A Late Presentation of Unilateral Idiopathic Retinal Vasculitis, Aneurysms, and Neuroretinitis (IRVAN) Syndrome

Zachary G. Walburg, OD; Robert H. Janigian Jr., MD; Joseph Mega, OD; Paul B Greenberg, MD, MPH; Amanda Hunter, OD

Abstract
Although uncommon, idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN) syndrome can lead to vision-threatening complications if not diagnosed and treated appropriately. This case report describes an atypical presentation of unilateral IRVAN syndrome, which resulted in significant visual loss in an elderly male.

Introduction
Idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN) syndrome is a rare and usually bilateral condition, which can result in a vision-threatening ischemic and exudative retinopathy. The clinical presentation of IRVAN syndrome is variable, which can potentially complicate the accurate diagnosis of the condition. Herein, we describe an atypical presentation of unilateral IRVAN syndrome in an elderly male.

Case Presentation
A 76-year-old male with longstanding visual loss in his left eye, presented for a follow-up examination secondary to complications from an unknown exudative retinopathy. The patient had no new complaints and reported stable vision in both eyes.

The retinopathy was noted when the patient initially presented to the eye clinic at 59 years of age. The rest of the patient’s past ocular history was notable for pseudophakia in both eyes, with cataract surgery performed three years prior to presentation, and retinal emboli in the left eye resulting from carotid occlusive disease. The patient’s medical history included hyperlipidemia, alcoholic cirrhosis with resolved hepatic encephalopathy seven years prior to presentation, peripheral sensory neuropathy, anemia, and bilateral carotid atherosclerotic disease. His medications included folic acid, simvastatin, gabapentin, spironolactone, thiamine, omeprazole, diphenhydramine, and furosemide.

On examination, the patient’s best-corrected visual acuity was 6/6 in the right eye and counting fingers at 0.3 meters in the left eye. The left pupil was fixed and dilated. A left relative afferent pupillary defect was noted by reverse testing. Confrontation visual fields were full and extraocular muscle motility testing revealed full range of motion in each eye. Slit-lamp biomicroscopy was remarkable for centered posterior chamber intraocular lenses in both eyes with early posterior capsular opacification centrally in the left eye.

On dilated fundus examination, the right eye was notable only for trace retinal pigment epithelium mottling in the macula. In the left eye, the media was clear, the optic nerve was pale, the retinal vasculature was attenuated with sheathed and sclerosed arterioles, and three incidental retinal emboli were noted: one at the first bifurcation of the superotemporal and superonasal arteries and one at the second bifurcation of the inferotemporal artery. Additionally, subretinal fibrosis and atrophy located at the fovea were noted with associated intraretinal hemorrhages, extensive lipid exudates and fibrotic macroaneurysms superior and nasal to the optic nerve. No neovascularization or cotton wool spots were appreciated (figure 1). The lipid exudates were improved compared to photos taken 20 months prior.

Zachary G. Walburg, OD1; Robert H. Janigian Jr., MD2,4; Joseph Mega, OD2,3; Paul B Greenberg, MD, MPH2,4; Amanda Hunter, OD2,3
1 Eye Clinic, Jacksonville Outpatient Clinic, North Florida/South Georgia Healthcare System, US Department of Veterans Affairs, Jacksonville, Florida USA; 2 Eye Clinic, Providence Veterans Affairs Medical Center, Providence, Rhode Island, USA; 3 New England College of Optometry, Boston, Massachusetts, USA; 4 Division of Ophthalmology, Alpert Medical School, Brown University, Providence, Rhode Island, USA

Correspondence to: Amanda Hunter, O.D., Eye Clinic Providence Veterans Affairs Medical Center, 830 Chalkstone Ave. Providence, RI 02908 Email: Amanda.Hunter2@va.gov
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Figure 1. Widefield fundus photographs of both eyes: the right eye was unremarkable; the left eye showed optic nerve pallor, attenuated and sheathed retinal vasculature, scattered retinal hemorrhages and exudates, macular retinal pigment epithelium atrophy, thrombosed arterial macroaneurysms superior, nasal inferotemporal to the nerve, and three emboli in the arterioles.
Optical coherence tomography (OCT) of the macula was unremarkable in the right eye. In the left eye, there was a hyperreflective band at the vitreoretinal interface consistent with an epiretinal membrane. There was intraretinal hyper-reflective material consistent with the lipid exudates seen clinically, as well as loss of the outer retinal layers with hyper-reflectivity consistent with RPE atrophy.

Fluorescein angiography (FA) demonstrated early phase occlusion of retinal vessels along the inferotemporal arcade. There was hypofluorescence due to dense lipid deposits and capillary non-perfusion, which was present in the early phase lasting through the late phases. The lipid deposits were appreciated along the superotemporal and inferotemporal arcades, while the capillary non-perfusion was present along the inferotemporal, inferonasal and superonasal arcades. There were scattered bulbous hyperfluorescent lesions consistent with macroaneurysms and microaneurysms. The macroaneurysms were located superior and nasal to the optic nerve and along the inferotemporal arcades, with the microaneurysms scattered throughout the posterior pole concentrated within the arcades. There was hyperfluorescent leakage of the retinal vasculature without disc leakage or leakage consistent with retinal neovascularization (figure 2).

The above findings were consistent with an atypical presentation of IRVAN syndrome. The patient was managed conservatively due to the relatively quiescent disease and the poor prognosis for visual recovery secondary to foveal atrophy and fibrosis.

**Discussion**

Idiopathic retinal vasculitis, aneurysms and neuroretinitis syndrome is a rare condition of uncertain etiology that can masquerade as a variety of conditions including retinal arterial macroaneurysms, Eale’s disease, Behçet’s disease, sarcoidosis, and adult-onset Coats’ disease. Several characteristics can help distinguish between these conditions and IRVAN syndrome (Table I).

**Table 1. Differential diagnoses for IRVAN Syndrome with the characteristics of each condition that differ from IRVAN syndrome**

<table>
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<th>Differential Diagnosis</th>
<th>Key Features</th>
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| Retinal arterial macroaneurysm | - associated with systemic hypertension  
- usually diagnosed in the 6th to 7th decade  
- intraretinal, preretinal and vitreous hemorrhages are present  
- no neuroretinitis |
| Eale’s Disease | - usually diagnosed in younger males  
- positive tuberculin test  
- vestibuloauditory deficits  
- cerebral infarction  
- periphlebitis without aneurysms |
| Behçet’s Disease | - occlusive pararteritis  
- oral aphthous ulcers  
- genital ulcers  
- hypopyon |
| Sarcoidosis | - systemic complications  
- usually diagnosed in the 3rd to 4th decade  
- African American race  
- hypopigmented chorioretinal scars |
| Adult-onset Coats’ Disease | - male predilection  
- typically does not progress after onset  
- typically localized to temporal retina |

IRVAN syndrome is classically diagnosed in the third to fourth decades of life, with a greater predilection for females. The majority of cases present bilaterally, although there have been reports of unilateral cases, as well as cases that began in one eye and progressed to involve the fellow eye.

This patient’s formal diagnosis of IRVAN syndrome was made 24 years after his initial presentation. This discrepancy was most likely related to the patient’s atypical presentation of IRVAN syndrome, including late presentation, male sex, and unilateral findings.

In contrast to these atypical findings, the patient’s sheathed and sclerosed vasculature from a history of vasculitis, multiple aneurysmal dilations, exudative retinopathy, and capillary non-perfusion as seen on FA were all consistent with IRVAN syndrome. No optic nerve edema was noted, but the presence of optic nerve pallor suggests a history of chronic optic nerve inflammation. The retinal emboli resulted from the patient’s established carotid artery disease and were unrelated to IRVAN syndrome.

As described by Samuel et. al. (2007), IRVAN syndrome can be categorized into five stages. Stage 1 is characterized by macroaneurysms, exudation, neuroretinitis and retinal vasculitis. Stage 2 is characterized by angiographic evidence of capillary non-perfusion resulting from occlusive retinal vasculitis. Stage 3 occurs when there is development of posterior segment neovascularization with or without a vitreous hemorrhage.
Stage 4 is characterized by the presence of anterior segment neovascularization, while stage 5 occurs with the development of neovascular glaucoma. Based on these stages, our patient had stage 2 IRVAN syndrome in his left eye.

The visual prognosis of IRVAN syndrome is related to the severity of the disease, and it correlates with the degree of retinal ischemia and the stage of the condition at the time of initiation of treatment. PAN retinal photocoagulation (PRP) is recommended if there is retinal ischemia involving two or more quadrants of the retina, as in stages 2 through 5.11

In a study by Samuel et. al. (2010), eyes treated at various stages of IRVAN syndrome were evaluated for long-term visual prognosis. They found that eyes treated at stage 2 maintained a best-corrected visual acuity (BCVA) of 20/20, whereas 25% of stage 3 eyes became 20/200 or worse, and treatment initiated in stages 4 or 5 resulted in 50% of eyes progressing to severe vision loss.2

Although retinal neovascularization may not impact the likelihood of progression of IRVAN syndrome,2 patients with active neovascularization are at risk for additional vision-threatening conditions, such as vitreous hemorrhage and retinal detachment. Thus, anti-vascular endothelial growth factor (anti-VEGF) agents are indicated in cases of active neovascularization (stages 3 through 5).2

As with other retinal vascular diseases, treatment of exudative maculopathy in IRVAN syndrome usually involves focal laser and/or anti-VEGF, but there have been promising results of treatment of macular edema with anti-tumor necrosis factor (anti-TNF) agents, such as infliximab, based on their ability to mediate ocular inflammation. Cheema et. al. (2011) reported two cases of macular edema in IRVAN syndrome that responded to treatment with the anti-TNF agent infliximab.

Despite the success of infliximab in treating macular edema caused by IRVAN syndrome, anti-TNF agents should be used with caution due to the risk of activation of opportunistic infections and latent tuberculosis. Additionally, while infliximab can be beneficial in managing macular edema, it does not have any impact on capillary nonperfusion, highlighting the necessity of combination therapy with laser photocoagulation or anti-VEGF agents to manage the risk of development of neovascularization.10 Direct photocoagulation of arterial macroaneurysms is generally not advised as there is a risk of occlusion of the blood vessel and worsening of retinal ischemia.10

Conclusion
Idiopathic retinal vasculitis, aneurysms, and neuroretinitis syndrome can be a highly variable disease with potentially devastating visual complications. Therefore, prompt diagnosis and management of IRVAN syndrome is important to prevent vision-threatening complications.

References