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Case Report Open Access

Vogt-Koyanagi-Harada Syndrome: Case Report

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Abstract

Vogt-Koyanagi-Harada syndrome (VKHS) is a multi-organ disorder with well-established diagnostic criteria, which is little known by the dermatologist.

We emphasize the importance of early recognition and treatment of VKHS, avoiding especially the ophthalmologic sequels.

Since vitiligo is closely related to the syndrome and other autoimmune disorders, we question the need for a better evaluation of patients with vitiligo by dermatologists.

Keywords: Vogt-Koyanagi-Harada Syndrome (VKHS); Bilateral Granulomatous Panuveitis Vitiligo (BPUG); Poliosis; Pigmentation

Introduction

Vogt-Koyanagi-Harada syndrome (VKHS) is a well-established multiorgan disorder that affects structures where there are melanocytes, as the eyes, internal ears, meninges and skin. VKHS is an autoimmune inflammatory condition, in which cytotoxic T-cells attack the melanocytes of genetically susceptible individuals [1]. Vitiligo is a disease that integrates the syndrome, when cutaneous melanocyte compromising exists, and has been considered a multifactor condition associated to polygenic alterations with a still not entirely clarified pathogenesis [2].

Case Report

A 54 year-old single black woman, living in Rio de Janeiro, Brazil, was seen at the Sector of Dermatology with achromic lesions on the face, which had appeared a few months earlier.

The examination revealed achromic macula grouped in the left mandibular region (Figures 1 and 2).

The patient is being followed up by the Sector of Ophthalmology of our Hospital for 14 years due to Bilateral Panuveitis Granulomatosa (BPUG). Before this, she referred presenting hyperemia and ocular pain, treated with eyewash in a public health unit. Six months after the first symptoms, new similar episodes occurred in a total of eight crises.

During the initial assessment by the Ophthalmologist, she complained about persistent tinnitus and headache, considered as unspecific by the Otorhinolaryngologist and Neurologist.

After the diagnosis of BPUG in the tertiary unit, oral prednisone was given in a daily dose of 1 mg/kg with frequent attempts of interruption without success.

Discussion

Although there are descriptions that could have been VKHS since the 12th century, the first cases were published by Alfred Vogt, a Swiss Ophtalmologist, and Jujiro Komoto, a Japanese Ophthalmologist, in the beginning of the 20th century. The disease, however, only became known after the publications of Yoshizo Koyanagi, also a Japanese Ophthalmologist, in 1914 and 1929, and of Einosuke Harada, a Japanese Surgeon, in 1926, based on series of cases [1,3].

VKHS is a rare disorder, but it is probably underdiagnosed. The disease is more common in certain ethnic groups, such as the populations of East and Southeast Asia, Middle East, India and Hispanics [4]. It was demonstrated that HLA-DRB1*0405 is the prevailing susceptibility allele in the Brazilian population [1].

Studies in animals have demonstrated that the proteins of the tyrosinase family, TRP1 and TRP2, found in the melanocytes, are of great relevance in the VKHS pathogenesis, for favoring their recognition by T-lymphocytes. Other proteins found in melanocytes may also function as auto-antigens, such as MART 1, PMel-17/gp100, Ku-Mel-1, PAX3 and the uveal auto-antigen (UACA). The lymphocytes of patients with VKHS demonstrated to be more resistant to apoptosis mediated by the anti-Fas antibody [1,5,6].

Four clinical stages of VKHS were described: prodromal phase, uveitic phase, chronic phase and recurrence [4,7].

1. The prodromal or meningeal phase has been identified in 50% of the cases, with average duration from days to weeks. The clinical presentation can be varied, ranging from symptoms similar to a viral infection, such as slight fever, asthenia, cephalea, muscular weakness; up to neurological symptoms as cerebellar ataxia, psychosis,

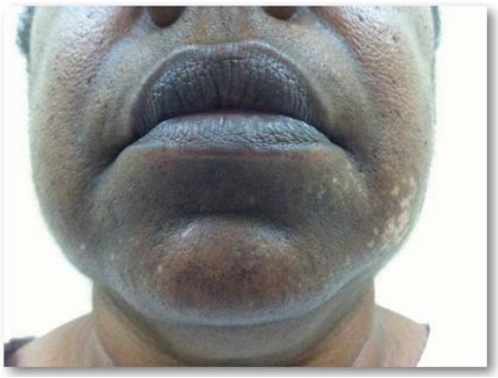

Figure 1: Small achromic lesions on the lower face.

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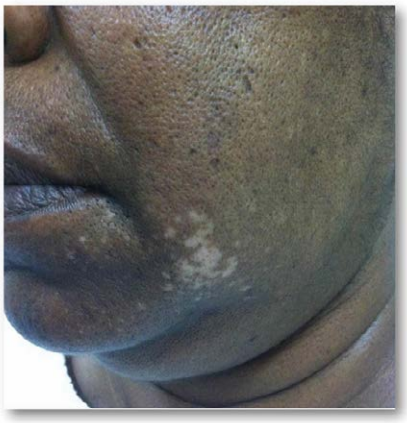

Figure 2: Side view of the achromic lesions, showing coalescence of the small lesion forming a patch.

meningism, among others. Analysis of the liquor demonstrated lymphocytic pleocytosis in over 80% of cases, increase of proteins and liquoric pressure [4];

2. The uveitic phase begins between the third and fifth day after the meningeal phase and persists for weeks. In 70% of cases there are complaints regarding bilateral visual turbidity. There are also reports of photophobia, conjunctive hyperemia, reduction of visual acuity and amaurosis. Otorhinolaryngologic manifestations may appear in this period. Patients may present neurosensory hearing loss, tinnitus, vertigo and other manifestations [4]:

3. The chronic phase occurs after months or years, when pigment alterations in melanocyte-bearing tissues are observed. The typical ocular alterations are sunset glow fundus, Dahlen-Fuchs depigmented chorioretinal scars, and migration or accumulation of pigment epithelium in the retina [7]. The cutaneous alterations, such as vitiligo, alopecia and poliosis, occur about 2 to 3 months after onset of the syndrome, with poliosis present in about 80 to 90% of the patients. Involvement of the scalp, eyelashes and eyebrows with variable extension can be observed in poliosis. Alopecia can begin suddenly, can be diffuse or in plaques and is rarely total [8]; and

4. The recurrence phase is characterized by sudden surges of ocular inflammation with complications such as glaucoma, retinal detachment or cataract [4].

Diagnosis is based on the diagnostic criteria revised by the International Nomenclature Committee in 2001. Major criteria are: 1. No history of penetrating eye trauma or surgery before the episode of uveitis, 2. No clinical or analytical evidence suggestive of other eye diseases, 3. Bilateral ocular involvement (choroiditis, uveitis, inflammatory vitreous reaction, serous retinal detachment), 4. Neurological and auditory findings (meningism, tinnitus, pleocytosis in cerebrospinal fluid), 5. Dermatologic findings (alopecia, poliosis, vitiligo), 6. Hypoxia, 7. Central nervous system depression, 8. Petechiae; and Minor Criteria: 9. Tachycardia (>120 beats per minute), 10. Fever (temperature >39°C), 11. Unexplained anemia, and 12. Thrombocytopenia (platelet count <150 × 109/L) [9]. In order to be classified as a complete syndrome, all the criteria need to be present [1,10]. Treatment should be early and aggressive, with minimum duration of six months to one year. Corticosteroids are used in immunosuppressive dosages, and, in severe cases, pulse therapy with methylprednisolone is applied [11]. Immunosuppressors as for instance: methotrexate, azathioprine, cyclosporine, cyclophosphamide, mofetil mycophenolate, tacrolimus, chlorambucil and biological medications such as: etanercept and adalimumab may be associated if necessary. The use of immunoglobulin has also been proposed [4]. Liu et al. [12] demonstrated that T CD4+ and CD8+ lymphocytes express IFN-γ and Interleukin 17, confirming involvement of Th1 and Th17 cells in the etiopathogeny of VKHS. These findings are important, for reinforcing the utility of immunosuppressive therapies [12].

The prognosis will depend on the earliness of the diagnosis and beginning of treatment. Some authors state that the otorhinolaryngologic alterations tend to recede, in opposition to cutaneous alterations which would be permanent [13]. Regarding ocular alterations, some factors are necessary for a good prognosis as for instance: good visual acuity after one month of treatment, early use of corticoids in high doses and patient age (the younger the better) [11,14].

Conclusion

It is important to highlight the existence of VKHS to the dermatologist, since vitiligo is a component of the disease, despite usually being a late manifestation [15]. An early diagnosis and systemic therapeutic intervention can change the course of the disease, especially those related to the ocular system.

Many cases diagnosed only as vitiligo may possibly be associated to the syndrome, since VKHS is the most common cause of uveitis in Brazil, which is cause of concern. The possibility of the dermatologist contributing with this diagnosis, in particular in cases of early appearance of the cutaneous manifestations, needs to be emphasized.

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