Case Report

Vogt-Koyanagi-Harada Syndrome With Severe Neurologic Impairment

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Abstract

Vogt-Koyanagi-Harada (VKH) syndrome is a rare systemic disease involving various melanocyt-containing organs with subacute chronic course. Bilateral uveitis associated with cutaneous, neurological and auditory abnormalities characterizes this syndrome. The degree of neurological symptoms may vary but they are usually mild. Here we report an unusual case with severe visual and neurological impairment such as bilateral amaurosis, recurrent status epilepticus episodes and progressive mental changes.

Keywords: Bilateral panuveitis, Status epilepticus, Vogt-Koyanagi-Harada syndrome

INTRODUCTION

Vogt-Koyanagi-Harada (VKH) syndrome is a rare systemic disease involving various melanocyt-containing organs with subacute chronic course. Bilateral uveitis associated with cutaneous, neurological and auditory abnormalities characterizes this syndrome. As first described by Vogt in 1906 and Koyanagi in 1929, predominantly anterior uveitis associated with poliosis, vitiligo, and auditory disturbances characterizes Vogt-Koyanagi syndrome. In 1926, Harada reported a patient with idiopathic uveitis affecting the posterior segment with retinal detachment and meningeal irritation. At present these two disorders are considered as variations of a single entity referred to Vogt-Koyanagi-Harada syndrome or uveomeningoencephalitis.

The degree of neurological symptoms may vary but they are usually mild. Generalized muscle weakness, headache, meningismus, vertigo, decreased visual acuity, hearing loss and mental changes ranging from mild confusion to psychosis, hemiparesis, dysarthria, aphasia and rarely seizures can be seen. Here we report an unusual case with severe visual and neurologic impairment and recurrent status epilepticus periods.
CASE PRESENTATION
33 years old male, had experienced an episode of bilateral panuveitis 10 years ago. Although he had been given the oral systemic corticosteroid therapy at that time, visual complications had progressed and eventually cataract and later amaurosis had occurred in both eyes within six years. During the following four years, mild skin changes, seizures (defined as partial and secondary generalized seizures), behavioral disturbances, hearing loss, recurrent status epilepticus episodes, progressive neurological disturbances and mental changes had developed. His first seizure occurred seven years after the onset of the ocular findings. He had status epilepticus episodes for three times which first episode occurred two years ago probably due to ineffective usage of antiepileptic drugs. All these status epilepticus episodes were in secondary generalized tonic-clonic pattern. He was admitted to hospital again because of a long lasting delusional state occurring after an episode of status epilepticus.

He had hypopigmented skin lesions defined as vitiligo (Figure-1) and frontal alopecia (Figure-2). The neurologic examination revealed bilateral pyramidal signs, quadripareisis, myoklonic jerks, athetoic movements, bilateral amaurosis, severe mental disturbance and delusional state. In physical examination cerebrospinal fluid (CSF) analysis showed mild lymphocytic pleocytosis and elevated protein levels but no melanin-laden macrophages (MLMs). In the brain MRI there was generalized brain atrophy, communicating hydrocephalus and bilateral multiple focal T2 hyperintense lesions in periventricular white matter. (Figure 3,4,5) There were generalized epileptiform discharges dominantly seen in bilateral temporal regions on EEG. Bilateral hearing loss was ascertained with brainstem evoked response audiometry (BERA). Ophthalmologic examination and ocular USG was compatible with sequel changes of bilateral panuveitis, retinal detachment and secondary cataract. Skin biopsy was compatible with vitiligo and the patherji test performed to exclude Behçet's disease was negative. There was also no history of oral and genital ulcers. Serologic markers for brucella in serum and CSF were negative. Immunologic markers including ANA, ANCA, Anti-ds DNA, RF, Anti-Ro, Anti-La were negative. In order to exclude the possibility of the sarcoidosis, thorax CT scan performed and the level of ACE in the CSF was controlled. They were also in normal limits.

Figure 1-2: Hypopigmented skin lesions defined as vitiligo and frontal alopecia
DISCUSSION
The etiologic and pathogenic factors in VKH syndrome are still unclear. The clinical course of VKH syndrome with an influenza like episode suggests a viral or post infectious origin. Some studies invoke a possible role of Epstein-Barr virus reactivation in this disease\(^{(9,10)}\). Although a viral cause has been proposed, no virus has been isolated or cultured from patients with VKH syndrome. Morris and Schlaegel found virus like inclusions bodies in the subretinal fluid of a patient with VKH syndrome\(^{(6)}\).

Clinical and experimental data continue to support an immunologic etiology. An autoimmune reaction seems to be directed against an antigenic component shared by uveal, dermal and meningeal melanocytes, possibly tyrosinase or a tyrosinase-related protein\(^{(7)}\). The possibility of autoimmune pathogenesis in VKH syndrome is also supported by the statistically significant frequency of HLA-DR4, an antigen which commonly associated with other autoimmune diseases.

It is suspected, but not definitely established, that this is a viral disease. It has been suggested that the disease results from an autoimmune response to uveal pigment. Hague\(^{(1)}\) considered the possibility of virus infection on the basis of involvement of the hypothalamus.

VKH syndrome occurs more frequently in individuals with darker pigmentation. It occurs most frequently in the Far East countries and South America and frequently in dark-skinned people. Women appear to be affected more frequently than men. The onset of VKH syndrome has been reported to range from 10-52 years, with a maximum frequency in the thirties, although often unrecognized VKH syndrome may affect children\(^{(5)}\).

VKH syndrome is not associated with mortality. Acute disturbances in hearing and vision may occur, and the cutaneous changes may be permanent.

The disease can be divided into three phases with a subacute chronic course: Acute ophthalmic, meningoencephalitic, and convalescent phase. The ophthalmic-auditory phase is characterized by common features such as decreased visual acuity, eye pain, eye irritation and loss of vision\(^{(7,10)}\). Dysacusis and tinnitus develop in 50% of patients. In the meningoencephalitis phase, the degree of neurological symptoms may vary\(^{(4)}\). Most of the neurological symptoms have been

Figure 3-4-5: Brain MRI; There was generalized brain atrophy, communicating hydrocephalus and bilateral multiple focal T2 hyperintens lesions in periventricular white matter.
directly attributed to inflammatory arachnoiditis or resulting subarachnoidal adhesions. The convalescent phase is characterized by cutaneous signs developing after uveitis begins to subside, usually within 3 months from the onset of the disease. Poliosis, which occurs in 90% of the patients, involves the eyebrows and eyelashes and, occasionally, the scalp and body hair. Vitiligo manifests in 63% of patients and is often symmetric. Halo nevi may be present. Pigmentary changes tend to be permanent. VKH syndrome may initially present as aseptic meningitis, without specific ophthalmological symptoms. In suspected cases a very detailed CSF cell analysis is needed, because the presence of MLMs can confirm the diagnosis(1). Cranial MRI may show multiple focal lesions and T2 hyperintense periventricular lesions(2,3).

Although there is no specific therapy at present, corticosteroids given during the early stages are effective. But it must be kept in mind that this stage may persist for months with or without exacerbations so the treatment may be required for longer periods. Surgical therapy for glaucoma is necessary in some patients. The goals of pharmacotherapy are to reduce morbidity and to prevent complications. The most important long-term complications include reversible and irreversible vision loss. Final visual outcome depends on the rapidity and congruity of the treatment(8).

The diagnosis of VKH which can be defined as chronic, bilateral granulomatous ocular and multisystem inflammatory condition, of unknown cause, is usually made on the basis of clinical findings and by excluding the other possible uveomeningoencephalitic syndromes(10,11). For this reason clinical criteria recommended by the American Uveitis Society can be used(7). Our case is also met this criteria. The diagnosis of VKH syndrome was made depending on the history, clinical signs and laboratory findings and by excluding the other degenerative, vasculitic, connective tissue diseases, chronic infectious and granulomatous diseases.

However the most interesting feature of our case was the severity of the neurologic impairment and relapsing status epilepticus attacks. There was also no report of status epilepticus with VKH syndrome in the literature. Therefore in case of bilateral visual loss, skin changes and neurological impairment even as status epilepticus, VKH syndrome should be remembered.

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