CASE REPORT

A Rare Case of Unilateral Progressive Vision Loss and Pachymeningitis

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ABSTRACT

We describe a 32-year-old man with presumed Vogt-Koyanagi Harada (VKH) syndrome, whose presenting symptoms were headache and progressive loss of vision in the right eye. Neuro-ophthalmic examination showed anterior and posterior uveitis, and retinal detachment in the right eye. Ocular coherence tomography (OCT) showed extensive submacular fluid in the right eye, while the fundus fluorescein angiogram (FFA) confirmed perifoveal retinal pigment epithelium (RPE) disruption and multifocal fluorescein leakage in the right eye. The brain MRI showed a small crescent of dependent fluid layering in the right posterior globe adjacent to the right optic nerve head, and pachymeningeal enhancement of the skull base dura along the clivus. This case demonstrates the utility of brain MRI and OCT findings in the early diagnosis of VKH syndrome, in the absence of prominent clinical signs of meningitis. Aggressive treatment is critical to preserve vision and prevent development of other systemic complications of the disease.

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Introduction

Vogt-Koyanagi-Harada (VKH) disease is a rare cause of visual loss in younger individuals. It typically affects women aged 20–50, with an incidence of 1–6 per million. Vogt-Koyanagi-Harada disease has predilection for Asian, Middle Eastern, Hispanic, and Native American populations.^{1–6} In Japan, VKH disease accounts for 7–9% of uveitis cases, whereas in the United States it remains close to 1–4%.^{7,8}

It is a multisystem disease of presumed autoimmune aetiology, with pathology directed against melanocyte-containing cells.^{9–12} Theories revolve around the possibility that a T-cell-mediated autoimmune reaction against antigens associated with melanocytes, melanin, and retinal pigment epithelium (RPE) may play a major role in the disease.^{12–14}

Clinically, it is characterised by bilateral granulomatous uveitis, meningitis, hearing loss, and cutaneous manifestations. Ophthalmic examination may reveal uveitis, retinal or optic nerve oedema, and in more serious cases, retinal detachment. Neuroimaging may demonstrate meningitis, and can detect subretinal fluid. Spinal fluid typically demonstrates

lymphocytic meningitis; this association is characteristic of VKH disease and excludes other choroidopathies associated with central nervous system (CNS) compromise.^{15–19}

Case report

A 32-year-old man presented with a 4-week history of severe headache and progressive loss of vision in the right eye. His past ocular history was unremarkable, without ocular surgery or trauma. His past medical history was significant for hypothyroidism, vitiligo, and poliosis. He has had no recent international travel, sick exposure, animal bites, or scratches.

In October 2012, he developed progressive generalised headache associated with low-grade fever, and nausea. This was followed a few days later by photosensitivity affecting both eyes, worse in the right. Over the course of 6 weeks, he developed cloudy vision in the right eye that progressed to total loss of vision. Other than photosensitivity, the left eye was normal. He denied eye pain or hearing loss. He has had no similar events in the past. Visual fields plotted in December 2012 by the

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referring ophthalmologist showed superior altitudinal defect in the right eye and mild central depression in the left eye.

The patient was evaluated at our neuro-ophthalmology clinic in January 2013, because of persistent monocular vision loss. He had been on low-dose oral steroids for 48 hours prior to our evaluation. Examination showed visual acuity of count fingers (CF) at 2 feet OD (right eye) and 20/20 OS (left eye). There was no relative afferent pupillary defect (RAPD). Colour and stereo vision were impaired in the right and normal in the left. Visual field testing of the right eye could not be plotted, whereas the left eye showed mild central depression. Extraocular motility was normal. Slit-lamp biomicroscopy revealed 2+ cells in the anterior and posterior chambers of the right eye and trace vitreous cell in the left. Dilated examination showed massive submacular swelling and serous retinal detachment in the right eye (Figure 1A). Ocular coherence tomography (OCT) showed extensive submacular fluid in the right eye (Figure 1B). Fundus fluorescein angiogram (FFA) confirmed perifoveal retinal pigment epithelium (RPE) disruption and multifocal fluorescein leakage in the right eye (Figure 1C). The patient's neurologic examination was unremarkable. He had no meningeal signs or cranial nerve deficits. Physical examination showed vitiligo and poliosis (Figure 2).

Lumbar puncture was performed and revealed normal opening pressure. Cerebrospinal fluid (CSF) constituents revealed 4 white blood cells per microliter with lymphocytic predominance; glucose and protein were within normal levels. The spinal fluid cytopathology, flow cytometry, and infectious work-up were unremarkable. Serum angiotensin-converting enzyme (ACE), aquaporin-4 antibody, antinuclear antibody (ANA), Quantiferon TB Gold, human immunodeficiency virus (HIV), and rapid plasma reagin (RPR) were negative. The brain magnetic resonance imaging (MRI) showed a small crescent of dependent fluid layering in the right posterior globe adjacent to the right optic nerve head (Figure 3A), and pachymeningeal enhancement of the skull base dura along the clivus (Figure 3B). There was no evidence of retro-orbital optic nerve contrast enhancement. These imaging findings correlate well with his clinical picture of meningitis and extensive submacular fluid seen on dilated eye examination.

Figure 1. (A) Right eye fundus photo shows serous retinal detachment (arrow), with improvement of serous fluid during treatment. (B) Macula OCT shows massive submacular fluid with resolution of submacular fluid during treatment. (C) Fundus fluorescein angiography shows focal RPE leak with resolution of RPE leak during treatment.

Figure 2. Poliosis and vitiligo.

Figure 3. (A) T2-weighted fat-suppressed orbit MRI shows a small crescent of dependent fluid layering in the right posterior globe adjacent to the right optic nerve head related to the submacular fluid seen on examination. (B) Contrasted T1-weighted coronal MRI shows pachymeningeal enhancement of the skull base dura along the clivus.

We felt that the right visual loss were combined effects of retinal detachment, macular oedema, and an acute papillitis. With his constellation of signs and symptoms, and characteristic imaging findings, there was concern for VKH disease. A number of diagnoses had been considered in this patient, including neurosarcoidosis, many infectious and autoimmune aetiologies, and demyelinating disease. Tumour, neoplasm, and immunodeficiency were ruled out by imaging, serology, and spinal fluid examination.

He was immediately started on 5 days of intravenous methylprednisolone (1 mg/kg/day) followed by high-dose oral prednisone. Treatment gradually induced remission of symptoms. At 1-month follow-up, best-corrected visual acuity was 20/50 OD and 20/20 OS. The right macula and optic nerve appeared normal without an afferent pupillary defect. Confrontational visual field testing showed central scotoma in the right eye and was normal in the left. Biomicroscopic examination improved, showing only trace cells in the anterior and posterior chambers, OU. Subsequent follow-up visits showed visual acuity of 20/20 in each eye.

A 2-year course of azathioprine 75 mg twice daily was initiated in lieu of prednisone due to significant hyperglycaemia that was difficult to control. A few weeks after discontinuing immunosuppression, he developed worsening vision in the right eye. On examination, best-corrected visual acuity was 20/20 in each eye. Humphrey visual field showed inferotemporal scotoma in the right eye and mild central depression in the left eye. He has been off of immunosuppression for more than a year now and remains asymptomatic, with stable visual afferent function.

Discussion

Vogt-Koyanagi-Harada (VKH) disease is defined as a bilateral granulomatous panuveitis with potential systemic manifestations affecting young adults. Extraocular manifestations include meningitis, hearing loss, vitiligo, and other dermatologic signs, including poliosis and alopecia. The disease is mediated by T-helper cell attack against melanocytes in the uvea, skin, central nervous system, and inner ear. [Tables 1](#) and [2](#) show ocular and extraocular manifestations of VKH disease.

The first diagnostic criteria created by American Uveitis Society in 1978 was revised because it failed to distinguish acute and chronic cases, and did not take into account ancillary ophthalmic procedures. Currently, the disease is classified into complete, incomplete, and probable VKH based on the 2001 revised diagnostic criteria of the International Nomenclature Committee.¹⁶

Table 1. Ocular manifestations of VKH disease.

Early ocular manifestations	Late ocular manifestations
Diffuse choroiditis	Recurrent or chronic uveitis
Vitreous inflammatory reaction	RPE clumping and chorioretinal scars
Optic disc hyperaemia	Neovascularisation
Subretinal fluid	Ocular de-pigmentation
Macular oedema	Cataract and glaucoma
Bullous retinal detachment	Choroidal and optic atrophy

Note. RPE = retinal pigment epithelium; VKH = Vogt-Koyanagi-Harada.

Table 2. Extraocular manifestations of VKH disease.

Systemic associations
Neurologic signs: fever, headache, nausea, vomiting, and neck stiffness
Dermal signs: vitiligo, poliosis, and alopecia
Auditory signs: sensorineural hearing loss, tinnitus, and vertigo

The clinical features of VKH disease varies depending on the stage of the disease. The prodromal stage resembles viral-like illness and can last 3–5 days. It usually presents with headaches, fever, nausea, dizziness, and light sensitivity. The second uveitic stage presents with decreased visual acuity. Vision loss begins in one eye, followed by the fellow eye in 1–2 weeks. A third stage designated as chronic or convalescent typically develops weeks to months after the uveitis. At this stage, the patient shows overt dermatologic manifestations (vitiligo, poliosis, and alopecia) and depigmentation of choroid. The final stage is characterised by uveitis exacerbations and threatening visual complications such as neovascularisation, glaucoma, and cataracts.¹¹

Diagnosis of VKH disease is made clinically. There are no serologic biomarkers available to confirm the diagnosis. In the past, melanocyte-specific proteins have been targeted as candidate autoantigens in the pathogenesis of VKH disease. We know from previous studies that HLA-DR4 (human leukocyte antigen) is strongly associated with VKH disease, but most recently three loci associated with *VKHD* gene susceptibility have been identified: IL23R-C1orf141, rs117633859; ADO-ZNF365-EGR2, rs442309; and HLA-DRB1/DQA1, rs3021304.^{20–22} Despite advances in research, we have yet to come up with a specific serologic testing to diagnose VKH disease. Ancillary ophthalmic examinations such as FFA, indocyanine green angiography (ICGA), electroretinography (ERG), ultrasonography, and OCT are often used to assist in the diagnosis and localisation of the pathologic process to the choroid.

To avoid overlooking systemic or neurologic disorders associated with posterior uveitis, a careful neuro-ophthalmic examination and imaging of the brain and orbit with gadolinium should be performed. This should be followed by serologic and CSF analysis to expeditiously define an aetiology and to initiate treatment. Table 3 shows a comprehensive differential diagnosis of VKH disease. This table includes the most common forms of posterior uveitis associated with neoplasm, autoimmunity, inflammatory, and infectious aetiologies in the immunocompetent and immunodeficient patients.

Brain MRI is especially useful in detecting collateral meningeal inflammatory process, generally

Table 3. Differential diagnosis of VKH disease.

Infection
• HIV
• Syphilis
• TB
• Herpes-type viruses (CMV, HSV1, and HHV6)
• Lyme disease
• Whipple's disease
• Cat-scratch disease
Autoimmune
• Behçet's disease
• Reiter's syndrome
• Sjögren's syndrome
• Birdshot chorioretinopathy
• Neurosarcoidosis
• Ankylosing spondylitis
• Lupus choroidopathy
• Multiple sclerosis (intermediate uveitis)
Neoplasm
• Intraocular lymphoma
• Acute leukaemia
• Metastatic carcinoma
• Uveal lymphoid infiltration
Other inflammatory processes
• Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)
• Uveal effusion syndrome
• Posterior scleritis

Note. CMV = cytomegalovirus; HSV1 = human herpes virus type 1; HHV = human herpes virus 6.

not found in other choroidopathies, thus improving diagnostic specificity for VKH disease. In our patient, the most distinguishing imaging feature of VKH disease were the presence of fluid in the posterior globe, pachymeningeal enhancement, and exclusion of demyelinating optic neuritis. Melanocytes within the dura are targets of VKH autoimmunity; hence, the pachymeningeal enhancement observed in our patient may be a marker of early CNS involvement, which is generally not present in other choroidopathies. The absence of brain parenchymal compromise and vasculitis excludes acute multifocal placoid pigmentary epitheliopathy (AMPPE).

High-dose systemic corticosteroids is the mainstay of treatment. A short course of intravenous methylprednisolone given 1 g daily for 3–5 days followed by 3–6 months prednisone taper (1–1.5 mg/kg per day) is recommended. In some cases, rapid discontinuation of systemic corticosteroid may lead to recurrences; therefore, the duration of steroid treatment depends on the degree of inflammation. Medications such as azathioprine, methotrexate, and mycophenolate may be considered as

steroid-sparing agents. Biologic agents such as infliximab and cyclophosphamide have also been proven effective for VKH disease. In general, the inflammatory process in VKH disease resolves within 1–2 years of treatment, and the visual outcome is good, with visual acuity better than 20/40 achieved in 50–90% of treated cases.²³

In summary, our experience in this case adds to the diagnosis of an unusual cause of visual loss in younger individuals. A careful neuro-ophthalmic history and examination, complimented by neuroimaging, and spinal fluid analysis facilitated the identification of a meningeal process, adding diagnostic specificity to our ancillary testing. In our case, brain MRI showed good concordance with the OCT findings, and was an important tool in the early diagnosis of this rare disorder even in the absence of prominent clinical signs of meningitis. Prompt and aggressive treatment is critical to preserve vision and prevent development of other systemic complications of VKH disease.

Declaration of interest

All authors examined and treated the patient and contributed to writing the manuscript. Jorge C. Kattah, MD, has been a consultant for Biogen, Bayer, and Teva. There are no specific disclosures in relation to this report.

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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