Vitiligo as a First Sign of Vogt-Koyanagi-Harada Disease

Dear Editor,

Vogt-Koyanagi-Harada (VKH) disease is a multisystem disorder characterized by bilateral granulomatous panuveitis resulting in serous retinal detachments, disk edema, and a sunset glow fundus development. Furthermore, it is associated with various extraocular findings, such as tinnitus, hearing loss, vertigo, poliosis, and vitiligo (1). VKH is considered to be an autoimmune disease mediated by T-cells targeting melanocyte antigen tyrosinase peptide (2). Moreover, VKH more often occurs in individuals with a genetic predisposition to the disease, including those of Asian and Hispanic heritage (3). Three disease categories have been recognized, including complete, incomplete, and probable VKH. Each category has different clinical features, varying from neurological and auditory manifestations to ophthalmologic and dermatologic findings (1). Herein, we present a case of chronic complete Vogt-Koyanagi-Harada disease, which started with vitiligo.

CASE REPORT

A forty-year-old female patient presented to the Department of Ophthalmology with photophobia, dull eye pain, and a gradual decrease in visual acuity over two months. In addition, at clinical examination, vitiligo spots were observed on the patient's hands and the periocular area.

The patient's medical history revealed she had vitiligo from a young age. Additionally, she developed generalized epilepsy and headaches in adolescence. The neurologic symptoms had been treated, whereas dermatologic workup and treatment were never performed. It was also found that our patient was of Hispanic heritage, which later helped establish a diagnosis.

Ophthalmologic examination revealed eye redness, hypotony, keratic precipitates, anterior chamber cells, and posterior synechiaes. Fundoscopy showed mild vitreous haze, optic disc and macular edema, chorioretinal thickening (also seen on eye ultrasound), and disturbance of retinal pigment epithelium (Figure 1).

A standard diagnostic protocol for uveitis was performed. Serology for infectious causes was performed, and IgG for CMV and HSV 1 were positive. Tuberculosis testing was negative. HLA testing showed positive HLA-DR1, HLA B13/18, and HLA DQ-1 antigens. There were no cells in the intraocular fluid, and PCR of the fluid was negative for CMV and HSV 1 and 2.

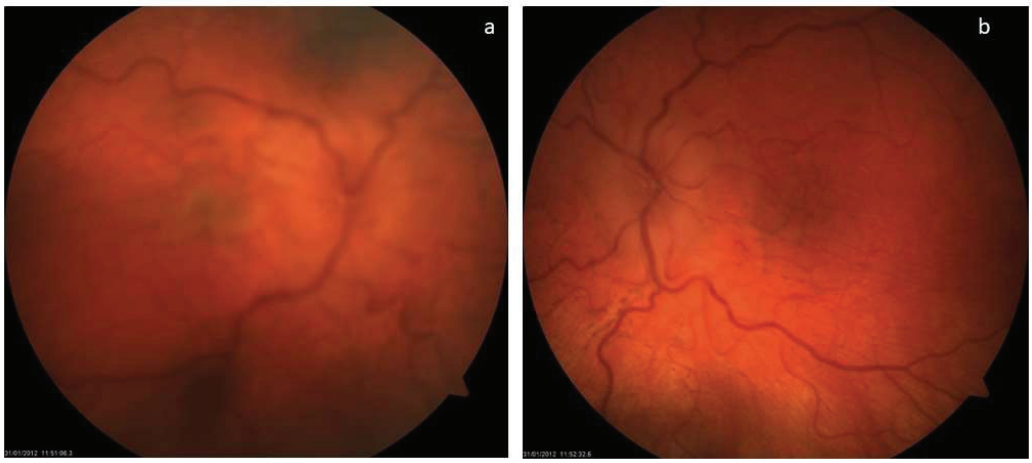

Figure 1. a) Right eye color fundus photography; b) left eye color fundus photography. Changes in retinal pigment epithelium, macular edema, and optic disc edema are visible.

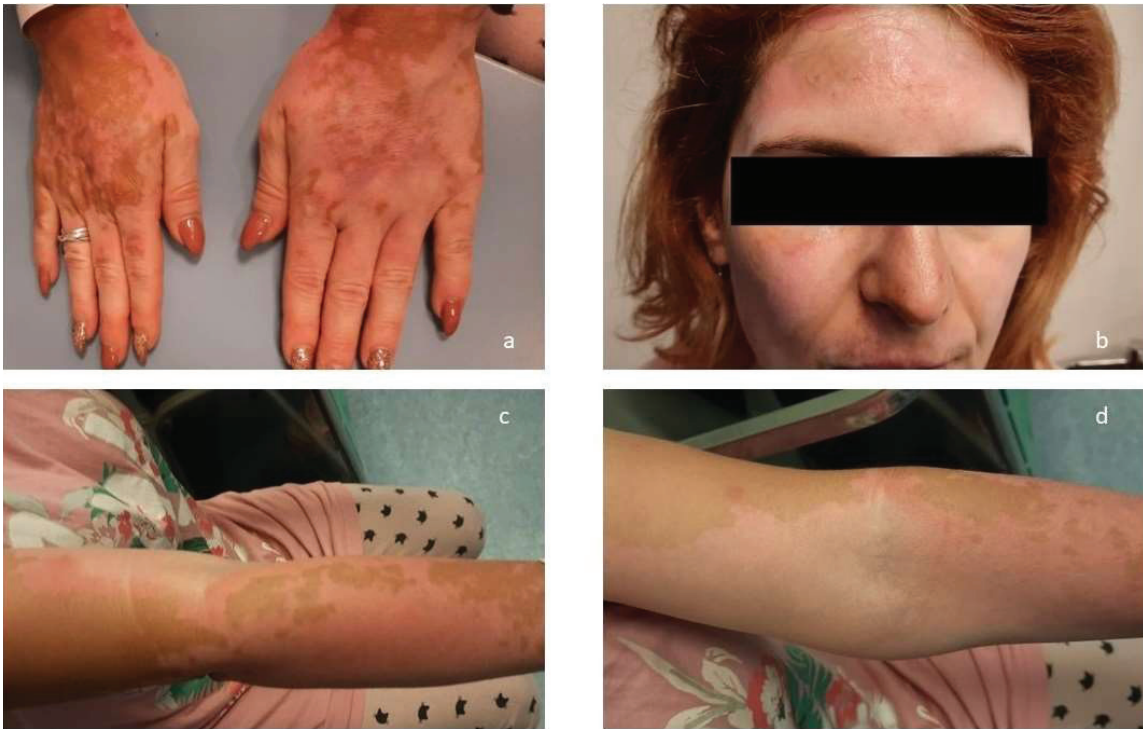

Figure 2. Vitiligo spots on a) the hands, b) the face, c) the right upper arm and forearm, d) the left upper arm and forearm.

Considering the noninfectious uveitis, a history of neurological and dermatological disorders, and the Hispanic heritage of our patient, the diagnosis of Vogt-Koyanagi-Harada disease was established.

Systemic methylprednisone in a 1.5 mg/kg dose was introduced during the first hospitalization. After slow tapering of the corticosteroid therapy, cyclosporine A in a 175 mg/day dose and azathioprine in a 100 mg/day dose were introduced for prolonged therapy.

Although signs of eye inflammation were reduced, poor prognostic signs such as hypotony and optic disc edema were persistent. Therefore, the TNF-α inhibitor adalimumab was introduced. After the introduction of adalimumab, the disease was considered stable with no worsening of visual function, but vitiligo spots continued to progress (Figure 2).

DISCUSSION

Our case presents a chronic stage Vogt-Koyanagi-Harada disease in a person with a Hispanic heritage.

VKH is a rare autoimmune disease that involves multiple organ systems, including the eyes, skin, and auditory and neurological systems. In the pathogenesis of the disease, there is an underlying granulomatous inflammation mediated by T-lymphocytes targeting melanocyte-specific antigens (4).

Besides the immune response, genetics is an integral part of the etiology of the disease. HLA-DR1 and HLA-DR4 have been associated with VKH disease, specifically in the Hispanic and Asian populations (3,5). Other studies have found that VKH is more common in people of Asian and Hispanic heritage than in Caucasian or African-American individuals (6). In our case report, the Hispanic origin of our patient was essential for the diagnosis of the disease.

There are four phases of VKH disease. The prodromal phase lasts a few days to a few weeks and is characterized by extraocular findings such as headache, vertigo, meningismus, and nausea (1). After the prodromal phase, the acute uveitic phase occurs, with sudden onset of blurred vision, conjunctival injection, and photophobia (1,7). Weeks to months after, the convalescent phase occurs, with signs of depigmentation such as vitiligo, poliosis, and vitiligo in the ocular limbal area, called the Sugiura sign. Finally, six to nine months after initial symptoms, the chronic recurrent phase occurs, leading to exacerbations of anterior uveitis (1).

Even though most patients develop skin changes in the convalescent phase, our patients experienced skin depigmentation years before ocular involvement.

VKH can be complete, incomplete, or probable. Our patient is an example of complete VKH, since she fulfilled all criteria for complete VKH, including 1) no history of penetrating ocular trauma or surgery, 2) no clinical or laboratory evidence of other ocular

diseases, 3) bilateral ocular involvement, 4) neurological findings, and 5) integumentary findings (8).

Treatment for VKH consists of high-dose systemic corticosteroids, administered orally or through intravenous delivery, followed by slow tapering of oral corticosteroids. Immunosuppressive therapy with cyclosporine and/or azathioprine is considered if the symptoms are persistent or worsening. In case of no improvement, biological agents such as infliximab and adalimumab are included (4).

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