

Vogt-Koyanagi-Harada (VKH) Syndrome – A Case Report in Southwestern Saskatchewan

Background

Vogt-Koyanagi-Harada (VKH) syndrome or uveoencephalitis is an extremely rare systemic disease, involving melanocyte-containing organs¹. The syndrome is so rare that data regarding its prevalence in Canada is presently unavailable. First described in 940-1010 AD, the syndrome was reported independently in the early 20th century by Vogt, Harada, and Koyanagi¹. VKH occurs most commonly in individuals with darker pigmentation (Asian, Native, Latin or African American), and rarely occurs in fair skinned individuals¹. Presentation of the syndrome characteristically occurs between the 2nd and 5th decades with a mean age of 30-40 years¹.

Pathogenesis

Although several theories exist, the etiology of VKH is unknown. Clinical data appears to support the theory of an autoimmune process directed against melanocytes, since lymphocytes from peripheral blood and CSF of VKH patients exhibit cytotoxic activity against B-36 melanoma lines¹. Although no virus has been isolated from patients with VKH, some researchers believe viral reactivation may be responsible because the clinical course of the syndrome presents with an influenza-like episode¹. Other researchers believe the syndrome may be inherited, likely as an autosomal recessive trait. Although familial cases are rare, Japanese researchers continue to explore this avenue²⁻⁵.

Clinical Presentation

VKH presents clinically with diverse symptoms but can usually be categorized into phases: prodromal, uveitic, and convalescent¹.

The *prodromal* phase, also known as the meningeal phase, generally lasts for a few days. In this phase the degree of neurologic symptoms vary¹. Patients may experience headache, fever, photophobia, and meningismus (a non-infective state resembling meningitis). Generalized muscle weakness, hemiparesis, dysarthria (difficulty speaking), and aphasia (loss of ability to comprehend or express speech and concepts) have also been reported. The patient's mental status may be altered and can range from mild confusion to psychosis. It is believed that most of the neurologic symptoms are directly attributed to changes in the cerebral spinal fluid (CSF), as there is often lymphocytic pleocytosis, increased pressure and protein levels¹.

The *uveitic* phase, lasting several weeks, is the phase during which most patients seek medical attention, usually presenting to their ophthalmologist. The common features of this phase include bilateral blurred vision, eye pain and irritation, and a loss of vision¹. Tinnitus and dysacusis (hearing impairment with distortion of frequency or intensity and

discomfort for certain sounds) develops in 50% of patients, and may appear during any of VKH's three phases¹⁻².

The *convalescent* phase usually occurs within three months of syndrome onset, and is characterized by cutaneous signs¹. Although this usually occurs after the onset of the uveitis, skin changes have been reported years before any ocular symptoms were experienced¹. Dermatological symptoms include patchy alopecia, poliosis (90% of patients) involving the eyebrows, eyelashes, body hair and scalp, and symmetrical vitiligo (63% of patients) over the head and trunk¹⁻².

Diagnosis

The American Uveitis Society recommends that the following criteria be used in diagnosing VKH:⁶

1. An absence of ocular trauma or surgery
2. Presence of at least three of the following four:
 - bilateral chronic iridocyclitis (inflammation of the iris and ciliary body)
 - posterior uveitis, including multifocal exudative retinal detachments, and disc hyperemia or edema
 - neurological signs of tinnitus, neck stiffness, cranial nerve or central nervous system dysfunction, or cerebrospinal pleocytosis
 - cutaneous findings of alopecia, poliosis, or vitiligo

The majority of diagnoses are made clinically through neurological and ophthalmologic examinations, with lumbar puncture often used to substantiate the diagnosis¹.

Prognosis

VKH is not associated with mortality¹. While acute disturbances in sight occur, ultimate vision outcomes depend on the rapidity and appropriateness of treatment. Hearing is almost always completely restored¹. Unfortunately, cutaneous pigmentary changes are often permanent¹. Although uncommon, long term complications may arise and include reversible and irreversible vision loss, intraocular pressure elevation, glaucoma, and cataracts¹.

Pharmacotherapy

The goal of therapy is to reduce morbidity and prevent complications. This is accomplished via suppression of the initial intraocular inflammation with early and aggressive systemic corticosteroids, followed by a slow taper over 3-6 months¹. Initial adult dose of prednisone generally ranges from 60-100 po daily, while pediatric doses are 0.14- 2.0 mg/kg/day divided three to four times daily¹. Patients who are unresponsive to high dose corticosteroids may respond to immunosuppression with azathioprine, cyclophosphamide, or methotrexate¹. Topical (ocular) therapy includes the use of corticosteroids, while cycloplegic-mydriatic eye drops may be used symptomatically¹.

Case Report

Our report of VKH occurred in a 16-year old Caucasian female, LS (name changed to maintain confidentiality) from a rural community in Southwestern Saskatchewan. The diagnosis proved to be a challenge not only because most physicians have no experience with VKH, but also because she did not present in the classic manner.

LS's medical history was unremarkable, although there is a family history of thyroid dysfunction. At the age of 6 months, LS developed the measles. It was undetermined whether she had ever experienced chickenpox. No other recent viral infections were noted. Until this point, LS had been considered a normal, healthy 16-year old.

The following outlines the progress of symptoms in the months leading up to LS's diagnosis as described by both LS and her medical charts:

Relevant Clinical Course:

Summer – LS noticed white patches of skin. However, as they were not bothersome, she did not seek medical attention.

November 10 – LS presented to her family physician with complaints of headaches, dizzy spells, and general malaise lasting approximately two weeks. Lab tests were conducted, including iron studies, electrolytes, CBC, albumin and thyroid levels, and a monospot. All tests came back normal, and the monospot was negative.

November 24 – LS became increasingly listless and fatigued. She experienced extreme muscle weakness and complained of decreased muscle control, where at times she was unable to move. LS was now having eye pain and described it as the eyes felt like they were “swelling”. Weight loss was also evident.

December 4 – LS was now sleeping 18 hours daily, and had lost all interest in social activities. She was depressed, and startled easily. LS was admitted to the local hospital and lab tests were repeated. Viral studies including hepatitis, HIV, and West Nile Virus were also conducted. All results came back within normal ranges, and all viral studies were negative.

December 20 – LS had an apparent focal seizure, where she was found staring and unresponsive. Some left arm weakness and left facial droop was noted, and slurring of words occurred. Symptoms lasted approximately 10 minutes then resolved fully.

December 23 – LS became restless and although she was fatigued, she was unable to sleep. Viral studies for Influenza A came back positive.

December 30 – Unable to determine a diagnosis, the local physician referred LS to the regional hospital under the care of an internist for further investigations. Upon admission a mild tremor on the left side was noted, but otherwise neurological findings were normal. A CT scan revealed diffuse edema with meningeal enhancement.

January 1 – Episodes of mild confusion occurred throughout the day. Later that evening LS was heard moaning and was found in a dazed state with her eyes rolled back. She appeared awake, but was uncommunicative. After an hour and a half symptoms resolved and LS returned to a normal state. It was undetermined whether LS had suffered a seizure and was found in the post-ictal state. Because of the inability to determine a diagnosis, LS was transferred to a major provincial health centre to be seen by a neurologist and pediatric neurologist.

January 2 – Upon initial physical examination LS appeared very drowsy. There was no evidence of any visual disturbances, although some tinnitus was present and there was decreased hearing in the left ear. No weakness or paresthesias was observed. Dermatological symptoms included diffusely scattered hypo-pigmented macules, occasional halo nevi, and some patches of hypo-pigmented hair.

Neurological examination determined mild meningismus. A MRI scan revealed some enhancement in temporal lobes bilaterally (left > right). LS appeared confused at times, then alert. A Mini Mental Status test was scored at 26/30, with points being lost for writing, drawing, reading and orientation to place. Sensations were intact. Fundoscopy revealed bilateral florid edema with some hemorrhages. Lab results were unremarkable and were not helpful in determining a diagnosis. Because of massive cerebral edema, a lumbar puncture was not possible.

Initially LS was treated as a chronic meningitis with cefuroxime and vancomycin, and for possible HSV encephalitis with acyclovir.

Several specialists were called in for consultations, including ophthalmology and dermatology. It was during the dermatological consultation that the similarity of LS's symptoms with those of VKH was noted. A working diagnosis of VKH was determined, although it remained uncertain as to whether LS had had uveitis. Therapy was initiated with dexamethasone, and a dramatic improvement was seen within the first day.

LS was discharged on prednisone 75mg daily, to be tapered by 5mg weekly until a dose of 50mg was achieved. Further tapering will be dependent on patient response. Unfortunately, prednisone is a drug with multiple side effects, and these complications have proven to be the most troublesome for our patient. LS experienced gastrointestinal upset from the prednisone, for which rabeprazole 20mg daily was successful in treating. She is also receiving treatment for steroid-induced acne, although her dermatologist has determined that no specific therapy of the vitiligo or halo nevi is required. As osteoporosis is a major concern for patients on chronic steroid therapy, calcium and vitamin D supplementation was initiated.

The rarity of VKH makes its diagnosis a challenge. However, when a patient does not present in the classical way, as was the case with LS, it makes the diagnosis even more difficult. Fortunately, LS was diagnosed and treated in a timely fashion, and because of this will likely not experience any further long-term complication from the syndrome. Since discharge, LS has continued to improve, and less than two months after diagnosis

has returned to school and part-time work, although she is still being followed closely by a neurologist, ophthalmologist, and dermatologist.

The fact that a variety of specialists were needed to determine the diagnosis is further evidence for the importance of collaboration among health professionals in providing optimal patient care.

References

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