A 28-Year-Old Female with Floaters and Neurologic Symptoms

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Introduction:

A 28 year-old female was referred to The Retina Institute with a 6 month history of floaters and a black spot in one of her eyes which was accompanied by headaches, dizziness, and tinnitus. Three months earlier, she received intravenous (IV) solumedrol for 5 days for a new diagnosis of multiple sclerosis after suspicious changes on her MRI brain (report and images not available). Family history consisted of a second cousin with multiple sclerosis and a review of systems was positive for vertigo. Her only medication included an estrogen/progesterone contraceptive pill.

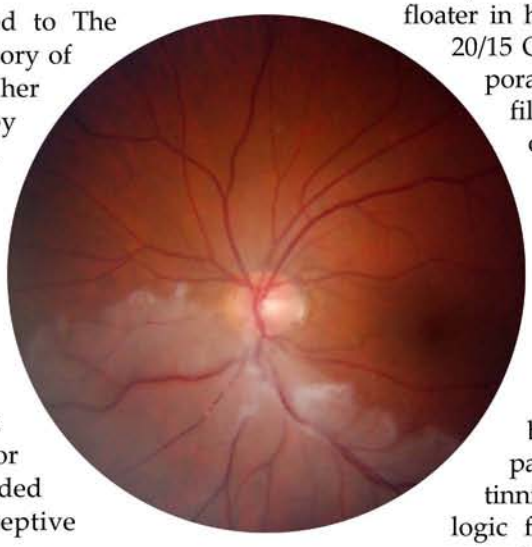

Figure 1: *Inferior branch retinal artery occlusion with opaque and edematous retina OS.*

Her visual acuity was 20/15 OU. There was no relative afferent pupillary defect. Intraocular pressure and anterior segment exam were normal OU. Dilated fundus exam was significant for 0.1, sharp, and pink optic nerves. As part of her systemic workup, her neurologist scheduled a cerebral angiogram so a fluorescein angiogram (FA) was obtained which showed no flow abnormalities OU.

Five months later, the patient returned with floaters and loss of her superior hemifield OS. She was being treated by her neurologist with intravenous immunoglobulin (IVIG) and another round of IV solumedrol. Visual acuity was 20/20 OU. Her right eye was unaffected but the left inferior retina was opaque and edematous (Figure 1). Her FA exhibited a branch retinal artery occlusion (BRAO) and hyperfluorescence of superior arterioles as well (Figure 2).

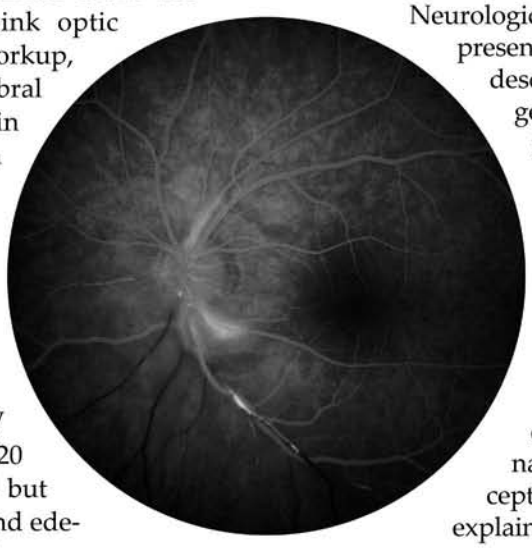

Figure 2: *Delayed filling in inferior arterioles OS. The superotemporal arteriole has subtle hyperfluorescence but appears normal on fundus photography.*

At a 2 month follow-up visit, despite being on 50 mg of Prednisone by her neurologist, she now reported a floater in her right eye. Her vision remained 20/15 OU but exam revealed a superotemporal BRAO OD with delayed arteriole filling and arteriole hyperfluorescence on FA (Figure 3, 4). The patient was subsequently started on aspirin 81 mg daily with continual close follow-up with retina, neurology and rheumatology.

Diagnosis:

This young woman presents with bilateral, sequential BRAOs accompanied by headaches, dizziness, and tinnitus. Based on the retinal and neurologic findings, the differential diagnosis includes cerebroretinal vasculopathy (CRV), Susac syndrome, multiple sclerosis (MS), or secondary clotting/thrombosis due to oral contraceptive use.

Neurologic and ophthalmic findings can be present in CRV and MS. However, CRV, as described by Grand et al., typically spans generations and presents with CNS pseudotumors (non-vasculitic fibrinoid necrosis of small vessel walls in white matter) as well as posterior pole capillary occlusion, microvascular abnormalities, and perifoveal capillary obliteration[1,2]. Meanwhile, MS typically exhibits periventricular white matter changes, optic neuritis, motility defects, intermediate uveitis, or retinal periphlebitis. While oral contraceptive related clotting/thrombosis could explain bilateral BRAOs[3], the patient's retinal vascular occlusive disease with headaches, dizziness, tinnitus, and MRI brain changes were more consistent with Susac syndrome.

Discussion:

The first case reports of two young women with the clinical triad of encephalopathy, multiple/sequential BRAOs, and hearing loss were published in 1979 by Susac. Susac syndrome is a multisystem, microvascular, occlusive endotheliopathy often affecting retinocochleocerebral vasculature with a suspected immune-mediated pathogenesis. Diagnosing Susac syndrome can be challenging, especially in patients presenting without all features of the clinical triad.

There is a 3:1 female to male predilection and no racial preference. Range at diagnosis is 20-40 years. Small precapillary arterioles less than 100 micrometers in diameter are typically damaged and endothelial cell necrosis with sloughing and denudement of capillaries and venules is present. Following immune-mediated injury, there is narrowing or occlusion of microvasculature resulting in ischemic injury of the brain, retina, cochlea and other organs.

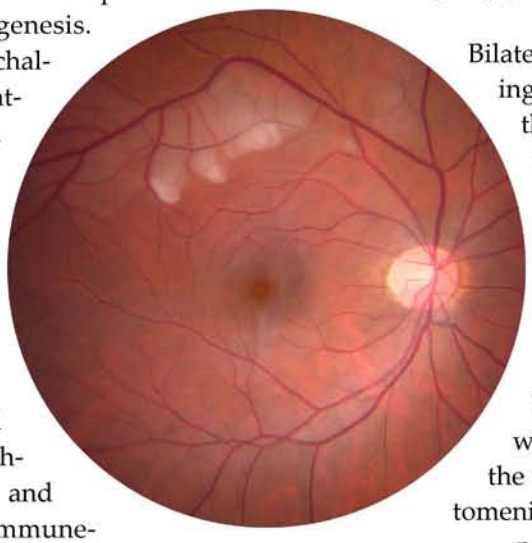

Figure 3: *Superior branch retinal artery occlusion OS.*

FA shows focal, nonperfused retinal arterioles with discrete areas of arteriolar wall hyperfluorescence in affected and normal appearing retinal arterioles indicating a diffuse endotheliopathy. Choroidal circulation is normal on indocyanine green angiography.

Histopathological changes include retinal peripheral capillary dropout and microvascular occlusion of arteries and veins. Areas of yellow-white retinal arteriolar thickening/plaques adjacent to areas of normal vessel wall may represent areas of lipid deposition called Gass plaques. Occluded arterioles appear as "ghost vessels or silver streaks". Electron microscopy revealed constricted vascular lumens with amorphous, periodic acid-Schiff positive, fluid-filled spaces located between the internal limiting membrane and outer vessel wall[4, 5].

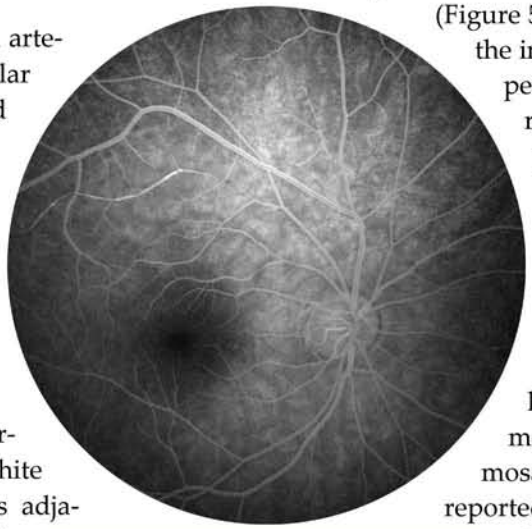

Figure 4: *Delayed filling and hyperfluorescence in superior arteriole.*

Neurologic Findings:

Encephalopathy in Susac syndrome manifests variably in acute and subacute forms with headache, confusion, memory loss, mood and personality change, seizures, ataxia, pyramidal tract signs, and dysarthria. Electroencephalograms may demonstrate generalized slowing implying widespread dysfunction.

Bilateral asymmetric sensorineural hearing loss results from microinfarction of the cochlear arterioles. Vertigo, tinnitus and vestibular nystagmus may be accompanying features. Permanent cochlear implants may be needed.

Neuroimaging:

Encephalopathy can manifest with widespread abnormalities involving the white matter, gray matter, leptomeninges, and facial/vestibulocochlear nerves. Patients may be misdiagnosed with MS in early stages like our patient. Characteristic MRI findings include small, multifocal, white matter changes preferentially involving the corpus callosum called "snowballs" and "spokes" (Figure 5). Microinfarcts can also involve the internal capusle giving a "string of pearls" appearance. Cerebral angiography may be normal in some patients, possibly because vascular changes may be beyond imaging resolution.

Systemic Findings:

Emerging literature has also highlighted skin and muscle involvement in Susac syndrome. Livedo racemosa affecting flanks and feet have been reported and muscle biopsy specimens can show subclinical microangiopathy of arterioles[4].

Laboratory:

Autoimmune markers can be elevated including erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, rheumatoid factor and anti-

phospholipid antibody levels. CSF may have elevated protein, mild lymphocytic pleocytosis, and oligoclonal bands during encephalopathic stages. Elevated levels of factor VIII and von Willebrand factor antigen have been reported[4].

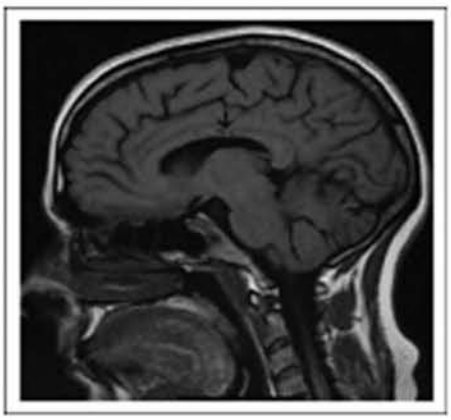

Figure 5: *Representative MRI shows microinfarctions called "snowballs or spokes" in the corpus callosum.*[4]

Treatment:

The natural course of Susac syndrome is unpredictable and typically follows one of the three major courses - monophasic (self-limited with no recurrences), polycyclic, or chronic continuous course.

Steroids, cyclosporine, cyclophosphamide, methotrexate, mycophenolate mofetil, azathioprine, infliximab, etanercept, rituximab have been used in various combinations to treat Susac syndrome. Upon diagnosis, aggressive treatment with IV methylprednisolone followed by high dose PO prednisone for 4 weeks and IVIG monthly for 6 months have been recommended. In severe cases, plasmapheresis has been used. Upon remission, slow taper of steroids over several months with sustained immunomodulatory therapy should be continued for about 2 years[4].

Daily aspirin is recommended but not proven to prevent BRAO and patients should be followed with serial FAs.

Conclusion:

Susac syndrome is a severe angiopathic disorder with a characteristic clinical triad that can lead to severe vision loss, hearing loss, encephalopathy, and rarely death. This diagnosis should be considered in patients with multiple sequential BRAOs and neurologic findings. Management and follow-up requires close collaboration between ophthalmology, neurology, audiology, and rheumatology. Early aggressive treatment with steroids, immunomodulators, IVIG, plasmapheresis, and daily aspirin is necessary to minimize debilitating sequelae. Chronic immunomodulators after a prolonged steroid taper can help prevent relapses.

References:

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