

Recurrent Vogt-Koyanagi-Harada disease presenting with diffuse orbital inflammation

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ABSTRACT

Purpose: To report diffuse orbital inflammation as a manifestation of recurrent inflammation in a patient with Vogt-Koyanagi-Harada (VKH) disease.

Observations: 20-year-old African American male, who was previously diagnosed with VKH, presented with right eye pain, swelling, and binocular double vision. He had run out of methotrexate while on steroid taper. Neuroimaging was consistent with diffuse orbital inflammation with myositis. He was started on intravenous steroids and then transitioned to oral steroids, with complete resolution of his symptoms.

Conclusions and importance: Central nervous system involvement as a manifestation of VKH has been previously reported, however, there have been no reports of orbital inflammatory syndrome resulting from VKH. Thus, in the appropriate clinical context, orbital signs may be recognized as features of recurrent VKH.

MeSH terms

Uveomeningoencephalitic Syndrome, Orbital Inflammatory Pseudotumor.

1. Introduction

Vogt-Koyanagi-Harada disease (VKH) is a rare condition that causes severe intraocular and extraocular inflammation. The disease process occurs due to a Th1-mediated autoimmune targeting of antigens associated with melanocytes that results in granulomatous inflammation.^{1,2} The disease is associated with HLA-DRB1*0405.³ The primary ocular manifestation is bilateral granulomatous inflammation, including: panuveitis, exudative retinal detachments, and eventual depigmentation of the choroid.^{1,2}

Additionally, several extraocular manifestations have been well described. Extraocular findings include poliosis, vitiligo, alopecia, meningismus, and hearing loss.^{1,3} Though many extraocular manifestations of VKH have been documented, there are presently no known cases described in the literature of a patient with recurrent VKH presenting with orbital inflammation.

2. Case

A 20-year-old African American male presented to the Emergency Department (ED) with right eye pain, swelling, and binocular double vision. Four months prior, he was diagnosed with incomplete VKH per the original criteria and early-stage VKH in the revised classification system.⁴ At the time of diagnosis, his presenting features were headaches/meningismus, bilateral panuveitis, peripapillary exudative retinal detachments, choroidal folds, and disc edema (see Fig. 1).

Lab results, at the time of initial presentation, included normal angiotensin converting enzyme levels, lysozyme levels, *Bartonella* antibody titers, anti-nuclear antibody titers (by immunofluorescent assay), Lyme disease antibody titers, HIV 1/2 antibody titers, syphilis antibody titers, anti-neutrophilic cytoplasmic antibody titers, anti-cardiolipin antibody titers, hepatitis B and C antibody titers, cyclic citrullinated peptide antibody titers, a negative QuantiFERON - TB gold plus test, and the absence of HLA B27. There was a positive lupus anticoagulant test that was later normal (indicating no clinical significance) and a positive rheumatoid factor without signs of rheumatoid arthritis.

Lumbar puncture demonstrated opening pressure of 25 cm water with pleocytosis. Cerebrospinal fluid analysis revealed negative cryptococcal antigen, bacterial culture, enteroviral assay, Lyme antibody study, and HIV 1/2 DNA test, as well as normal myelin basic protein and

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cerebrospinal fluid immunopathology studies.

He was started on 90 mg (1mg/kg) prednisone to which he had a favorable clinical response. His prednisone dose was slowly tapered as he was transitioned to 15 mg methotrexate weekly.

Within the few weeks prior to the ED visit, he was tapered from 40mg to 20mg of prednisone but had run out of methotrexate for 2–3 weeks. He resumed his methotrexate 2 days prior to presenting to the ED. In the ED, he complained of one week of blurry vision, pain with eye movements, and vertical and horizontal diplopia. He then developed right periorbital pain with redness and swelling of this right eye. On examination in the ED, he was lethargic and had periorbital swelling, redness, and mild proptosis by appearance, though no exophthalmometer measurements were taken. His near visual acuity (no available distance acuity chart was available at the time) was J1+ OU, while the pressure in the right eye was 21 mmHg compared to 17 mmHg in the left eye. His pupils were equal and reactive with no afferent pupillary defect. On the right side, he had decreased motility in all directions of gaze (see Fig. 2), serous chemosis, upper and lower lid edema, and rare cell in the anterior chamber.

Head CT with contrast revealed absence of sinus involvement while MRI orbits revealed enhancement of the optic nerve and signs of inflammation involving the orbital fat and extraocular muscles (see Fig. 3). Imaging was consistent with diffuse orbital inflammation with myositis. The patient was started on 250 mg of intravenous methylprednisolone every 6 hours. The following day, the patient had marked resolution of his ophthalmoplegia and orbital swelling. He was discharged on 80 mg of prednisone daily.

Two months later, the patient returned to the ED with left eye blurriness and double vision. His prednisone was tapered to 20 mg shortly before this visit and methotrexate had been recently increased to 25 mg. In the ED, he was noted to have a left esotropia with –1 restriction of motility in all directions of gaze and choroidal folds in the macula of both eyes. MRI was not repeated given clinical findings of the

left eye and recent similar episode in the right eye. He was given a 1-g bolus of intravenous methylprednisolone and his oral prednisone was increased to 60 mg to allow for the increased dose of methotrexate to take effect.

Additionally, rheumatology started the patient on subcutaneous adalimumab and his prednisone was tapered off. He has had no additional recurrences in the following 10 months and is stable on 25 mg of oral methotrexate weekly and 40 mg subcutaneous adalimumab every 14 days at his last clinic visit.

3. Discussion

Vogt-Koyanagi-Harada (VKH) disease was classically recognized to have 4 stages or phases: prodromal, acute, chronic convalescent, and chronic recurrent.^{3,5} Each stage has its own unique features, but the stages do not necessarily present in the same order with each patient.⁵ Updated criteria by the Standardization of Uveitis Nomenclature (SUN) Working Group recommended placement into one of two categories: early-stage or late-stage VKH.⁴

Based on the prior classification system, our patient met diagnostic criteria for incomplete VKH disease based on his features at the onset of disease which included uveitis without a history of ocular trauma or surgery, uveitis without clinical or laboratory evidence of other ocular disease, bilateral uveitis with retinal detachment, and the presence of neurologic features which included meningismus and pleocytosis of CSF. However, he did not meet criteria for complete VKH given the absence of the integumentary features of vitiligo, poliosis, or alopecia. In addition, with our patient experiencing multiple recurrences of these flares, he was within the chronic recurrent phase of the disease. The chronic recurrent phase of VKH is characterized by exacerbations of granulomatous anterior uveitis that oftentimes may be resistant to systemic steroid therapy. Additionally, other complications such as retinal pigment epithelial proliferation, subretinal fibrosis, subretinal

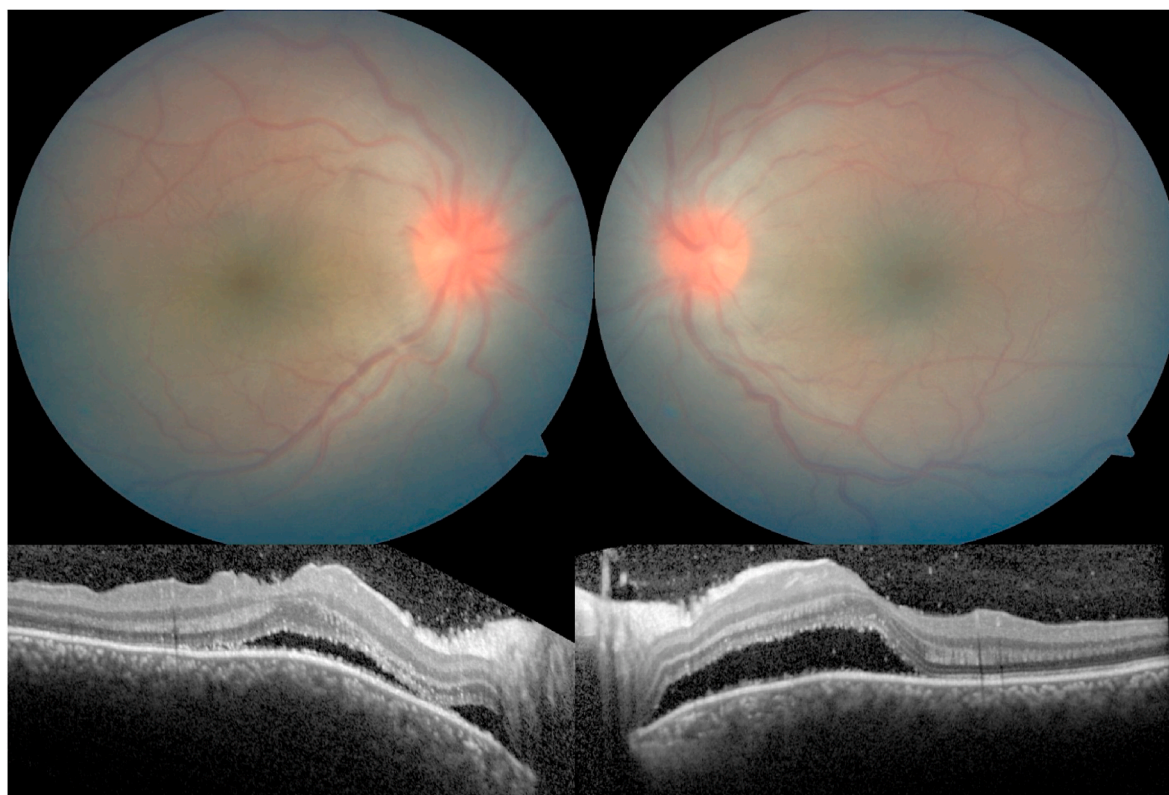


Fig. 1. Fundus photographs and optical coherence tomography, at the time of initial presentation and diagnosis, demonstrating bilateral optic disc edema, choroidal folds, and sub-retinal fluid.

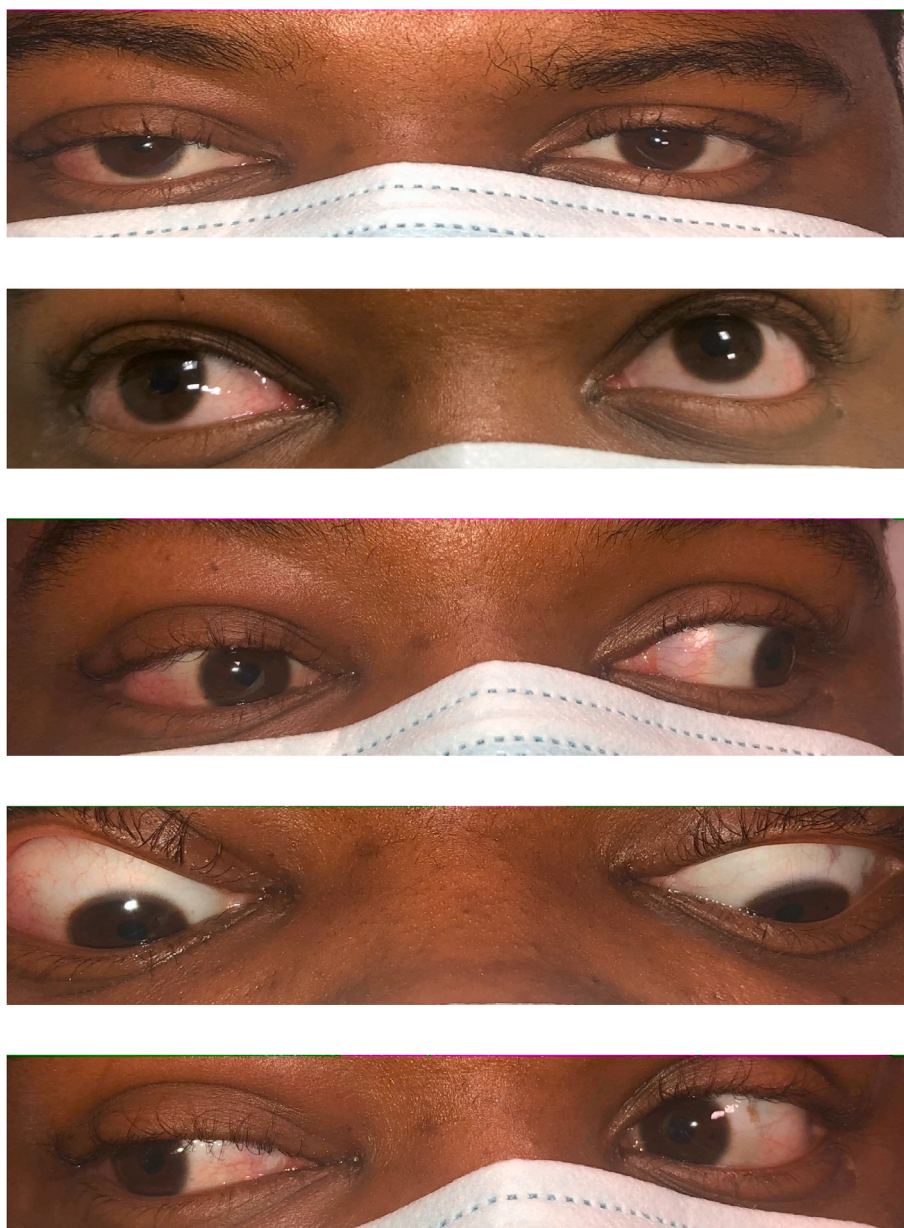


Fig. 2. Color external photographs of patient in primary gaze, then performing ductions: up gaze, left gaze, down gaze, and right gaze. These photographs display the patient's right eye restrictions in extraocular movements during the first episode of orbital inflammation.

neovascular membranes, posterior sub-capsular cataract, posterior synechiae, open and closed angle glaucoma often can arise during the recurrent phase.^{1,6,12} Recurrences often result from early or abrupt discontinuation of steroid therapy or in rapid tapering such as in our patient.¹³

In the present schema, our patient would be placed in the early-stage VKH classification based on the above features. Subsequent integumentary features or ocular/intraocular depigmentation reflect chronic disease and are included in late-stage VKH based on the revised classification.

Our case is the first to demonstrate orbital inflammation as a sign of recurrent VKH. Our patient's pain in the right eye both at rest and with extraocular movements, alongside external ophthalmoplegia, are unique features to this patient's VKH flare when considering the available literature. While there are reports of parenchymatous involvement of the brain as a manifestation of VKH, there have been no reports of orbital inflammatory syndrome resulting from VKH. Some related studies discuss meningeal involvement of VKH with brainstem

involvement; however, those patients did not exhibit orbital signs.^{9,10} Other cases involve nerve palsies or restricted eye movements of various combinations without MRI findings to suggest an orbital inflammatory syndrome.⁸ In one case, a patient with VKH presented with ophthalmoplegia in the setting of suspected brainstem encephalitis.¹¹ The patient was felt to have VKH-related symptoms, for which the patient was also treated with steroids, and improved.¹¹

In our case, the diagnosis was made based on clinical findings suggestive of diffuse orbital inflammation and the orbital MRI which showed signs of orbital fat stranding and myositis. [Figs. 2 and 3]. Typical MRI findings in VKH often include choroidal thickening and Tenon's capsule thickening.⁷ Idiopathic orbital inflammation (IOI) is also referred to as orbital pseudotumor, idiopathic orbital pseudotumor, inflammatory orbital pseudotumor, idiopathic orbital inflammatory syndrome, and nonspecific orbital inflammation.¹³ The term pseudotumor comes from the presence of mass effect in many, but not all, cases of IOI. IOI has been classified by some based on location of the orbital inflammation: idiopathic dacryoadenitis, idiopathic myositis, idiopathic



Fig. 3. Axial and coronal T1-weighted fat saturated contrasted (left images) and post-contrast (right images) MRIs during patient's first episode of orbital inflammation. The post-contrast images display right-sided contrast enhancement and hyperintensity throughout the orbit, including intraconal fat. There is subtle right-sided enhancement of the extraocular muscles indicating myositis. Perineural enhancement is also seen in the post-contrast images. Additionally, there is mild right-sided proptosis. These findings of diffuse hyperintensity are indicative of an orbital inflammatory process.

perineuritis, and diffuse when multiple structures are involved.¹³ Based on the clinical manifestations and MRI findings, our case represents diffuse orbital inflammation.

In conclusion, in the appropriate clinical context, orbital signs may be recognized as features of recurrent VKH. Given the rarity of the occurrence of inflammatory orbital inflammation in VKH, misdiagnosis and mistreatment may occur in caring for patients with VKH presenting with orbital symptoms. Prompt recognition is important as the patients respond quickly to steroids and not antibiotics, for instance. Consequently, early recognition of this rare presentation and initiation of appropriate treatment is paramount to preventing sight threatening complications in patients with recurrent VKH.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Patient consent

Consent to publish this case report has been obtained from the patient(s) in writing.

Declaration of competing interest

The following authors have no financial disclosures: BF, AF, VB, HZ.

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