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Optic disc edema with peripapillary serous retinal detachment as the presenting sign of necrotizing herpetic retinitis

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ABSTRACT

Purpose: To describe an atypical case of necrotizing herpetic retinitis (NHR) that presented initially with mild anterior uveitis, optic disc swelling, and peripapillary serous retinal detachment (SRD).

Observations: A 48-year-old Asian Indian man presented with blurred central vision and pain in his left eye. Examination revealed mild anterior chamber inflammation, optic disc swelling, and a peripapillary SRD in the affected eye. Multimodal imaging, including widefield fluorescein angiography, showed optic disc leakage and confirmed the presence of a peripapillary SRD, but was otherwise unremarkable with no evidence of retinitis. The patient was diagnosed with presumed Vogt-Koyanagi-Harada disease and was treated with systemic corticosteroids. While there was objective visual improvement initially, the patient subsequently noted peripheral vision loss and was found to have peripheral necrotizing retinitis and occlusive retinal vasculitis in affected eye. Polymerase chain reaction-based testing of aqueous humor detected varicella zoster virus DNA, confirming the diagnosis of NHR.

Conclusion and importance: Optic disc edema and peripapillary SRD may precede the development of overt retinitis in some patients with NHR.

1. Introduction

Herpetic eye disease can produce corneal pathology, as well as anterior or posterior uveitis.[1] While uncommon, direct and indirect optic nerve involvement has been described in select patients with necrotizing herpetic retinitis (NHR).[2–9] We describe an immunocompetent patient who presented with isolated papillitis with peripapillary serous retinal detachment (SRD) as the sentinel sign of necrotizing herpetic retinitis (NHR).

2. Case report

A 48-year-old Asian Indian man with history of gastroesophageal reflux disease presented with blurred central vision and pain in his left eye. His visual acuity was 20/20 in each eye, and intraocular pressures (IOP) were 15 mm Hg on the right and 21 mm Hg on the left. There was no relative afferent pupillary defect, extraocular motility was full and without pain, and confrontational visual fields were normal. A comprehensive examination of the anterior and posterior segments of each eye was performed. While no pathology was identified in the right eye, examination of the left eye revealed moderate conjunctival injection, trace cells in the anterior chamber, scattered vitreous cells, and moderate optic disc swelling with a peripapillary SRD (Fig. 1). This constellation of findings was thought to be characteristic of Vogt-Koyanagi-Harada (VKH) disease and the patient was treated with high-dose systemic corticosteroids. While the vision improved to 20/16 on the left two days later, the patient's IOP remained slightly elevated at 24 mm Hg and he continued to complain of blurred vision on the left. On examination, the optic disc swelling and peripapillary SRD in the left eye resolved, but there was mild late staining of the optic disc on wide-field fluorescein angiography (FA; not shown). The patient returned emergently three days later complaining of new onset of peripheral vision loss. Vision in his left eye had declined to 20/63 and IOP increased further to 27 mm Hg. Examination revealed panuveitis with peripheral

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necrotizing retinitis and occlusive retinal vasculitis in the left eye (Fig. 2). Polymerase chain reaction-based testing of aqueous humor detected presence of varicella zoster virus (VZV) DNA. The patient's diagnosis was changed to NHR, his systemic corticosteroids were discontinued, he was started on valganciclovir 1000 mg orally three times daily, and he was given an intravitreal injection of ganciclovir. Shortly after initiation of anti-viral therapy, the patient returned to India and was lost to follow up.

3. Discussion

A 48-year-old Asian Indian man with mild anterior chamber inflammation, minimally elevated IOP, papillitis, and peripapillary SRD was suspected to have early VKH disease and was treated with systemic corticosteroids, leading to objective improvement in visual acuity. The patient's IOP remained slightly elevated, however, and he then developed areas of necrotizing retinitis and occlusive retinal vasculitis, ultimately found to be caused by VZV.

While uncommon, multiple manifestations of optic nerve involvement have been described in ocular herpesvirus infection. Herpes simplex virus, VZV, and cytomegalovirus (CMV) can each result in neuroretinitis, a condition characterized by optic disc edema, early peripapillary SRD, and subsequent development of stellate maculopathy.[2] Ipsilateral optic nerve inflammation or infarction may occur following herpes zoster ophthalmicus.[3] The optic nerve is frequently involved in acute retinal necrosis and can manifest as pallid or hyperemic disc edema, with peripapillary hemorrhages in some cases, or normal in those with retrobulbar involvement.[4] Early optic disc involvement has been described in immunocompetent individuals with concurrent acute retinal necrosis (ARN).[5–7] While isolated optic neuropathy without peripapillary SRD has been described to precede ARN, those patients had acquired immunodeficiency syndrome.[8] A variety of mechanisms have been proposed to explain the optic nerve involvement seen in patients with ocular herpesvirus infection, and it is likely that each or a combination of these theories explains herpetic optic neuropathy in different clinical settings. Direct infection of the optic nerve may be the primary etiology in cases of neuroretinitis and peripapillary retinitis.[2,4] Persistent optic neuropathy, as evidenced by the presence of a relative afferent pupillary defect or visual field defect, can be caused by direct infection, arteritic optic neuropathy from vasculitis, or both.[4] Secondary optic disc edema may arise from spillover inflammation in the anterior chamber or from the vitreous.[9–11] Lastly, it is known that herpesviruses, especially VZV, can enter the eye through the optic nerve without direct infection and eventually incite acute retinal necrosis or necrotizing herpetic retinitis.[12] In select individuals, the viral transit through the optic nerve may result in exudation within the optic nerve sheath, resulting in non-neuropathic swelling.[4] For our patient, the resolution of optic disc edema and peripapillary SRD following corticosteroid therapy suggests that either one or both of the latter mechanisms was the primary etiology.

Early optic disc involvement in patients with NHR is a challenging diagnosis to ascertain and can be mistaken for more common causes of optic neuropathy that are treated with systemic corticosteroids. Benz et al.[13] described a woman with multiple sclerosis who developed sudden onset of decreased vision and eye pain in the setting of a relative afferent pupillary defect and was diagnosed with retrobulbar optic neuritis. Nine days following initiation of systemic corticosteroid treatment, her vision declined to count fingers and she was found to have progressive outer retinal necrosis in the affected eye. In another case, an elderly woman with history of rheumatoid arthritis treated with etanercept experienced sudden, progressive vision loss and was found to have optic disc edema with an afferent pupillary defect, vascular attenuation, and midperipheral retinal hemorrhages; she was treated with oral corticosteroids for presumed arteritic anterior ischemic optic neuropathy and developed NHR six days later.[13] Of note, while optic disc edema was noted at presentation in our patient, he lacked an afferent pupillary defect or any findings typical of NHR on extensive examination of the posterior segment and widefield imaging.

Optic disc edema, SRD, and mild non-granulomatous anterior uveitis are the most common early findings of VKH disease.[14] In 2001, the international Nomenclature Committee established that bilateral involvement is necessary for a diagnosis of VKH disease.[15] However, cases of unilateral VKH and delayed fellow eye involvement have since been reported.[16] Despite a wide array of possible autoimmune and infectious causes, uveitic SRD is by far most often observed in patients with VKH disease.[17] A review of clinical findings at presentation of all patients with uveitis seen at a tertiary referral center over 24 years yielded just one patient with NHR and clinically detectable SRD at initial examination.[17] Consideration of the above points along with the patient's ethinicity, good health, and lack of exposure to tuberculosis and sexually transmitted infections, lead to the initial diagnosis of presumed early VKH disease. While it remains possible that our patient possessed both VKH and NHR, the unilateral presentation and lack of a prodrome are atypical of VKH and the rapid development of NHR three days after presentation are more consistent with solely herpesviral ocular infection.

While, in retrospect, our patient did not have VKH disease, NHR has been reported to occur in patients being managed for VKH disease while being treated with corticosteroids and/or immunosuppressive agents. Yokoi et al.[18] described a patient diagnosed with unilateral, incomplete VKH disease based on the presence of anterior uveitis, SRD, a choroidal lesion, pinpoint areas of leakage on FA, and pleocytosis of cerebrospinal fluid, who was monitored for eight days, given systemic corticosteroids, and developed ARN eight days later. Gupta et al.[19] reported a patient

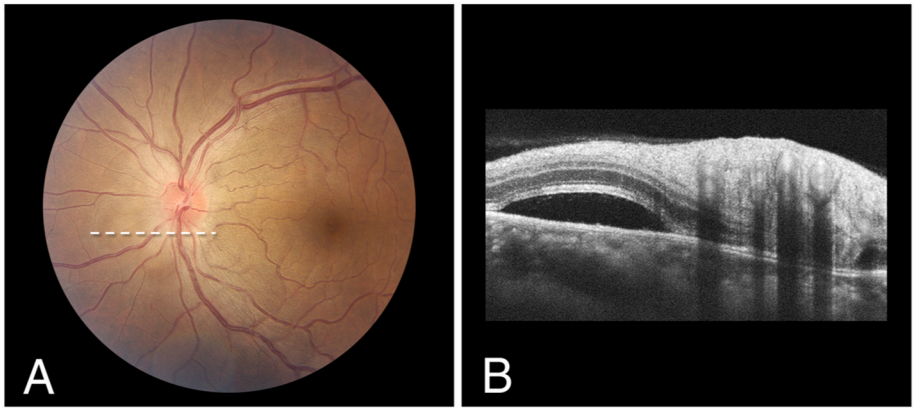

Fig. 1. A: Fundus photograph of the left eye showing optic disc swelling with multiple pockets of peripapillary serous retinal detachment. B: Spectral domain optical coherence tomography (SD-OCT) showing optic disc edema with adjacent subretinal fluid. (Dashed line in panel A corresponds to the location of the SD-OCT cut).

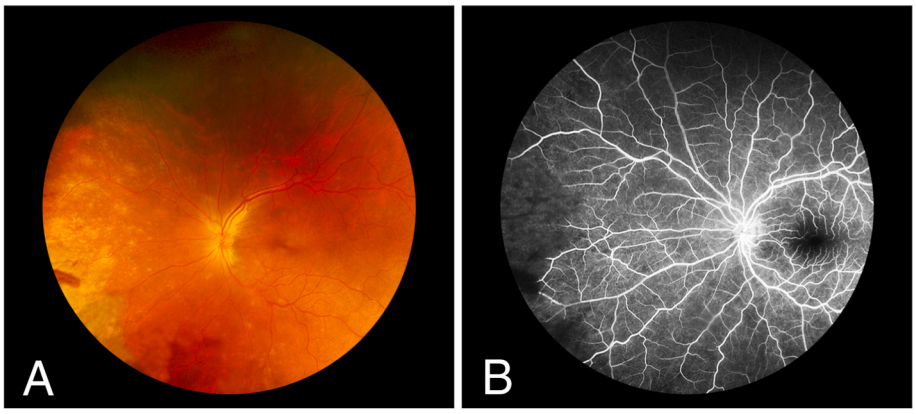

Fig. 2. A: Wide-field fundus photograph of the left eye showing peripheral retinitis with intraretinal hemorrhages. B: Wide-field fluorescein angiogram of the left eye showing peripheral nonperfusion consistent with occlusive vasculitis in the setting of necrotizing retinitis.

with bilateral, probable VKH disease, based on the presence of anterior uveitis, optic disc edema, multiple areas of SRD, choroidal thickening with RPE undulations, and pinpoint leaks on FA, who was started on corticosteroids and immunosuppressants and then developed chicken pox followed by ARN one month later. Takakura et al.[20] described an Asian man with longstanding VKH disease on infliximab, methotrexate, and prednisone who was given periocular and intravitreal corticosteroids following an uneventful cataract surgery and developed PCR-proven CMV NHR seven weeks later. Our patient may also have developed NHR precipitated by profound immunosuppression due to high dose corticosteroids, but the occurrence of NHR within 3 days of starting corticosteroids seems unlikely.

4. Conclusion

In summary, NHR may present initially with papillitis and we now show that such optic disc involvement can produce peripapillary SRD. Patients who present with optic disc swelling in the setting of uveitis should be monitored closely for the development of NHR, particularly when treated with high-dose systemic or regional corticosteroids.

Patient consent

The patient was lost to follow up and unable to be reached for consent. No personal identifiers were utilized in the writing of this case report.

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Authorship

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

Credit author statement

Caleb C Ng: Conceptualization, Visualization, Writing – original draft presentation, Writing – review & editing. H Richard McDonald: Writing – review & editing. Robert N Johnson: Writing – review & editing. Emmett T Cunningham, Jr: Writing – review & editing, Visualization, Supervision

Declaration of competing interest

None of the authors have any financial disclosures.

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