Case Study: An Atypical Presentation of Neuroretinitis

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Background

Uveitis is often associated with systemic manifestations which may pose a risk for morbidity and mortality if not adequately recognized and treated. In early stages, many etiologies of uveitis can be difficult to distinguish. We present a case with an atypical presentation of neuroretinitis.

Patient Case

Our patient is a 30-year-old female who presented to our clinic as a referral from an outside ophthalmologist for the management of acute anterior uveitis. About 3-4 weeks prior, the patient had been diagnosed with bilateral acute anterior uveitis and was started on prednisolone acetate 1% eyedrops every two hours while awake, and cyclopentolate 1% at night in both eyes. It was noted by the referring provider that the patient's anterior chamber cell and symptoms had initially improved after a week of therapy, and therefore, the patient had been started on a gradual taper of the prednisolone acetate. One week prior to referral to our clinic, while the patient was taking prednisolone acetate four times daily, she noticed that the visual acuity in the right eye precipitously dropped, which she described as "smoke" in her vision. Optical Coherence Tomography (OCT) imaging of the retina, as well as widefield fundus photos were obtained, and it was noted that the patient had developed optic nerve edema and radially oriented macular exudates in both eyes. In the left eye there was subretinal fluid in the space surrounding the optic nerve. Upon referral to our clinic, the patient's exam was significant for a best corrected visual acuity of 20/40 in the right eye, and 20/20 in the left eye. Anterior chamber showed a 2+ cell reaction, 1-2+ optic nerve edema, and a radial pattern of retinal exudates in the macula of both eyes. No periauricular, submandibular or cervical lymphadenopathy was present. Repeat testing confirmed the referring provider's findings (Figures 1 and 2).

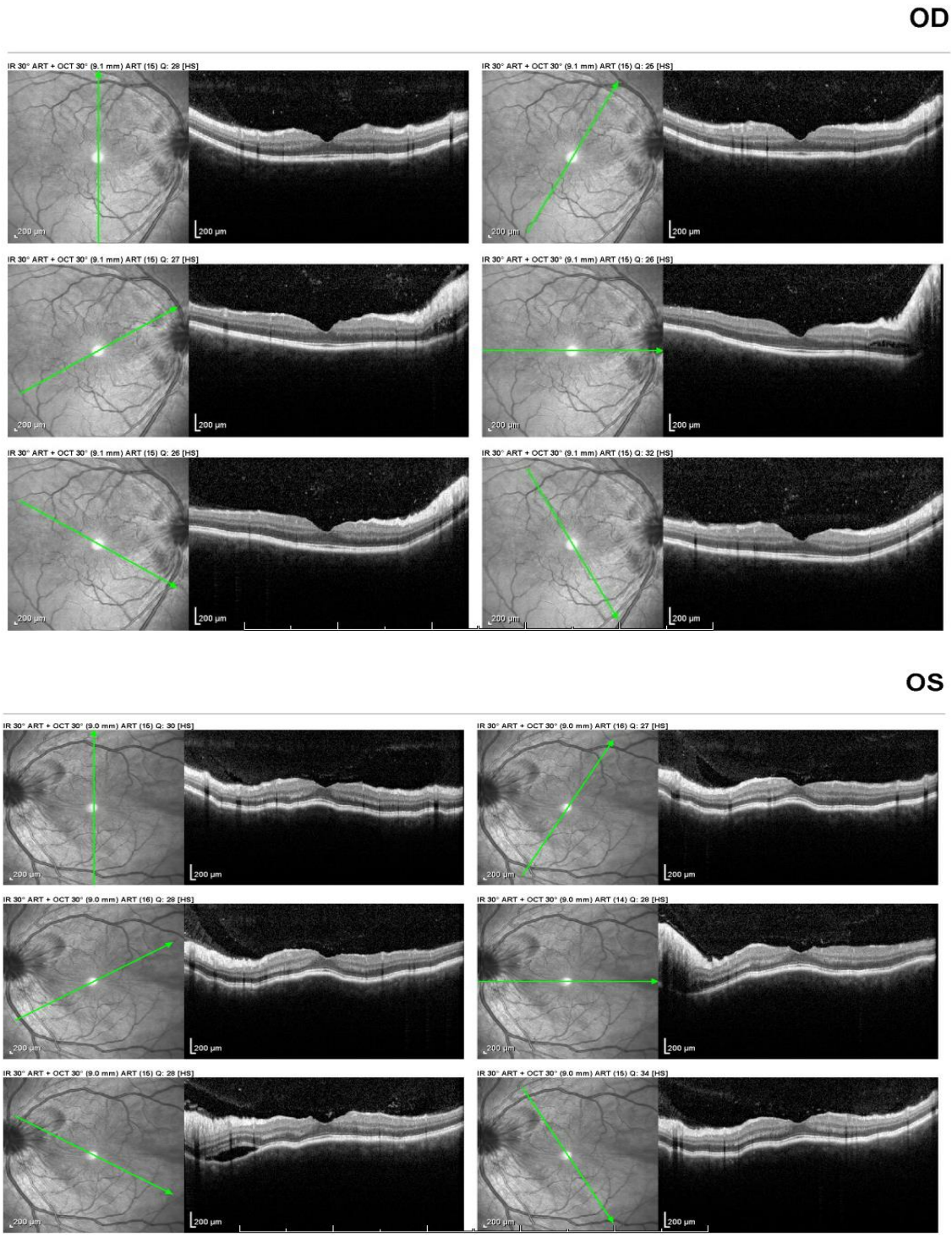

Figure 1: *Optical Coherence Tomography (OCT) of the retina of both eyes upon presentation showing bilateral optic nerve edema and subtle macular exudates. There is peripapillary subretinal fluid in the left eye.*

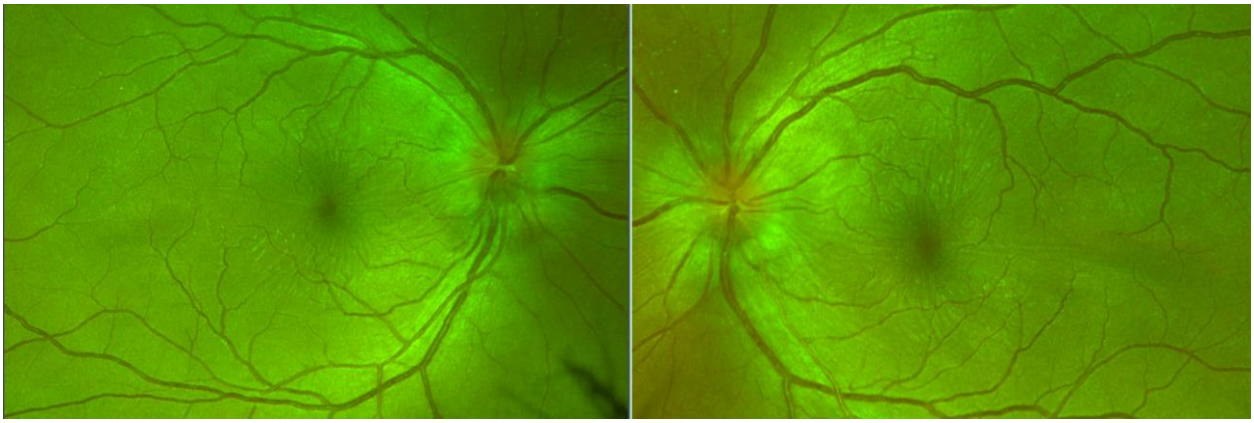

Figure 2: *Widefield fundus photos of both eyes upon presentation showing bilateral optic nerve edema and macular exudates.*

Upon discussion with the patient, she described progressive declining vision in both eyes, right greater than left, accompanied by occasional photopsias in both eyes. Four months prior to the development of her anterior uveitis, the patient attended a minute clinic and was diagnosed with a mild viral illness. She claimed a 15 pound weight gain over the prior two months, but denied symptoms of pulsatile tinnitus, binocular diplopia or transient visual obscurations. The patient also complained of headaches. She described a history of exposure to her sister's kitten about four weeks prior to her presentation to the outside provider. The patient also states that the cat both licked and scratched her. Additionally, she recently exposed to another cat owned by a friend but did not recall if she had been scratched. The patient had recent travel to Cabo San Lucas, Mexico a few months prior, but stated that she did not have exposure to the water and did not eat any exotic food. She had received the Pfizer COVID-19 Booster vaccine two months prior.

Broad testing was performed, including CBC, CMP, pregnancy testing, Bartonella Henselae and Bartonella Quintana IgM and IgG, ACE, Lysozyme, Quantiferon Gold, Syphilis Antibodies, Chest X-ray, and Toxoplasma IgG, and Lyme Antibodies, all of which were negative. MRI of the brain and orbits with and without contrast, as well as MRV of the brain were unremarkable. While the Bartonella testing was pending, the patient was started on an empiric dose of Doxycycline 100mg PO twice daily yet did not show signs of improvement and actually manifested worsening of the subretinal fluid. On this regimen she progressed to a serous retinal detachment involving the fovea in the left eye (Figure 3). After infectious etiologies were ruled out with negative lab results, doxycycline was stopped, and the patient was started on oral prednisone. Over the course of four weeks she experienced resolution of her subretinal fluid and improvement of the optic nerve swelling, headaches, photopsias, and visual acuity.

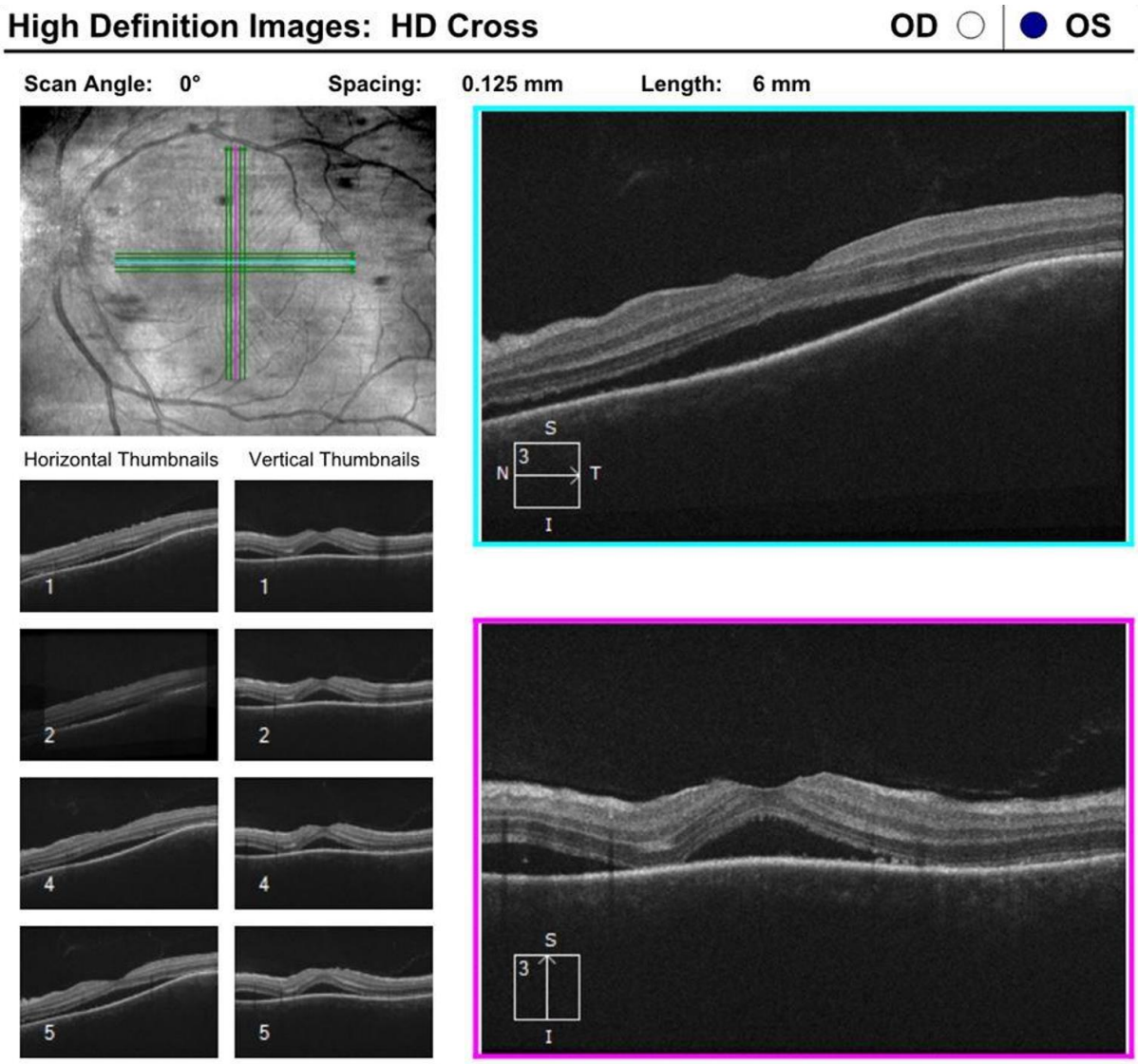

Figure 3: *Optical Coherence Tomography (OCT) of the retina of the left eye two weeks after the prior study (Figure 1) demonstrating serous retinal detachment involving the fovea.*

Discussion

The combination of optic nerve head swelling and the presence of a macular star is termed neuroretinitis, and carries a broad differential diagnosis (Table 1)[1]. Unilateral presentations tend to be infectious, with the most typical cause being infection by Bartonella species. Bilateral presentations may be inflammatory, a masquerade syndrome, or most commonly, idiopathic.

Idiopathic cases of neuroretinitis typically are self-limited and do not recur. In 1916, Leber described the entity Leber's Idiopathic Stellate Neuroretinitis (LISN), characterized by unilateral disease, stellate macular exudates, spontaneous resolution, and unknown etiology[2]. While it was later shown that many of these cases were secondary to Bartonella infection, not all were attributable to this etiology. Idiopathic neuroretinitis tends not to recur. However, cases of

recurrent idiopathic neuroretinitis portend poorer visual outcomes and may require systemic immunomodulatory treatment[3].

The most common cause of unilateral neuroretinitis occurs in cat scratch disease, which is caused by Bartonella henselae and Bartonella quinata species. It is transmitted by the scratch, licks, and bites of young kittens. The most common posterior finding is the macular star, although patients may also experience local areas of retinitis[5]. Anterior uveitis is also common. The diagnosis is made via a positive IgM or IgG antibody for Bartonella species[1,6]. Bartonella neuroretinitis is a self-limited disease that spontaneously resolves within months. Nevertheless, the typical treatment is doxycycline 100mg PO BID for 4-6 weeks. In children 8 years or younger, azithromycin is typically used instead. Steroids are also commonly used, although their role is unclear.

Bilateral neuroretinitis has been associated with Bartonella infection, but is less well described. Other causes of bilateral neuroretinitis include VKH, DUSN, Sarcoidosis, COVID-19, Mumps, Toxoplasmosis, and as an adverse reaction to medication. [7-13]. In our patient, the preceding viral illness, negative Bartonella species antibodies and extension of the subretinal fluid raised concern for VKH as the causative etiology based upon a diagnosis of exclusion. In summary, cases of neuroretinitis are uncommon with bilateral disease even more rare. The ophthalmologist should consider this diagnosis in a case of combined optic nerve and macular edema.

Table 1: Summary of differential diagnoses for neuroretinitis[1,14]

Inflammatory

- Vogt-Koyanagi-Harada (VKH) Syndrome
- Sarcoidosis
- Bechet's Disease
- Idiopathic Retinitis, Vasculitis, and Neuroretinitis (IRVAN)

Bacterial

- Bartonella Henselae
- Bartonella Quintana
- Mycobacterium Tuberculosis
- *Spirochetes*: Syphilis, Lyme, Leptospirosis

Parasitic

- Toxoplasmosis
- Diffuse Unilateral Subacute Neuroretinitis (DUSN)

Viral

- Herpes viruses: HSV, VZV, EBV
- Human Immunodeficiency virus (HIV)
- Hepatitis B Virus
- Influenza A
- Measles, Mumps, Rubella

Fungal

- Histoplasmosis
- Coccidicomycosis
- Actinomycosis

Masquerade

- Leukemia
- Malignant hypertension
- Branch Retinal Vein Occlusion (BRVO)
- Idiopathic intracranial hypertension (IIH)
- Diabetic papillopathy
- Anterior ischemic optic neuropathy (AION)

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