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Clinical Record

Deafness in Vogt–Koyanagi–Harada syndrome

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Abstract

Sudden onset sensorineural hearing loss is a well recognized entity frequently encountered in otolaryngological practice. However, the combination of such deafness as part of a wider systemic disorder is fortunately rare. Almost 100 years after the syndrome was classified, we describe a case of Vogt–Koyanagi–Harada syndrome occurring unusually in a Caucasian woman and characterized by sudden hearing loss. A brief review of this rare condition is presented.

Key words: Vogt Koyanagi Harada; Sensorineural Deafness, Syndrome; Autoimmune; Uveitis

Introduction

Vogt–Koyanagi–Harada Syndrome (VKH syndrome) is a rare conglomeration of signs and symptoms which was first described by Vogt in 1906 and modified by Koyanagi and Harada. Essentially, it comprises a combination of uveitis with other clinical features: vitiligo, alopecia and cerebrospinal fluid (CSF) changes, plus deafness in about 30 per cent of cases. Our case was made unusual by the absence of skin changes, deemed to be a very important feature of this syndrome, and also by the fact that our patient was Caucasian; all other cases we found in the literature described occurrence of this syndrome in pigmented individuals. Vogt–Koyanagi–Harada syndrome is practically unknown in Caucasians. Our Caucasian patient did not have skin changes but nevertheless was deemed to have 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.

Case report

A 58-year-old woman attended the ENT clinic with a two-month history of bilateral, sudden onset hearing loss, worse in the right ear, preceded by a general history of malaise, anorexia and gait ataxia. She had no tremor or other cerebellar symptoms or signs and the ataxia was thought to be associated with vestibular disease; she also suffered from episodes of positional vertigo and bilateral tinnitus, which fluctuated in intensity. These features were associated with a concurrent history of joint pains, backache and pain in the eyes plus acute loss of vision. The patient had also suffered from occasional breathlessness and had hypertension, controlled on appropriate medication. A few years previously, she had suffered an episode of high fever, headaches and myalgia, which was controlled by systemic antibiotics, with a presumptive diagnosis of chest infection. A total abdominal hysterectomy with bilateral salpingo-oophorectomy had been performed for ovarian cancer two years previously and she was thought to be clear of disease. She had undergone a lobectomy of the left lung in childhood for recurrent lung infections.

On examinaton, otoscopy was normal and the pure tone audiogram showed a 50–70 dB sensorineural loss, with the right side 5–10 dB worse than the left. A test of loudness recruitment (the short increment sensitivity index) suggested that the deafness was retro-cochlear. The neuro-otological examination was otherwise normal and there was no neurological deficit.

Following admission to the ward for further detailed investigation, an ophthalmological opinion was sought and bilateral anterior uveitis was diagnosed. Review by the neurologists at this stage was unremarkable, and a magnetic resonance imaging (MRI) scan of the brain was normal. A lumbar puncture was performed which showed a mild lymphocytosis. C-reactive protein concentration was slightly elevated, suggestive of a mild inflammation, and an autoantibody screen, erythrocyte sedimentation rate (ESR), syphilis serology and serum calcium were normal.

The patient was commenced on systemic steroids, initially dexamethasone 4 mg three times a day. Her constitutional symptoms improved after two days and she was discharged home on oral prednisolone 40 mg daily, gradually tapering down to 10 mg, for three weeks. She was kept under review and her deafness gradually improved and her imbalance settled.

However, three weeks after withdrawal of the steroids, she developed recurrent, severe ocular symptoms and was found to have bilateral anterior and posterior uveitis, pars planitis and multifocal choroiditis, with a swollen, haemorrhagic right disc and thickening in the left macular region. A chest X-ray showed diffuse fine nodular shadowing. A conjunctival biopsy showed inflammatory changes without granulomatous foci, excluding sarcoidosis, an opinion reinforced by a normal angiotensin-converting enzyme concentration and a normal transbronchial biopsy, although serum calcium concentration was raised.

The symptoms again subsided on the steroid regime that had been used previously. In view of the good response to steroids and the association of sudden onset sensorineural

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hearing loss with uveitis, retinopathy and neurological symptoms, a presumptive diagnosis of VKH syndrome was made, consistent with the criteria established by the American Uveitis Society.[1]

The patient continued on low dosage topical and systemic steroids. The ocular symptoms subsided, and she subsequently managed well with a hearing aid.

Discussion

A recurrent inflammatory syndrome comprising of bilateral uveitis, sensorineural deafness, and retinopathy was first described in 1906. Subsequently, in 1926, Harada described what he believed to be a distinct entity comprising bilateral retinopathy, uveitis and dysacousis.[2] In 1929, a variant of this initial description was added by Koyanagi, who also described vitiligo and alopecia in association with the same condition.[2]

This condition is thought to be the result of an inflammatory process affecting cells of neural crest origin.[3] The principal feature is prolonged bilateral uveitis, which often progresses to blindness. Shucknecht suggested that the disease occurs in three stages, starting with a meningeal or prodromal phase and progressing to an ophthalmic or uveitic phase and then to a convalescent phase.[2]

The first, or meningeal, phase is present in approximately 50 per cent of cases, may last for up to four weeks and is characterized by headache, fever and meningism in varying degrees of intensity. This usually progresses to the ophthalmic stage, with bilateral uveitis and other ocular signs, including choroidal thickening, hyperaemia of the discs and cyclitis as well as bilateral retinal detachment, inflammatory signs in the aqueous and vitreous humour, and ocular or systemic signs of depigmentation.[4] Involvement of the ears has been shown to be present in almost 30 per cent of patients early in the course of the disease, and any hearing loss is usually associated with the ocular signs and is most normally retro-cochlear.[5] The hearing loss may be sudden in onset and is frequently associated with tinnitus and vertigo. This is followed by the convalescent phase, which is characterized by patchy alopecia and poliosis (absence and/or loss of pigmentation of hair) and perilimbal vitiligo, which is followed one to two months later by depigmentation in the fundus ('sunset glow fundus'). The vision often returns to normal in a matter of months, but glaucoma and cataract are potential complications.

The disease is more prevalent amongst pigmented races and is thought to be rare in Caucasians. A Japanese study proposed an autoimmune aetiology involving melanocytes.[6] VKH syndrome has been linked to the incidence of cranial nerve palsies.[7] 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. In addition, recent studies have also suggested an autoimmune reaction in melanocytes in this condition, as anti-retinal antibodies have been detected and there have been reports of co-existent autoimmune disorders such as Hashimoto's thyroiditis.[8,9] In addition, lymphocytes from peripheral blood and from the CSF of such patients have been shown to exhibit cytotoxic activity to B-36 melanoma cell lines[8] and there is a strong association with certain human lymphocyte antigen types and the development of Vogt–Koyanagi–Harada syndrome.[5,10]

There are few autoimmune disorders which involve both the eyes and ears. Perhaps the most common is Cogan's syndrome, which links interstitial keratitis with vestibular and auditory dysfunction.[2] In this condition, however, the sensorineural loss is progressive and is associated with tinnitus and vertigo and, typically, the cornea is affected and the uveal tract is spared. In addition, the deafness is normally cochlear in type.

The clinical manifestations are varied and the American Uveitis Society has therefore adopted relatively broad-based diagnostic criteria.[1] These include a lack of history of ocular surgery or trauma (to exclude patients with sympathetic ophthalmia) and at least three of four other criteria. These four criteria are: bilateral chronic iridocyclitis or posterior uveitis (including retinal detachments and disc hyperaemia or oedema); neurological signs (including tinnitus, cranial nerve or central nervous system dysfunction, and CSF pleocytosis (presence of abnormal type and number of cells)); and cutaneous changes (alopecia, vitiligo or poliosis). In addition, these features may be complete, incomplete or probable.[11]

We consider that our patient developed all three stages of the disease. Her initial symptoms of fever, prostration, headache and myalgia could have represented the early meningeal phase, although signs of meningeal irritation were certainly not elicited. The second stage, which seemed more obvious in our patient, was characterized by severe uveitis and sensorineural deafness. The latter appeared to be of retro-cochlear origin on a short increment sensitivity index (SISI) test. Certainly, we could not demonstrate any alternative explanation for the hearing loss. In particular, an MRI scan was normal, sarcoid was excluded on biopsy, and syphilis and non-specific vasculitis or systemic lupus erythematosis were excluded by serological testing. A viral aetiology was also excluded in our patient, and we do not feel that she could have had Cogan's syndrome as she had uveitis with a normal cornea and also a normal ESR (ESR is usually raised markedly in Cogan's syndrome patients). In addition, we think it likely that our patient probably had retro-cochlear pathology rather than a hearing loss of cochlear origin.

Other pathologies were considered. However, we feel that multiple sclerosis was excluded in the absence of any neurological deficit and a normal scan and, while the granulomatous element might raise the suspicion of herpetic or fungal infection, viral serology was normal and the absence of neurological deficit, haemorrhagic CSF and necrotizing retinitis precluded the possibility of herpetic infection. Similarly, the absence of features of a space-occupying lesion in the brain precluded the diagnosis of a fungal infection.

In conclusion, on the basis of systematic exclusion and the signs and symptoms exhibited by our patient, we feel that our patient suffered a variant of Vogt–Koyanagi–Harada syndrome. It is certainly true that she did not have any typical cutaneous features; however, as has been demonstrated in a retrospective series of 20 cases, integumentary signs may be present in less than half of patients with the syndrome.[12] The findings of a hearing loss in association with bilateral posterior uveitis, CSF pleocytosis and iridocyclitis are in keeping with the VKH syndrome diagnosis. Although she was Caucasian (which is certainly atypical), in all other respects our patient appeared to satisfy the criteria for diagnosis of Vogt–Koyanagi–Harada syndrome. After full investigation, and in the absence of any alternative diagnosis, we therefore feel that our patient's case represents an incomplete variant of this rare and interesting condition.

Conclusion

We present an interesting case of Vogt–Koyanagi–Harada syndrome, a rare condition of probable autoimmune aetiology involving melanocytes and possibly other cells derived from the neural crest. Autoimmune disorders presenting as

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sudden sensorineural deafness are uncommon, and a high index of suspicion is required to correlate the other characteristics of this condition into a unified diagnosis. The possible implication of melanocytes in the aetiology of the disorder is in keeping with its predilection for the pigmented races; in this respect, our Caucasian patient was atypical.

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- **Vogt–Koyanagi–Harada syndrome is a rare disorder of probable autoimmune aetiology affecting cells of neural crest origin**
- **In general, it comprises an association of deafness and uveitis with vitiligo and alopecia, together with other neural involvement**
- **The pathogenesis is unknown, and it is a diagnosis of exclusion. An association with HLA DR4 has been demonstrated**
- **In this patient, clinical diagnosis was based on the 1978 diagnostic criteria of the American Uveitis Society**
- **This disorder typically occurs in the pigmented races; the patient reported was, atypically, a Caucasian female**
- **The case suggests that this patient had all three stages of this syndrome**

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