioretinitis in OD and chronic, inactive scar in OS. Intravitreal clindamycin 1 mg/0.1 mL and dexamethasone 0.4 mg/0.1 mL in OD were injected for vision-threatening retinitis. Topical dorzolamide-timolol drops were given twice daily in OD. In addition, from when the diagnosis was made, the patient was also treated with trimethoprim-sulfamethoxazole 800/160 mg twice daily, clindamycin 300 mg three times daily, and topical prednisolone and cyclopentolate for 42 days; afterward, prophylactic trimethoprim-sulfamethoxazole 800/160 mg was administered three times weekly. Three months from presentation, there was resolved retinitis with visual acuity of 20/20 in OD.

The patient returned 9 months from initial presentation with 2 weeks of blurry vision OD. Visual acuity was 20/20, but the patient described a peripheral scotoma in OD. Anterior segment examination was unremarkable in both eyes. Fundus examination of OD demonstrated retinal whitening and edema along the superior arcade adjacent to an inactive retinal scar (Fig. 2a). Fluorescein angiography demonstrates an artery traversing through the toxoplasmosis lesion, with blockage of perfusion distally (Fig. 2b). OCT revealed a hyperreflective band in the inner nuclear layer around the area of whitening, sparing the fovea (Fig. 2c, d). A 12 × 12 mm en face structural SS-OCT of the middle retina demonstrated paracentral acute middle maculopathy (PAMM) with non-perfusion in an arteriolar distribution (Fig. 3a–c). A diagnosis of BRAO was made and the patient was started on 81 mg of aspirin daily as an antiplatelet agent for secondary prevention of another ischemic event. Six months later, the en face structural SS-OCT and corresponding B-scans showed resolution of PAMM with interval development of retinal thinning (Fig. 2e–g, 3d–f). Visual acuity continued to be 20/20 in the affected eye.

Case Rep Ophthalmol 2023;14:369–375
DOI: 10.1159/000528787

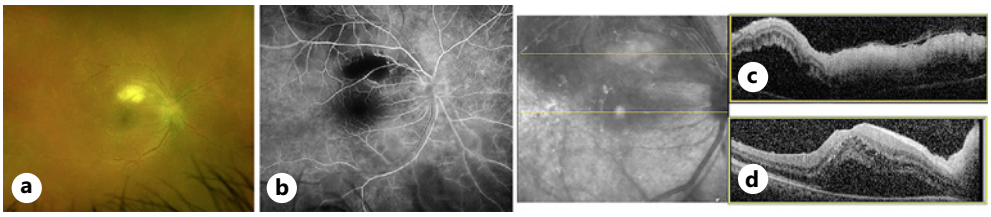

Fig. 1. Initial Presentation. **a** Fundus photography of OD demonstrates a hazy view with a yellow, creamy lesion near the superior arcade. **b** Early-phase fluorescein angiography of OD demonstrates leakage surrounding a central hypofluorescent lesion, along with leakage of the optic disc. **c** OD optical coherence tomography (OCT) B-scan on the lesion shows hyperreflectivity of the inner retina representing necrosis. **d** OCT B-scan on the macula shows subretinal and intraretinal fluid.

Discussion

RAO associated with ocular toxoplasmosis is a rare phenomenon that was first described by Gass in 1967 [3]. Multiple reports describing RAO in ocular toxoplasmosis have been published since then (Table 1). All of these cases of RAO occurred at the time of presentation of the toxoplasmosis chorioretinitis except one case which occurred 6 weeks after presentation [4]. Theodossiadis et al. [2] in 1995 reported that in 64 eyes with toxoplasmosis chorioretinitis, 92% of vascular events in their cohort occurred in the same quadrant as the active infectious retinitis. There were 3 cases of occlusive retinitis, all of which involved vessels traversing the active lesion. The acute vascular event resolved along with the active retinal lesion in 22% of cases [2].

The present case describes a young individual with active toxoplasmosis and a BRAO immediately adjacent to the infectious lesion that developed 9 months later with toxoplasmosis being quiescent. This is the first case describing a delayed-onset arteriolar occlusion in the absence of active toxoplasmosis. Like the other cases reported, the offended artery does traverse through the toxoplasmosis lesion and the ischemia occurs in the same quadrants as the healed toxoplasmosis lesion [2]. Previous reports have hypothesized that in active toxoplasmosis, the occlusive event may be due to the acute necrotizing reaction from the toxoplasmosis lesion that causes inflammation, resulting in contraction of the arterioles as a subsequent response [4]. These so-called "Kyrieleis plaques" are well-described foci of segmental periarteritis and endothelial inflammation, classically associated with toxoplasmosis chorioretinitis but also present in other infectious posterior uveitis including herpetic, syphilis, tuberculosis, and rickettsial disease [15, 16]. In addition, the viscosity of blood increases during active inflammation due to a release of heparin from mast cells, inhibiting coagulation of the viscous blood and causing a delay in blood flow [4].

In our case, although there could have been a subclinical focus of reactivation, the toxoplasmosis lesion appeared inactive at the time the RAO developed. We hypothesize that the process of a toxoplasmosis lesion forming into a chorioretinal scar may also involve external compression and manipulation of the involved artery, resulting in an occlusive event. Furthermore, the periarteriolitis and local necrosis associated with the original toxoplasmosis chorioretinitis may have led to chronic vascular endothelial injury which led to delayed occlusion and PAMM formation.

This is the first report describing PAMM from toxoplasmosis using widefield SS-OCT. En face structural OCT focusing with segmentation in the middle retina has previously been shown to detect PAMM with its distinct patterns, such as globular, arteriolar, and fern-like patterns [17]. In this case, we demonstrate an arteriolar pattern of PAMM using the SS-OCT, as the ischemia revolves around the artery involved. 12 × 12 mm SS-OCT can

Case Rep Ophthalmol 2023;14:369–375
DOI: 10.1159/000528787

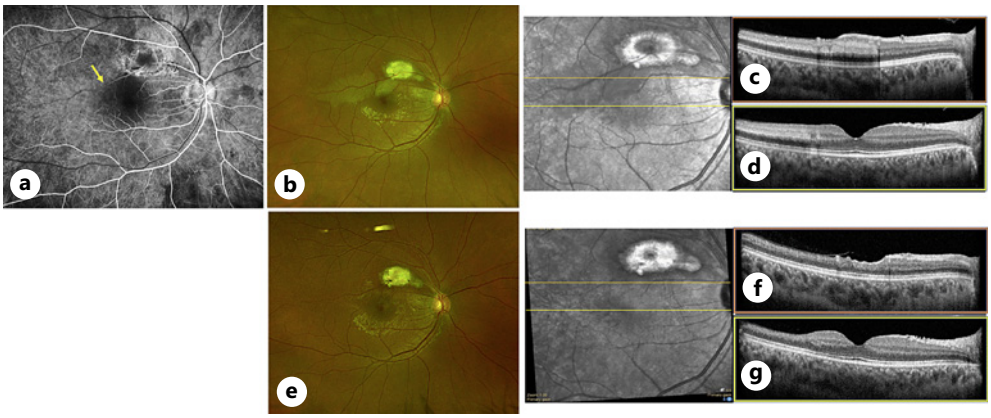

Fig. 2. 9-month follow-up of OD. **a** Early-phase fluorescein angiography demonstrates an artery traversing through the toxoplasma lesion becoming occluded (yellow arrow) and not perfusing distally. **b** Fundus photography demonstrates a superior, inactive yellow toxoplasmosis lesion with an extension of whitening along the superior arcade. Note that the whitening follows the artery that traverses through the toxoplasmosis lesion. **c** OCT B-scan on the area of whitening demonstrates hyperreflectivity of the inner nuclear layer, representing paracentral acute middle maculopathy (PAMM). **d** OCT B-scan on the fovea shows resolution of the macular edema with temporal PAMM. **e** Fundus photography 6 months later demonstrates resolution of the whitening. **f** OCT B-scan on the area of whitening demonstrates resolution of PAMM with now inner retinal thinning. **g** OCT on the fovea shows temporal thinning corresponding to previous PAMM.

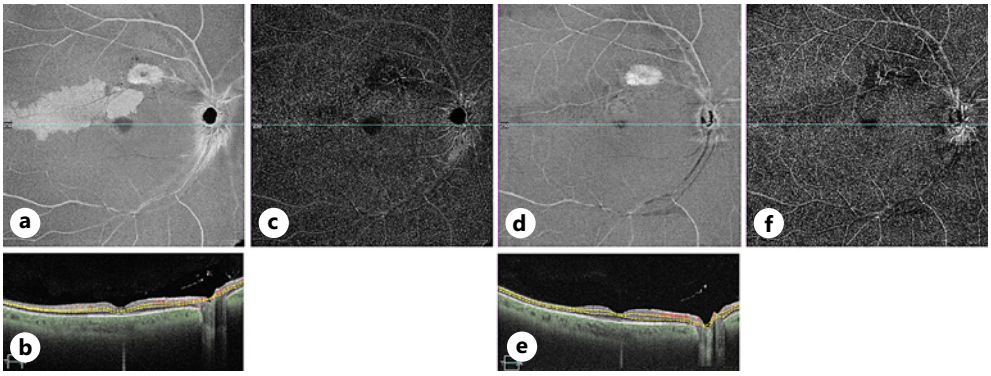

Fig. 3. a, **b** 12 × 12 mm en face structural SS-OCT demonstrates an arteriolar pattern of PAMM, with corresponding B-scan segmented in the middle retina. **c** 12 × 12 mm en face OCT angiography demonstrates areas of hyporeflectivity representing non-perfusion. **d**, **e** 6 months later, there is resolution of the arteriolar pattern PAMM on en face structural SS-OCT, with corresponding B-scan showing temporal thinning. **f** En face OCT angiography shows increased areas of non-perfusion around the affected retinal artery.

also detect wider areas of ischemia in PAMM compared to traditional 6 × 6 mm scans [18]. Without the widefield scans, it would not be possible to capture the extent of PAMM that is involved in this case. In addition, clinically widefield SS-OCT is advantageous because it can capture vascular and structural changes using one machine in a noninvasive manner. The SS-OCT also demonstrates resolution of PAMM in our patient after 9 months of follow-up (Fig. 3).

In most cases of RAO in toxoplasmosis, visual acuity can improve with time as long as there is no foveal involvement (Table 1). Despite a favorable outcome, the ischemic event can render the retina atrophic once the RAO is resolved. SS-OCT is a useful tool in documenting PAMM and its

Case Rep Ophthalmol 2023;14:369–375
DOI: 10.1159/000528787

Table 1. Summary of published cases of RAOs occurring in toxoplasmosis chorioretinitis

Study	Patients, *n*	Time frame to RAO	Visual acuity during RAO	Treatment	Final visual acuity
Gass [3] (1968)	N/A	N/A	N/A	N/A	N/A
Willerson et al. [5] (1977)	1, 17-year-old M, OS	During presentation	20/200	Sulfadiazine, pyrimethamine, folinic acid and prednisone	N/A
Braunstein and Gass [4] (1980)	1, 53-year-old F, OD	During presentation	CF	Pyramithamine, sulfadiazine, and topical steroid	20/30
	1, 24-year-old M, OS	6–8 weeks post episode	20/30	Steroid therapy	N/A
	1, 42-year-old F, OS	During presentation	HM	N/A	N/A
Haefliger and Müller [6] (1980)	3, 21-year-old M, rest in German	During presentation	N/A	Antibiotics and steroids	N/A
Morgan and Gragoudas [7] (1987)	1, 50-year-old F, OS	During presentation	3/200	Pyrimethamine, sulfadiazine, oral prednisone	10/200
Pakalin and Arnaud [8] (1990)	1, N/A in French	N/A	N/A	N/A	N/A
Theodossiadis et al. [2] (1995)	3, N/A	N/A	N/A	N/A	N/A
Gentile et al. [9] (1997)	1, 34-year-old M, OS (combined RAO and RVO)	During presentation	20/40	Trimethoprim-sulfamethoxazole 800/160 mg, prednisone 80 mg	20/20
	1, 14-year-old M, OS (combined RAO and RVO)	During presentation	20/100	Sulfadiazine, pyrimethamine, clindamycin, and prednisone	20/20
Kucukerdonmez et al. [10] (2004)	1, 22-year-old F, OD	During presentation	20/200	Trimethoprim/ sulfamethoxazole 1,600/320 mg, clindamycin 300 mg, prednisone 80 mg	20/30
Chiang et al. [11] (2012)	1, 17-year-old M, OD	During presentation	CF 10	Azythromycin 500 mg, prednisone 40 mg	20/70
Kianersi et al. [12] (2013)	1, 45-year-old F, OS	During presentation	20/50	Sulfadoazome 4 g, pyrimethamine 50 mg, folinic acid	20/25
Tolou et al. [13] (2015)	1, 60-year-old F, OS	During presentation	20/50	Anti-parasitic treatment and oral corticosteroids	20/20
Aggio et al. [14] (2016)	1, 22-year-old M, OS	During presentation	20/400	Pyrimethamine 50 mg, sulfadiazine 2 g, folinic acid 15 mg, prednisone 60 mg	20/30

(Continued on following page)

Table 1. (continued)

Study	Patients, *n*	Time frame to RAO	Visual acuity during RAO	Treatment	Final visual acuity
Neiweem and Jusufbegovic [15] (2020)	1, 38-year-old M, OD	During presentation	20/40	Trimethoprim/ sulfamethoxazole (1,600/ 320 mg orally twice daily)	N/A
Present study	1, 21-year-old M, OS	9 months	20/70	Aspirin 81 mg Previously oral trimethoprim-sulfamethoxazole, clindamycin; intravitreal clindamycin/dexamethasone	20/20

resolution caused by BRAO in cases of ocular toxoplasmosis. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000528787).

Acknowledgments

The authors would like to thank Department of Photography at Bascom Palmer Eye Institute, Miami, FL, USA.

Statement of Ethics

The authors have no ethical conflicts to disclose. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. All medical interventions have been carried out according to the latest protocols of therapy. Reporting and writing are all in compliance with the Declaration of Helsinki. The study protocol was reviewed and the need for approval was waived by the University of Miami/Bascom Palmer Ethics Committee.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was supported in part by an unrestricted grant from Research to Prevent Blindness GR004596 to University of Miami (New York, NY, USA) and NIH Center Core Grant P30EY014801 (Bethesda, MD, USA).The sponsor or funding organization had no role in the design or conduct of this study.

Author Contributions

Prashanth Iyer, MD; Noy Ashkenazy; Jeremy Liu, MD, MD; Diana Laura, MD; Marilyn Ann Marquez, MD; and Thomas Albini, MD, meet the ICMJE criteria including substantial contributions to the conception of the work, drafting the work critically, final approval of the version to be published, and agreement to be accountable to all aspects of the work regarding accuracy and integrity of the manuscript. Thomas Albini, MD, is the corresponding author.

Data Availability Statement

All data generated or analyzed during this study are included in the article and its online supplementary material. Further inquires can be directed to the corresponding author.

References

1 Gass JDM. Stereoscopic atlas of macular disease: diagnosis and treatment. CV; 1997. Vol. 2; p. 938–51.
2 Theodossiadis P, Kokolakis S, Ladas I, Kollia AC, Chatzoulis D, Theodossiadis G. Retinal vascular involvement in acute toxoplasmic retinochoroiditis. Int Ophthalmol. 1995;19(1):19–24.
3 Gass J. Fluorescein angiography in endogenous intraocular inflammation. Clin Methods Uveitis. 1968:202–29.
4 Braunstein RA, Gass JD. Branch artery obstruction caused by acute toxoplasmosis. Arch Ophthalmol. 1980; 98(3):512–3.
5 Willerson D, Aaberg TM, Reeser F, Meredith T. Unusual ocular presentation of acute toxoplasmosis. Br J Ophthalmol. 1977;61(11):693–8.
6 Haefliger E, Müller O. Branch artery occlusion due to focal necrotizing retinitis: probably caused by toxoplasmosis (author's transl). Klin Monbl Augenheilkd. 1980;176(4):613–8.
7 Morgan CM, Gragoudas ES. Branch retinal artery occlusion associated with recurrent toxoplasmic retinochoroiditis. Arch Ophthalmol. 1987;105(1):130–1.
8 Pakalin S, Arnaud B. Arterial occlusion associated with toxoplasmic chorioretinitis. J Fr Ophtalmol. 1990; 13(11–12):554–6.
9 Gentile RC, Berinstein DM, Oppenheim R, Walsh JB. Retinal vascular occlusions complicating acute toxoplasmic retinochoroiditis. Can J Ophthalmol. 1997;32(5):354–8.
10 Küçükerdönmez C, Yilmaz G, Akova YA. Branch retinal arterial occlusion associated with toxoplasmic chorioretinitis. Ocul Immunol Inflamm. 2004;12(3):227–31.
11 Chiang E, Goldstein DA, Shapiro MJ, Mets MB. Branch retinal artery occlusion caused by toxoplasmosis in an adolescent. Case Rep Ophthalmol. 2012;3(3):333–8.
12 Kianersi F, Ghanbari H, Beni AN, Beni ZN, Fesharaki H, Ahmadi M. Macular branch retinal artery occlusion as the first manifestation of ocular toxoplasmosis. Retin Cases Brief Rep. 2013;7(4):391–4.
13 Tolou C, Salmon L, Mahieu L, Couzinet A, Soler V. Spectral-domain optical coherence tomography appearance of preretinal granulomas in toxoplasma posterior uveitis with arterial occlusion. J Fr Ophtalmol. 2015;38(9): 889–91.
14 Aggio FB, Novelli FJ, Rosa EL, Nobrega MJ. Combined branch retinal vein and artery occlusion in toxoplasmosis. Arq Bras Oftalmol. 2016;79(3):189–91.
15 Neiweem AE, Jusufbegovic D. Branch retinal artery occlusion associated with toxoplasma retinitis. Korean J Ophthalmol. 2020;34(4):341–2.
16 Pichi FVC, Veronese C, Lembo A, Invernizzi A, Mantovani A, Herbort CP, et al. New appraisals of Kyrieleis plaques: a multimodal imaging study. Br J Ophthalmol. 2017;101(3):316–21.
17 Sridhar J, Shahlaee A, Rahimy E, Hong BK, Khan MA, Maguire JI, et al. Optical coherence tomography angiography and en face optical coherence tomography features of paracentral acute middle maculopathy. Am J Ophthalmol. 2015;160(6):1259–68.e2.
18 Iyer PG, Swaminathan SS, Trivizki O, Shi Y, Shen M, Kansora M, et al. Widefield en face optical coherence tomography monitoring of the peri-venular fern-like pattern of paracentral acute middle maculopathy. Am J Ophthalmol Case Rep. 2021;22:101047.