Published in final edited form as:

Retin Cases Brief Rep. 2016 ; 10(1): 58–62. doi:10.1097/ICB.0000000000000161.

Sequential Central Retinal Vein and Ophthalmic Artery Occlusions in a Pediatric Case of Primary Antiphospholipid Syndrome

Rony Gelman, MD, MS* and Stephen H. Tsang, MD, PhD*,†

*Bernard & Shirlee Brown Glaucoma Laboratory and Barbara & Donald Jonas Stem Cell Laboratory, Department of Ophthalmology, Edward S. Harkness Eye Institute, Columbia University College of Physicians and Surgeons, New York, New York

†Department of Pathology and Cell Biology, Institute of Human Nutrition, Columbia University College of Physicians and Surgeons, New York, New York

Abstract

Purpose—To report a case of sequential central retinal vein occlusion and ophthalmic artery occlusion in a patient with primary antiphospholipid syndrome.

Methods—Observational case report. Color fundus photography, fluorescein angiography, and optical coherence tomography were used to document the progression of a central retinal vein occlusion and sequential development of an ophthalmic artery occlusion within a 1-week period in a patient with primary antiphospholipid syndrome.

Results—A 15-year-old boy presented with unilateral blurry vision due to a central retinal vein occlusion along with other systemic symptoms. Within a 1-week period, he developed an ophthalmic artery occlusion in the same eye, with resulting bare light perception vision. Extensive evaluation by the pediatrics and rheumatology services led to a diagnosis of primary antiphospholipid syndrome as the etiology for the occlusions.

Conclusion—This case report illustrates the rapid sequential venous and arterial ocular thrombosis in a patient with primary antiphospholipid syndrome.

Keywords

antiphospholipid syndrome; central retinal vein occlusion; ophthalmic artery occlusion

Antiphospholipid syndrome (APS) leads to a hyper-coagulable state and recurrent thrombosis.¹ Anti-phospholipid syndrome is known to be associated with both arterial and venous occlusions, with an increased risk of venous thrombosis of up to 10-fold.² Antiphospholipid syndrome may be associated with an underlying systemic autoimmune condition, such as systemic lupus erythematosus, or can occur in an isolated form called primary APS.

Reprint requests: Stephen H. Tsang, MD, PhD, Department of Ophthalmology, Edward S. Harkness Eye Institute, 635 W. 165 Street, New York, NY 10032; sht2@columbia.edu.

None of the authors have any conflicting interests to disclose.

Ocular complications of APS include amaurosis fugax, transient diplopia, visual field loss, ischemic optic neuropathy, retinal and choroidal vascular occlusions, and peripheral proliferative retinopathy. A previous study has shown the high prevalence of APS-related antibodies in patients with vaso-occlusive retinopathy without conventional risk factors and the importance of a systemic evaluation for APS in this group of patients given the diagnostic and therapeutic implications.³

We present a case of 15-year-old boy presenting with blurry vision due to a central retinal vein occlusion (CRVO). Extensive diagnostic evaluation revealed primary APS as the etiology of the occlusion. We illustrate the rapid progression of the patient's underlying thrombotic state as his vision drastically declined over the course of a week because of the development of a subsequent ophthalmic artery occlusion despite systemic immunosuppression and anticoagulation.

Case Report

A previously healthy 15-year-old Hispanic male born at full term presented to our emergency department complaining of blurry vision in his right eye with dark spots for 3 days. He denied eye pain or photopsias. He endorsed a history of an approximate 100-pound weight loss over the previous 6 months, fevers, fatigue, epigastric pain, and frequent nonbloody vomiting. He reported an intermittent erythematous macular rash on his arms, legs, and belly but sparing his palms and soles. He was born in the United States and had no recent travel history.

His vision was 20/30⁻² in the right eye and 20/20 in the left eye. Intraocular pressure and anterior segment examination were within normal limits. No neovascularization of the iris, anterior chamber cell, or vitreous cell was noted. Dilated fundus examination showed mild blurring of the optic disk margins, scattered intraretinal hemorrhages, some of which were Roth spots, and mild tortuosity of the retinal vessels in the right eye. These findings appeared consistent with a CRVO in the right eye. The left eye appeared normal.

The following day, he reported sudden worsening vision in the right eye. Visual acuity declined to 20/200 in the right eye, and fundus examination showed worsening of the baseline retinal findings (Figure 1). Fluorescein angiography confirmed the diagnosis of a nonischemic CRVO (Figure 2). Optical coherence tomography showed lack of cystoid macular edema (Figure 3).

The patient was admitted to the pediatrics service, which conducted a thorough evaluation for his ocular and systemic symptoms. Extensive diagnostic testing was performed, and consultations were obtained from the infectious disease, hematology/oncology, cardiology, neurology, and rheumatology services.

Blood cultures and serology studies excluded an infectious etiology, including syphilis, tuberculosis, HIV, toxoplasmosis, Bartonella disease, and Lyme's disease. An echocardiogram revealed no cardiac vegetations or a patent foramen ovale but showed left ventricular dilation, trivial aortic insufficiency, and mild mitral regurgitation, which

cardiology attributed to a panvalvitis/pancarditis because of his underlying inflammatory process.

Laboratory results were consistent with a normocytic anemia, thrombocytopenia, and hyperbilirubinemia. He had an elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), prothrombin time (PT), partial thromboplastin time (PTT), and immunoglobulin levels, whereas levels of Factor VII and IX were low. Factor V Leiden was negative. Triglyceride and homocysteine levels were normal. Serological markers of systemic lupus erythematosus, sarcoidosis, Wegener's granulomatosis, and polyarteritis nodosa were negative.

A peripheral blood smear showed reactive inflammatory cells without evidence of malignancy. A bone marrow biopsy showed hypocellular bone marrow and was not consistent with an oncologic process. Lupus anticoagulant and anticardiolipin IgG and IgM antibodies returned markedly positive.

A magnetic resonance imaging of the brain and orbits and a magnetic resonance venography study did not show vascular occlusions or other abnormalities. Neurologic testing showed no deficits other than his vision loss. A computed tomography of the chest was suggestive of small infarcts of the lower lung lobes. Computed tomography of the abdomen showed innumerable ill-defined small hypoenhancing lesions in the liver. A positron emission tomography scan revealed hypodense regions in the liver that likely represent regions of vasculitis with thrombosis.

Treatment recommendations from the rheumatology service included IVIG infusion and 3 days of intravenous SoluMedrol followed by maintenance on oral prednisone. He was also placed on systemic anticoagulation.

On hospital Day 8, the patient reported diminished vision in his right eye. Visual acuity declined to bare light perception in the right eye. Examination showed worsening of the CRVO and the development of an ophthalmic artery occlusion (Figure 4). An optical coherence tomography scan showed diffuse macular edema and retinal thickening (Figure 5). He was medically stabilized and discharged home on anticoagulation and immunosuppressive therapy with outpatient ophthalmology follow-up. No acute ophthalmic intervention was indicated, as he had no evidence of neovascularization, and intravitreal bevacizumab was deferred given his underlying medical issues.

The patient, however, was subsequently lost to follow-up and returned approximately 8 months later complaining of pain in the right eye. He was found to have neovascular glaucoma and underwent prompt panretinal photocoagulation and an intravitreal bevacizumab injection. Despite repeated efforts to reach his family, he was lost to follow-up thereafter. Review of his medical record showed that he was admitted to the pediatrics service about 1 month later for chest pain. Cardiology deemed his symptoms to be due to myocarditis. Evaluation by the rheumatology service during this hospitalization showed persistently elevated levels of lupus anticoagulant and anticardiolipin IgG and IgM antibodies and positive beta 2-glycoprotein antibodies. Reinvestigation by the pediatrics and rheumatology service for an underlying etiology was unrevealing. This led to a diagnosis of

primary APS by rheumatology. No ophthalmology consultation from pediatrics was made during this hospitalization.

Discussion

Pediatric retinal vascular occlusions are uncommon, with the literature limited to case reports. Previous reports have described retinal arteriolar occlusions in pediatric APS.^{4,5} Hartnett et al⁶ described a case of retinal venous thrombosis with subsequent neovascularization in a 6-year-old patient with primary APS. Consecutive CRVO and ophthalmic artery occlusion have been described in a 60-year-old patient with primary APS.⁷ However, to our knowledge, no such case in the pediatric population has been described before. In this report, we documented the development of a sequential CRVO and ophthalmic artery occlusion in a pediatric patient with primary APS.

Catastrophic antiphospholipid antibody syndrome is characterized by multiple vascular occlusive events, usually affecting small vessels and developing over a short period.⁸ Catastrophic antiphospholipid antibody syndrome is a rare life-threatening form of APS in which widespread intravascular thrombosis results in multiorgan ischemia and failure.⁹ Diagnostic criteria for catastrophic antiphospholipid antibody syndrome include 1) involvement of 3 or more organs/tissues, 2) development of manifestations in less than a week, 3) histologic evidence of intravascular thrombosis, and 4) presence of antiphospholipid antibodies on 2 occasions 6 weeks apart.¹⁰ Although our patient had multiorgan involvement and presence of antiphospholipid antibodies on 2 occasions 6 weeks apart, he did not fulfill the other items in the diagnostic criteria for catastrophic antiphospholipid antibody syndrome.

In summary, we present a case of rapid sequential unilateral CRVO and ophthalmic artery occlusions in a patient with primary APS. Despite immuno-suppression and anticoagulation, the patient's ocular thrombosis worsened, illustrating this devastating complication of APS. This case emphasizes the importance of systemic evaluation, including APS testing, in patients with vaso-occlusive retinopathy without conventional risk factors, especially in the pediatric population.

Acknowledgments

The Bernard & Shirlee Brown Glaucoma Laboratory and Barbara & Donald Jonas Stem Cell Laboratory are supported by NIH core grants 5P30CA013696 and 5P30EY019007 and unrestricted funds from Research to Prevent Blindness, New York, NY. S. H. Tsang is a member of the RD-CURE Consortium and is supported by the Tistou and Charlotte Kerstan Foundation. This work is also supported by NIH R01EY018213, the Research to Prevent Blindness Physician-Scientist Award, the Nancy and Kobi Karp Foundation, the Schneeweiss Stem Cell Fund, New York State (N09G-302), the Foundation Fighting Blindness New York Regional Research Center Grant (C-NY05-0705-0312), the Joel Hoffman Fund, Charles Culpeper Scholarship, the Irma T. Hirschl Charitable Trust, the Professor Gertrude Rothschild Stem Cell Foundation, and Gebroe Family Foundation. R. Gelman was supported by a Foundation Fighting Blindness Alan Laties Career Development Program Award.

References

1. Durrani OM, Gordon C, Murray P. Primary anti-phospholipid antibody syndrome (APS): current concepts. *Surv Ophthalmol.* 2002; 47:215–238. [PubMed: 12052409]

2. Wahl DG, Guillemin F, de Maistre E, et al. Meta-analysis of the risk of venous thrombosis in individuals with antiphospholipid antibodies without underlying autoimmune disease or previous thrombosis. *Lupus*. 1998; 7:15–22. [PubMed: 9493144]
3. Cobo-Soriano R, Sanchez-Ramon S, Aparicio MJ, et al. Antiphospholipid antibodies and retinal thrombosis in patients without risk factors: a prospective case-control study. *Am J Ophthalmol*. 1999; 128:725–732. [PubMed: 10612509]
4. Uysal Z, Dogu F, Kurekci AE, et al. Recurrent arterial thrombosis in a child: primary antiphospholipid antibody syndrome. *Pediatr Hematol Oncol*. 2002; 19:59–66. [PubMed: 11787868]
5. Saxonhouse MA, Bhatti MT, Driebe WT, et al. Primary antiphospholipid syndrome presenting with a branch retinal artery occlusion in a 15-year-old male. *J Child Neurol*. 2002; 17:392–394. [PubMed: 12150590]
6. Hartnett ME, Laposata M, Van Cott E. Antiphospholipid antibody syndrome in a six-year-old female patient. *Am J Ophthalmol*. 2003; 135:543–544.
7. Ang LP, Lim AT, Yap E. Central retinal vein and ophthalmic artery occlusion in primary antiphospholipid syndrome. *Eye (Lond)*. 2004; 18:439–440. [PubMed: 15069448]
8. Asherson RA. The catastrophic antiphospholipid syndrome. *J Rheumatol*. 1992; 19:508–512. [PubMed: 1593568]
9. Nayer A, Ortega LM. Catastrophic antiphospholipid antibody syndrome: a clinical review. *J Nephropathol*. 2014; 3:9–17. [PubMed: 24644537]
10. Asherson RA, Cervera R, de Groot PG, et al. Catastrophic antiphospholipid syndrome: international consensus statement on classification criteria and treatment guidelines. *Lupus*. 2003; 12:530–534. [PubMed: 12892393]

Fig. 1. Color montage photograph of the right eye on presentation showing vascular tortuosity, vessel sheathing, white-centered intra-retinal hemorrhages, blurring of the optic disk margins, and peripapillary edema. These findings appeared consistent with a CRVO.

Fig. 2. Fluorescein angiogram (FA) at presentation of the right eye. **A.** Early and **(B)** late frames. **C.** A montage FA. There is delayed filling of the venules, venous congestion, and phlebitis consistent with a nonischemic CRVO.

Fig. 3. Time-domain optical coherence tomography at presentation of the right eye. **A.** A temporal-to-nasal scan through the fovea shows no central cystoid macular edema. **B.** Retinal thickness map shows peripapillary retinal thickening.

Fig. 4.

A. Color photograph of the right eye 1 week after presentation shows retinal whitening, diffuse intraretinal hemorrhages, macular edema, and severe vascular tortuosity, congestion, and sheathing. **B–D.** Fluorescein angiogram reveals markedly delayed and incomplete retinal and choroidal vascular filling with severe ischemia, consistent with worsening of the CRVO and the development of an ophthalmic artery occlusion.

Fig. 5. Spectral domain optical coherence tomography through the fovea of the right eye at 1 week after presentation shows diffuse retinal edema and disturbance of all retinal layers.