

## ORIGINAL ARTICLE

### Vogt-Koyanagi-Harada Syndrome

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Vogt-Koyanagi-Harada syndrome is generally a rare multisystemic autoimmune disorder involving with pigmented structures, such as the eye, meninges, inner ear and skin. The syndrome typically presents as an episode of bilateral panuveitis after prodromal symptoms similar to aseptic meningitis. Auditory disturbances include tinnitus, hearing loss and vertigo. We report the case of a 74-year-old woman with blurred vision, two month history of sudden onset hearing loss and tinnitus in the right ear.

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#### Introduction

Vogt-Koyanagi-Harada syndrome is generally a rare multisystemic autoimmune disease affecting eyes, meninges, ears and skin<sup>[1]</sup>. In 1906, Vogt first described a patient with bilateral uveitis, poliosis (whitening of the eyelashes), dysacusia and vitiligo<sup>[2]</sup>. Subsequently, in 1926, Harada described what he believed to be a distinct entity comprising bilateral retinopathy, uveitis and dysacusis<sup>[3]</sup>. In 1929, a variant of this initial description was added by Koyanagi, who also described hearing loss, vitiligo and alopecia in association with the same condition<sup>[4]</sup>. It has been described as an inflammatory condition of autoimmune nature in which cytotoxic T cells target melanocytes. The observed increased prevalence in pigmented races favours such a theory and is reinforced by the finding of a positive correlation between abnormal inner-ear function and loss of melanocytes<sup>[5]</sup>.

In this paper we report a case of hearing loss and tinnitus associated with VKH syndrome on the basis of both the diagnostic criteria established by the American Uveitis Society in 1978 and the revised diagnostic criteria published in 2001<sup>[6]</sup>.

#### Case Report

A 74-year-old woman was admitted to the ENT department with right-sided sudden onset hearing loss, tinnitus and bilateral blurred vision for two months. She had no history of vertigo, head and neck trauma, acoustics trauma, upper respiratory tract infection. She had hypertension, controlled on appropriate medication. She had undergone appendectomy forty years previously and bilateral cataract operation four years ago.

On examination, otoscopy was normal. She underwent full audiologic evaluation with standard techniques (0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz). Audiologic assessment was conducted in a double-walled sound booth (IAC, Denmark) using a commercially available AC40 clinical audiometer (Interacoustics, Denmark). The asymmetric sensorineural hearing loss is noted on the right ear. Pure tone audiometry resulted in a hearing loss averaging 38 dB HL and 18 dB HL at 500-1,000-2,000 Hz in the right and left ears, respectively. Within the high frequencies, the patient had 70 dB loss in the right side and 20 dB loss in the left side at 6 kHz, 60 dB loss in the right side and 35 dB loss in the left side at 8 kHz. Majority of elevated pure-tone threshold was at 6 kHz. Speech discrimination level was 84% in

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the right ear and 96% in the left ear (Figure 1). She did not have an audiologic evaluation previously.

The video electronystagmography (VNG) (Micromedical Technologies, USA) test was performed. An abnormal saccadic response was observed. It was characterized by abnormal peak velocity and latency. Saccadic pursuits were observed on tracking test. The VNG findings are in accordance to sensorineural system involvement. Since the patient could not tolerate the caloric test, we do not have the caloric responses. Vestibular evoked myogenic potentials (VEMP) were recorded through surface EMG activity of the sternocleidomastoid muscle using a Smart EP device (Intelligent Hearing Systems, Miami, FL, USA). Background electromyographic activity was monitored visually for consistent tonic contraction. The amplifier gain was set to 100,000, and signals were bandpass-filtered at 10 to 3,000 Hz. Short tone bursts (100 dB nHL, 500 Hz each, with a 1 ms raise-fall time and a 2 ms plateau time) were delivered monaurally via TDH 49P earphones. The stimulation rate was 5 Hz; the analysis time was 60 ms. A total of 128 responses were averaged, and measurements were repeated twice to check wave reproducibility. Latencies of the peak p13 and n23, interpeak p13-23 interval, and p13- n23 amplitudes were measured. Mean latency values for p13 and n23 were 13.07 and 22.0 ms, 14.87 and 21.67 ms on the right and left side respectively. She had bilateral normal VEMPs. Neurologic examination revealed no deficit. Bilateral panuveitis was diagnosed an ophthalmologic consultation.

A magnetic resonance imaging (MRI) scan of the brain revealed minimal diffuse cerebellar atrophy.

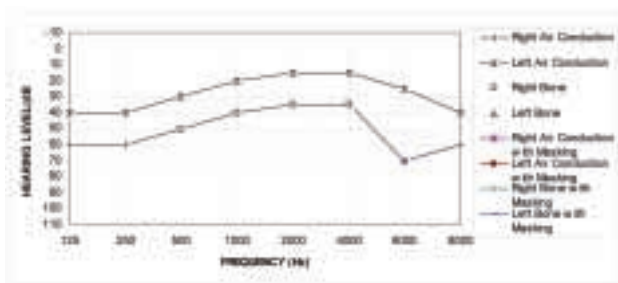


Figure 1. Audiogram of the patient on admission.

Abdominal ultrasonography and chest X-ray were normal. Serum alkaline phosphatase and lactate dehydrogenase were elevated. Serum C-reactive protein concentration was slightly elevated, suggestive of a mild inflammation. Autoantibody screen and serum calcium were normal.

The patient was treated with oral prednisolone 1mg/kg/day, topical prednisolone acetate and oral cyclosporine 200 mg. Prednisolone was gradually tapered down to 10 mg. She had control examinations with an interval of one week. Hearing loss and subjective tinnitus symptoms were recovered with medical therapy within a month. The ocular symptoms subsided. We continue to follow up the patient in the outpatient clinic. At one year follow up audiogram the hearing level on the right side rised to the hearing level on the left side. Hearing became symetric in both ears (Figure 2).

In view of the good response to steroids and cyclosporine, association of sudden onset sensorineural hearing loss and tinnitus with bilateral panuveitis, a diagnosis of incomplete VKH syndrome was made, consistent with the criteria established by the American Uveitis Society [6].

## Discussion

In 1906, Vogt first described a patient with bilateral uveitis, poliosis (whitening of the eyelashes), dysacusia and vitiligo [2]. Subsequently, in 1926, Harada described what he believed to be a distinct entity comprising bilateral retinopathy, uveitis and dysacusia [3]. Three years later, in 1929, Koyanagi described 6 patients with bilateral chronic iridocyclitis, patchy depigmentation of the skin, patchy hair loss and

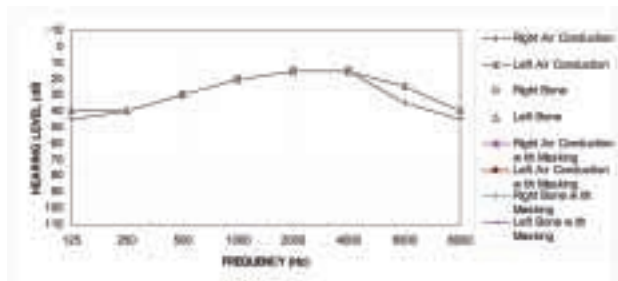


Figure 2. Audiogram of the patient at one year-follow up.

whitening of the hair<sup>[4]</sup>. Babel in 1932 and Bruno and McPherson in 1949 combined the findings and suggested that these process represent a continuum of the same disease, thereafter recognized as VKH syndrome<sup>[7,8]</sup>.

Vogt-Koyanagi-Harada syndrome is generally a rare multisystemic autoimmune disease affecting eyes, meninges, ears and skin. Asian, Hispanics, Asian Indians and those with Middle Eastern heritage are most frequently affected. However, black people are uncommonly affected<sup>[6]</sup>. Women seem to be affected more frequently than men, and VKH disease predominantly affects those in their third to fourth decades of life, although children as young as 4 years of age have been diagnosed with VKH syndrome<sup>[5,9]</sup>.

The etiology and pathogenesis of this syndrome is unknown; various investigators have suggested an underlying autoimmune or infectious process. The disease is thought to be a T-cell-mediated autoimmune process directed against one or more antigenic components of melanocytes, a cell shared by the involved regions. An association with HLA-DR1 and -DR4 has been found among 84% of Southern Californian Hispanic patients with VKH syndrome<sup>[10]</sup>. However Alaez et al found an association with HLA-DRB1\*0101 in Mexican Mestizos and identified a motif that is shared with DRB1\*0405 in Japanese patient with VKH<sup>[11]</sup>. Simultaneous onset of VKH syndrome among coworkers, friends and neighbours has been reported, suggesting a viral etiology<sup>[12]</sup>.

The VKH syndrome was divided into 3 categories: complete, incomplete and probable. For all types, there must be no penetrating ocular trauma or surgery at the initial onset of uveitis and no laboratory evidence for other ocular disease. There must be ocular involvement in all types. Complete VKH must include neurologic, auditory and integumentary findings. Incomplete VKH must have at least one of these findings; and probable VKH has none<sup>[6]</sup>. Our patient fulfilled the criteria for suffering incomplete VKH syndrome.

VKH syndrome is characterized primarily as a syndrome with ocular manifestations, but hearing loss may occur as well<sup>[13]</sup>. In 1958, Lehnhardt observed sudden,

progressive hearing loss in 13 patients and hypothesized that antiochlear antibodies caused contralateral hearing loss after ipsilateral cochlear destruction<sup>[14]</sup>. Melanocytes have been found in the endolymphatic sac, osseous spiral lamina, modiolus, stria vascularis, Reissner's membrane, ampullae, saccule, crus commune and utricle<sup>[15,16]</sup>. The melanocytes in the cochlea play an important role in hearing, as evidenced by the sensorineural deafness which occurs in some congenital pigmentary disorders, including Waardenburg syndrome<sup>[17]</sup>. Inflammatory cells infiltrated the cochlea through the spiral modiolar vein, and that inner ear memory responses in quinea pigs immunized against VKH produced hearing deficits and relevant cochlear histopathology<sup>[18]</sup>. However, findings of another study suggest that the melanocytes of the cochlea and vestibular organ in the inner ear play important roles in both hearing and equilibrium<sup>[19]</sup>.

In VKH syndrome hearing loss is seen in almost 30 % of patients during early phase of the disease. This loss is usually retrocochlear and most commonly associated with ocular findings.<sup>[20]</sup> Ondrey FG et al. (2006) reported 24 patients with this syndrome and were analyzed for auditory system abnormalities. Elevated pure-tone threshold were prevalent in eight of 24 (33.3 %) of the patients. With regard to patient-reported auditory symptoms in addition to hearing loss, two of 24 (8.3 %) experienced tinnitus and one of 24 (4 %) had vertigo. One patient experienced progressive hearing loss over the 2-year treatment course of illness that partially reversed with steroids. They concluded that a significant number of patient with VKH experience sensorineural hearing loss<sup>[13]</sup>.

Since clinical manifestations may vary, the American Uveitis Society has adopted relatively broad-based diagnostic criteria<sup>[6]</sup>. We consider that our patient was characterized by sudden onset hearing loss, tinnitus and panuveitis for two month. A viral etiology, noise exposure or head injury were also excluded. The patient has no history of vertigo or cerebellar symptoms. VNG showed some abnormalities such as abnormal latency and peak velocity of saccades and saccadic pursuits in the tracking test. These findings may be relevant to involvement of the cerebellar system and the brainstem pathways. Our patient

demonstrated normal VEMP results. VEMPs have been validated as being demonstrative of the sacculocolic reflex thus providing information about the inferior vestibular nerve function. Since the VEMPs were normal, one may assume that the inferior vestibular nerve has not been affected. MRI scan was normal. We could not demonstrate any alternative explanation for the hearing loss. The signs and symptoms of our patient show an incomplete Vogt-Koyanagi-Harada syndrome.

Although there is no specific treatment for VKH syndrome, symptoms usually can be controlled by corticosteroids, cytotoxic agents and/or immunosuppressants<sup>[5]</sup>. Corticosteroids for idiopathic, bilateral progressive SNHL were first advocated by McCabe<sup>[21]</sup>. A recent multicenter international study on the treatment of VKH syndrome showed that high-dose oral corticosteroids were as effective as intravenous corticosteroid intervention<sup>[1]</sup>. Treatment of the ocular manifestations of VKH can be successfully accomplished with corticosteroids. It is unknown whether steroid use halts progression of SNHL<sup>[13]</sup>. The patient was treated with oral prednisolone 1mg/kg/day tapered down to 10 mg/day, topical prednisolone acetate and oral cyclosporine 200 mg. Patient is doing well at one year follow up.

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