CASE STUDY

Sensorineural Hearing Loss Evolution in Vogt–Koyanagi–Harada Syndrome

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Abstract Vogt–Koyanagi–Harada syndrome is an autoimmune multisystem disease, characterized by the association of ocular inflammatory manifestations (uveitis and retinal detachment) and extraocular lesions such as meningismus and tegumentary or auditory findings. We report the case of a Hispanic woman with this syndrome.
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Introduction

Vogt–Koyanagi–Harada (VKH) syndrome is a multisystem autoimmune disease that is manifested by an inflammatory reaction affecting pigmented organs, especially the uvea and retinal pigment. In addition, it variably affects the 2nd and 8th cranial nerves (unilateral or bilateral sensorineural hearing loss), meninges, brain, skin and appendages (vitiligo, poliosis, alopecia and greying).1–6

Depending on organ involvement, it is classified as type 1 (ocular involvement without ear or skin involvement), type 2 (ocular findings and at least 1 ear or skin manifestation) or type 3 (ocular signs with 2 or more ear or skin manifestations).2,5,6 Although the precise aetiology is unknown, it is attributed to an autoimmune response against pigmented cells, with destruction of melanocytes by T lymphocytes directed against an unidentified antigen. There have been reports of circulating anti-retinal, anti-choroid and anti-cochlear autoantibodies, as well as the
participation of HLA II (DR1, DR4, DR53, DQA1, DQB1). Allergic mechanisms and viral infections by cytomegalovirus and Epstein Barr virus have also been involved.\textsuperscript{2,5}\n
It predominates in patients aged between 20 and 50 years, although there have been cases reported in patients as young as 4 years, with the evolution being more aggressive in such cases. It is more common in Native Americans, Hispanics and Asians.\textsuperscript{1,2,6}\n
Clinically, it presents 3 stages:

- Stage 1 or prodromal, with headache, fever, periorbitai pain, epiphora and photophobia.

- Stage 2 or ophthalmic, with bilateral uveitis, blurred vision, photophobia, dysacusia, Koepp e nodules (nODULES at the edge of the pupil), corneal keratin precipitates, papilloedema with non-haemorrhagic retinal detachment, involvement of cranial nerves (2 through 7), meningoencephalitis, cerebellar and spinal involvement, cutaneous involvement with polyosisis, vitiligo, alopecia, endocrine alterations and neurogenic bladder.

- Stage 3 or convalescence, which can last for weeks, months or become chronic, manifesting with uveitis, dysacusia, polyosisis, vitiligo or alopecia.\textsuperscript{1,4,9} Involvement of the 8th cranial nerve causes unilateral or bilateral sensorineural hearing loss, tinnitus, horizontal nystagmus, alteration of the vestibulo-ocular reflex and slow eye-tracking.\textsuperscript{1,4,6,9}\n
The diagnosis is clinical and relies on blood tests and CSF as well as electrophysiological, ophthalmologic, auditory and vestibular caloric testing.\textsuperscript{1,6,9}\n
Treatment is based on high doses of corticosteroids, immunosuppressants (cyclophosphamide, azathioprine, chlorambucil, immunoglobulins) and photodynamic therapy.\textsuperscript{1,2,4,9}\n
Clinical Case

We present the case of an Argentinean female, 42 years old, diagnosed with VKH syndrome, and who presented with bilateral panuveitis and serous detachment of posterior poles. She was treated by the Ophthalmology Department from April 2008 with mega doses of methylprednisolone (250 mg every 6 h for 3 days) followed by prednisone (60 mg every 24 h), adalimumab (40 mg every 15 days), cyclosporine A (150 mg every 12 h) and methotrexate (15 mg every week). Oral corticosteroids were discontinued 4 months later and an intraocular treatment with ranibizumab and triamcinolone was subsequently initiated with good response. In September 2008, she was referred to the ENT service due to hearing distortion and bilateral tinnitus. She did not suffer vertigo or instability.

We performed otoscopy and tympanometry with normal results. On the first visit, the mean hearing threshold (250–8000 Hz) was of 43.6 dB in the right ear (RE) and 47.9 dB in the left ear (LE) with a vocal discrimination percentage of 100% at 50 dB in RE and 60 dB in LE.

Subsequent audiometric controls showed fluctuating hearing with mild to moderate sensorineural hearing loss. We performed PEAT on the first visit to ENT (6 months from the onset of the disease) and 2 months later. In the first case we obtained, in both ears, curves in which it was not possible to distinguish waves I–V, and it was not possible to assess latencies. In the second case, we obtained curves with normal latency of wave V in both ears, and with difficulty to distinguish waves I–IV. The patient presented a mean hearing threshold of 41.4 dB in RE and 43.6 dB in LE when the first PEAT study was performed, and of 25.7 dB and 33.6 dB in the second study. The videonystagmography test results were normal for the slow and fast eye-tracking test; absence of spontaneous nystagmus; caloric testing (irrigation with 150 cm\textsuperscript{3} of water at 30 °C and 44 °C for 40 s) with normal bilateral vestibular excitability; damped pendulum kinetic test normal in amplitude, phase and predominance.

In October 2009, the treatment included cyclosporine A (150 mg every 12 h), methotrexate (2.5 mg every 24 h), adalimumab (40 mg every week) and prednisone (60 mg). Significant variations of the hearing threshold were noted in subsequent audiometric controls, with fluctuation of mild to moderate bilateral sensorineural hearing loss, as well as improvement in ophthalmologic symptoms (Table 1 and Fig. 1).

### Discussion

Auditory involvement in VKH syndrome is manifested as sensorineural hearing loss of varying degrees, accompanied by tinnitus and dysacusia.\textsuperscript{1,2,5–10} In our case, the patient showed mild to moderate hearing loss in audiometric testing, with hearing fluctuations related to treatment with immunomodulators.

In 1958, Lehndhard\textsuperscript{11} suggested the presence of anticoagulant antibodies that affected the inner ear. In 1979, McCabe presented 18 patients with asymmetric bilateral
Sensorineural hearing loss of unknown origin, which improved after treatment with corticosteroids, alone or in combination with cyclophosphamide. More recently, a protein of 68 kDa (heat shock protein 70) has been described, which correlates with the progression and degree of sensorineural hearing loss response. According to Niparko et al., treating hearing loss with steroids in autoimmune diseases produces a modulation in the inflammatory cascade, as well as reparative effects on the transendothelial barrier, enabling a recovery of hearing. Ondrey et al. published a case in which they observed how hearing loss could be partially reversible after treatment with corticosteroids, although they did not know if the use of corticosteroid therapy halted the progression of sensorineural hearing loss.

The patient we present referred suffering from hearing loss since presenting VKH syndrome, but we were unable to observe auditory fluctuations until we started monitoring her. Once she was treated at the ENT service, we observed that during those periods when she received immunomodulatory treatment for her ophthalmologic problem, which was the most severe, she experienced a significant hearing improvement both subjectively and in auditory controls. This appeared as a clear case of immunologically mediated sensorineural hearing loss, which could benefit from immunomodulatory therapy. However, we could not point out the individual effectiveness of each of the drugs used, since we prescribed a combination of various drugs at each point in time.

A recent controlled, randomized study showed that treatment with methotrexate was no more effective than with prednisone in maintaining hearing improvement. With respect to the site of involvement, we believe that both cochlear and neural involvement could coexist, since the alteration of melanotic cells characteristic of the syndrome would be more coincident with cochlear damage; however, the alteration of auditory evoked potentials evidences a neural injury that has also been described in immunological processes. We believe that audiometric testing is essential in patients with VKH syndrome who are being treated with corticosteroids or immunomodulators to prevent inadequate therapeutic advice, such as the prescription of a hearing prosthesis, since an improvement of the patient is possible, based on the response to treatment.

Figure 1 Changes in macular width and hearing over time. X-axis: time in months, from April 2008 until November 2009, with the treatments applied. Y-axis: macular width in microns. Z-axis: hearing in dB. Solid lines express the variation of macular width over time: marked with squares for the right eye and with diamonds for the left eye. Dotted lines correspond to the variation of mean hearing (125–8000 Hz) over time, marked with circles for the right ear and with crosses for the left ear.
Conflict of Interests

The authors have no conflicts of interest to declare.

References