Case report

Vogt-Koyanagi-Harada Syndrome: A case report and review of literature.

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Abstract Vogt-Koyanagi-Harada (VKH) syndrome is a rare multisystem disorder in which cell-mediated autoimmunity against melanocytes affects the eyes, inner ears, central nervous system and skin. Alopecia, poliosis and vitiligo are the cutaneous manifestations. Visual and hearing loss is the important complications which can be prevented by early diagnosis and aggressive systemic therapy. We report a case of VKH syndrome in which alopecia was the only cutaneous manifestation and early diagnosis and prompt systemic corticosteroid therapy prevented the visual loss and reduced the morbidity.

Key word
Vogt-Koyanagi-Harada syndrome

Introduction

Vogt-Koyanagi-Harada (VKH) syndrome is a rare systemic disease characterized by bilateral uveitis associated with poliosis, vitiligo, alopecia, and central nervous system and auditory signs. The syndrome was first described by Ali-ibn-Isa (940-1010 AD), an Ophthalmologist, and reported independently by Vogt, Harada, and Koyanagi in 1906, 1926 and 1929 respectively. In 1932, Babel classified the disease as Vogt-Koyanagi-Harada syndrome.[1]

VKH is currently considered to be a cell-mediated autoimmune disease with genetic predisposition. The autoimmunity appears to be directed against melanocytes. It occurs more commonly in darkly pigmented individuals including Asians, Native Americans, and Latin Americans. Clinical manifestations are variable and race-dependent. Typical cases are uncommon. Because of the wide spectrum of the disease, the American Uveitis Society adopted a diagnostic criteria (table I) in 1978 for the diagnosis of VKH syndrome.[2] Visual loss is the major complication, which is due to cataract, glaucoma and choroidal neovascularization. The key to successful therapy of VKH syndrome is early and aggressive treatment with systemic corticosteroids.

We describe a patient of VKH syndrome in which alopecia is the only cutaneous manifestation in addition to the ophthalmic and auditory involvement. This is the first case report in Pakistan in which early diagnosis and prompt systemic therapy improved the prognosis.

Case history

A 20-year-old young man presented in the dermatology OPD with a 3-month history of gradually increasing alopecia of scalp, which started with the feeling of pain in the hair roots. Since then he also had

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bilateral progressive hearing loss and tinnitus. For the last 5 months, he had 4 - 5 episodes of increasing severity of pain, photophobia and redness in both eyes with progressive decrease in the visual acuity. He was not evaluated for alopecia and the ear complaints before, but he did receive topical treatment from various ophthalmologists with waxing and waning of the eye symptoms. Two years ago, he had recurrent episodes of headache, which were usually relieved by analgesics. These lasted for one year. Attacks of headache were not accompanied by nausea, vomiting or neck stiffness and were never investigated. There was no history of any motor or sensory loss, seizures, unconsciousness or any impairment in the memory. The patient also denied of photosensitivity, or any other skin eruption, joint pains, fever, intraocular surgery or penetrating trauma to the eyes. History of any other systemic symptom could not be elicited.

On examination he had patchy diffuse alopecia of scalp without any signs of active inflammation, scaling or scarring. There were neither poliosis, vitiligo, halo naevi, nor any other cutaneous eruption. Ophthalmological examination revealed bilateral anterior and posterior uveitis, without any retinal detachment. The visual acuity of right eye was to projected light only and of the left eye was 4/60. Optic discs were edematous. There was bilateral complicated cataract (right > left) and the intraocular pressure was 17.3 mm Hg in both eyes (by Schiotz's tonometry). ENT examination and audiometry showed moderate sensineural deafness. Higher mental functions were normal and there was no neurological deficit. Examination of other systems was unremarkable. There was no abnormality in routine blood and urine examination. Blood sugar, blood urea, serum creatinine, Liver function tests and serum complements (3 & 4) were within normal range. ANA, Anti-DNA and VDRL test were negative. Scraping for fungus from the scalp was also negative. X-ray chest and CT scan of brain were normal.

Table 1 Diagnostic criteria of VHK syndrome

In the absence of prior trauma or surgery, at least three of the following four criteria must be present:

1. Bilateral chronic iridocyclitis.
2. Posterior uveitis, including multifocal exudative retinal detachments, retinal pigment epithelial changes, and disc hyperemia or edema.
3. Neurological signs of tinnitus, neck stiffness, cranial nerve or central nervous system dysfunction, or cerebrospinal fluid pleocytosis.
4. Cutaneous findings of alopecia, poliosis, or vitiligo.

The diagnosis of Vogt-Koyanagi-Harada syndrome was made based on the criteria of American Uveitis Society for the diagnosis of VKH syndrome (**Table 1**) and by exclusion of other possible etiologies on the basis of clinical and laboratory findings. The patient was managed in collaboration with the ophthalmology department. Oral steroids (prednisolone 60 mg/day) were started. Within a week his visual acuity started improving and after 4 weeks it became 6/60 in the right and 6/12 in the left eye. The intraocular pressure decreased from 17.3 to 8.5 mm Hg bilaterally and the ocular inflammation had settled. Up till that time the alopecia also moderately improved and the deafness became less

subjectively as well as on audiometry. On further improvement, after another four weeks, he was discharged on the same dose of oral steroids to be tapered very slowly according to the clinical status. The ophthalmology department has also planned cataract surgery with IOL after complete resolution.

Discussion

Vogt-Koyanagi-Harada (VKH) syndrome is a rare systemic disease involving various organs containing melanocytes. Granulomatous panuveitis with exudative retinal detachments in association with cutaneous, neurologic, and auditory abnormalities characterize this syndrome. VKH is more common in darkly pigmented races, including Asians particularly Japanese, Latin Americans, Native Americans, and African Americans. It is rarely seen in Northern European individuals. The incidence of VKH in USA is 1-4% and in Japan 7-8% of all uveitis cases.[3] Females are slightly more affected than males. The age of onset is usually between the second and fifth decades, with a mean age of 30 to 40 years, however, children as young as 4 years have been reported with VKH syndrome.[4]

The strong association between VKH and certain racial and ethnic groups and the statistically significant frequency of HLA-DR4 (an antigen commonly associated with other autoimmune diseases) suggests the immunogenetic predisposition in the development of this disease.[5] Granulomatous inflammation and loss of melanocytes has been described in a number of tissues, including the skin, inner ear, meninges, and uveal tract.[1,6] The histopathologic changes, clinical and experimental data suggest an infectious or autoimmune basis for the disease. Though a viral aetiology has been suggested[7] but majority of the evidences are in favour of autoimmune process.[8,9,10,11] In view of these findings, the pathogenesis of VKH syndrome is considered to be a cell-mediated autoimmune process against the melanocytes, with strong genetic predisposition. Despite its diverse manifestations, the clinical course of VKH syndrome has been categorized into four phases; prodromal, uveitic, chronic and recurrent (**Table 2**).[1] Except for the sensitivity to touch of the hair and skin in the prodromal phase, the major dermatological manifestations, i.e., alopecia, poliosis and vitiligo, develop in the third phase. In general the cutaneous signs occur several weeks to months after the onset of ocular inflammation, but in some patients skin changes were observed many years before uveitis appeared. According to a Japanese study,[12] alopecia may be patchy or diffuse and affects 50% of the patients. Poliosis usually appears after the onset of alopecia. It occurs in 90% of the patients and involves the eyebrows and eyelashes, and occasionally the scalp and body hair extensively. Vitiligo presents in 63% of the patients and is often symmetrical. It usually occurs over the head, face and trunk. The sacral region is the common site on the trunk. Atypical variants of vitiligo with inflammatory raised borders and plaque-type inflammatory erythema also have been reported. Halo naevi and perilimbal vitiligo in the eye (The Sugiura's Sign) may also occur.[13]

The differential diagnosis of VKH syndrome includes diseases of eye, CNS and skin, and systemic inflammatory or

Table 2 Phases of VHK syndrome

1. Prodromal phase

- Lasts for few days
- Headache, fever, meningismus, confusion
- Photophobia, orbital pain
- Auditory symptoms (at any stage): nausea, vertigo, tinnitis, dysacusis
- Skin and hair sensitive to touch
- Lymphocytic pleocytosis in CSF
- Uncommon: cranial nerve palsies and optic neuritis.
- These prodromal symptoms may not develop or pass unnoticed by some patients.

2. Uveitic phase:

- Lasts for several weeks
- Pain & redness in eyes, blurring of vision
- Photodysphoria, decreased visual acuity
- Posterior uveitis with retinal edema
- Optic disc hyperemia or edema
- Exudative retinal detachments
- Anterior uveitis often accompanies
- Intraocular pressure may be elevated

3. Chronic Phase

- Lasts for several months to years
- Dermatologic changes: alopecia, poliosis, vitiligo, halo naevi
- Uveal depigmentation

4. Recurrent Phase

- Chronic panuveitis
- Recurrent granulomatous anterior uveitis
- Rarely, recurrent posterior uveitis with retinal detachment
- Complications of VKH: cataract, glaucoma, choroidal neovascularization, subretinal fibrosis

Table 3 Differential diagnosis of VKH syndrome

Inflammatory diseases

- Systemic lupus erythematosus
- Sarcoidosis
- Ocular Lyme borreliosis
- Multiple sclerosis
- Behcet's disease
- Inflammatory bowel disease

Infectious diseases

- Syphilis
- Tuberculosis
- Herpes Simplex encephalitis
- Whipple disease
- Cryptococcal meningitis
- HIV meningitis
- CMV infection
- Toxoplasmosis

Eye/CNS diseases

- Sympathetic ophthalmia
- Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)
- Multifocal secondary retinal and pigment epithelial detachment in:
  Grade IV systemic hypertension and pregnancy-induced hypertension

Dermatological diseases

- Vitiligo
- Piebaldism
- Alezzandrini syndrome
- Alopecia areata
- Tinea capitis

infectious diseases (**Table 3**). The diagnosis is made clinically based upon a constellation of clinical signs and symptoms with no confirmatory tests. However, several diagnostic tests and procedures may be useful to substantiate the diagnosis. Depending upon the clinical features and stage of the disease at the time of presentation, fluorescein angiography, ultrasonography, CSF examination, MRI, electrophysiological studies and specific tests for inflammatory or infectious diseases may be helpful. Due to its varied clinical manifestations and absence of any confirmatory laboratory test, a diagnostic criteria (**Table 1**) was adopted by the American Uveitis Society for the diagnosis of VKH syndrome.[2]

The goal of therapy in VKH syndrome is to reduce morbidity and to prevent complications. Topical therapy only is not associated with complete recovery without complications. The key to

successful therapy is early and aggressive use of systemic corticosteroids. Treatment with corticosteroids may shorten the duration of the disease, prevent complications, and decrease the occurrence of extraocular signs.[3] The usual treatment includes systemic steroids with average initial dose of 1-2 mg/kg of oral prednisone per day. For most severe cases, some authors recommend pulse therapy with methyl prednisolone (up to 1 g/day) for several days before beginning oral prednisone. If patients are resistant to steroids, addition of intravenous immunoglobulins (IV IgG) may be helpful.[14] The length of treatment and subsequent tapering must be individualized for each patient. Most patients require therapy for 6 months and occasionally up to 1 year before successful tapering of systemic corticosteroids. In general, systemic therapy should not be discontinued during the 3 months following the onset of the disease because of the risk of recurrence. Alternatively, immunosuppressive therapy, such as cyclosporin, tacrolimus, azathioprine, cyclophosphamide or methotrexate, may be required in patients who fail to respond to high-dose systemic corticosteroids or develop significant adverse effects.[15] Topical therapy for eyes includes corticosteroids and cycloplegic-mydriatic eye drops. For pigmentary changes, treatment options are the same as for vitiligo.[13]

Most signs and symptoms resolve with corticosteroid therapy. Final visual outcome depends on rapid and appropriate treatment. Hearing is restored completely in most of the patients. Pigmentary changes are usually permanent. Long term complications include reversible and irreversible vision loss, glaucoma and cataract. Ocular complications are more severe in children than in adults, leading to rapid deterioration in vision.[16]

Our patient did not report any prodromal symptom of 1st phase, which is possible as these symptoms may not develop or pass unnoticed by the patient.[3] The clinical features and time frame of episodic headache (two years before) did not fit in the prodromal phase. In the 2nd phase he received topical treatment for recurrent uveitis from various sources. It was the start of 3rd phase when he presented in the dermatology OPD with alopecia of scalp. Development of alopecia after the uveitis is in accordance with the usual course of the disease. All the cutaneous manifestations are not present in every case. The poliosis usually appears after the alopecia and the frequencies of alopecia, poliosis and vitiligo are reported as 50%, 90% and 63%, respectively.[12] These findings can explain the absence of poliosis and vitiligo, and alopecia as the sole cutaneous sign in the reported case. Consistent clinical features, exclusion of other possible causes by clinical/laboratory findings, and the fulfillment of diagnostic criteria by American Uveitis Society were the basis for the diagnosis of VKH

syndrome in our patient. Treatment with systemic corticosteroids not only prevented the visual loss but also resulted in the marked improvement of all the ophthalmic parameters as well as deafness and alopecia. A local case of VKH syndrome was also reported previously in which visual and auditory loss could not be prevented due to late diagnosis and treatment.[17] To our knowledge, this is the first case report in Pakistan in which alopecia is the sole cutaneous manifestation and early diagnosis and prompt systemic corticosteroid therapy reduced the morbidity.

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