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Vogt-Koyanagi-Harada Disease: A Disorder Unfamiliar to Dermatologists☆

Enfermedad de Vogt-Koyanagi-Harada. Una entidad poco conocida para el dermatólogo

To the Editor:

Vogt-Koyanagi-Harada disease is a rare condition that is characterized by bilateral uveitis, meningitis, auditory symptoms, and skin disorders such as vitiligo, poliosis, and alopecia.[1] This report aims to draw attention to a condition that is widely discussed in the literature yet unfamiliar to dermatologists.

We present the case of a 37-year-old man from Bolivia who was seen in the emergency department with vertigo, headache, eye pain, and loss of vision in both eyes that had begun a week earlier. Three months later he was referred to the dermatology department with rapid-onset alopecia of the scalp. Physical examination revealed horizontal rotatory nystagmus at rest and on looking upward and to the right. Ophthalmological examination revealed a marked loss of visual acuity in both eyes; anterior pole biomicroscopy revealed Tyndall phenomenon with posterior synechiae (Fig. 1). Nonscarring diffuse alopecia was also observed on the scalp, together with poliosis of the right eyebrow (Fig. 2, A and B). The results of the blood workup—complete blood count, biochemistry, clotting, protein analysis, antibodies to antinuclear antigen and extractable nuclear antigen, serology for syphilis and viruses (hepatitis A, B, and C viruses; human immunodeficiency virus; Epstein-Barr virus; cytomegalovirus), and thyroid hormones—were negative or normal. Cerebral magnetic resonance imaging ruled out meningeal or encephalic disease. Histocompatibility testing was positive for HLA-DR4 and HLA-DR53. These findings enabled a diagnosis of Vogt-Koyanagi-Harada disease to be confirmed. Treatment with intravenous methylprednisolone (1 g) was prescribed for 3 days, with subsequent oral administration tapered over 12 weeks. The patient's clinical condition improved considerably, not only in terms of systemic manifestations, but also with complete resolution of the alopecia. However, the new hair remained whitish-gray in color (Fig. 3).

Vogt-Koyanagi-Harada disease, which was first reported in 1951, is a rare systemic inflammatory disorder mediated by T lymphocytes acting against pigmented cells in the uvea, skin, inner ear, and leptomeninges.[1]

It has an incidence of 6.5 cases per million and is more common in Hispanic and Native American individuals and Asian women aged between 20 and 50 years. Although its etiology is unknown, immunogenetic analysis suggests a strong association with some HLA antigens (DR4, DRB1, and DR53) and genes of the tyrosinase family that cause susceptibility to the disease.[2] It is associated with various infectious diseases and other disorders whose pathogenic mechanisms are of immunological origin, such as autoimmune thyroid disease, psoriasis, linear immunoglobulin A bullous dermatosis, and inflammatory vitiligo as a consequence of the destruction of melanocytes by cytotoxic $CD8^+$ T lymphocytes.[2–4]

Diagnosis is based essentially on clinical manifestations, as there are no specific confirmatory tests, and the diagnostic criteria include dermatologic findings (alopecia, poliosis, and vitiligo) (Table 1). Typical extracutaneous clinical manifestations include disorders of the eyes (bilateral granulomatous uveitis, retinal detachment, and loss of vision) and neurological and auditory conditions (headache, aseptic meningitis, vertigo, nystagmus, and hypoacusis).[5]

Alopecia can be seen in 70% of cases within weeks or months after the onset of ocular symptoms. It resolves completely after a variable period. Alopecia and the poliosis traditionally reported by ophthalmologists were recently considered to be alopecia areata with subsequent growth of white hair.[6] Vitiligo affects almost half of all cases; it is often symmetrical and the pigmentary changes may be permanent.

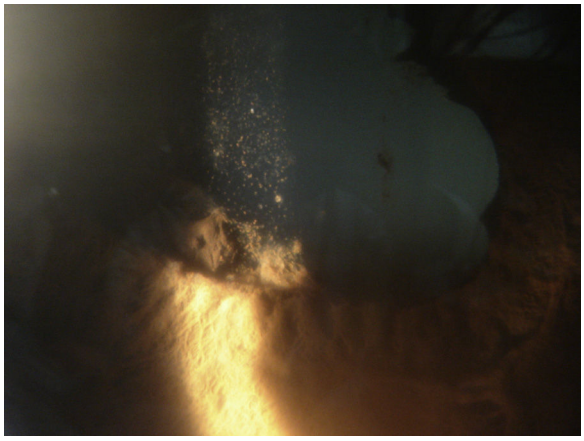

Figure 1 Tyndall phenomenon with the presence of posterior synechiae characteristic of anterior uveitis.

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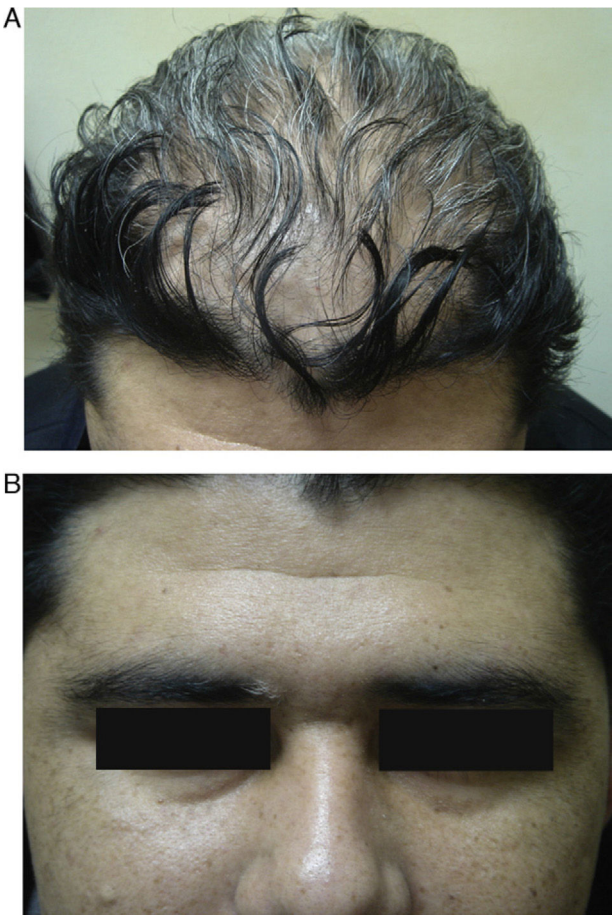

Figure 2 A, Diffuse rapid-onset alopecia on the scalp. B, Poliosis of the left eyebrow.

Early high-dose systemic corticosteroids are the treatment of choice in patients with active Vogt-Koyanagi-Harada disease. In cases of recurrent or corticosteroid-refractory disease, other immunosuppressive agents such as ciclosporin, cyclophosphamide, or azathioprine can be added to the treatment. A favorable response has been reported with adalimumab and rituximab in refractory cases.[7] Prognosis is relatively benign, and although the most common complications are visual, total blindness is now rare. Patients may also experience personality disorders, psychosis, and deafness, as occurred in the Spanish painter Francisco de Goya when creating his famous black paintings.[8]

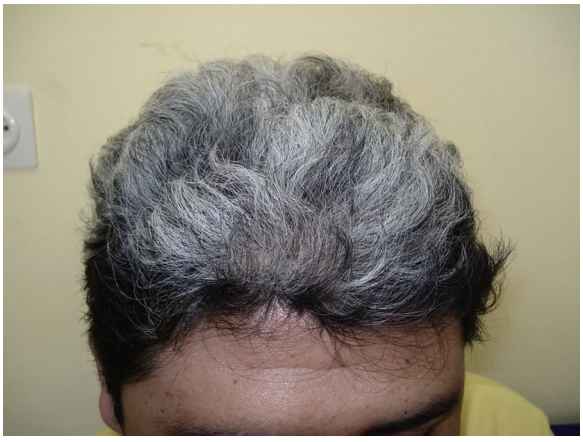

Figure 3 Complete resolution of alopecia after treatment, with growth of whitish-gray hair.

Table 1 Diagnostic Criteria of Vogt-Koyanagi-Harada Disease.

Major Criteria

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

Minor Criteria

9. Tachycardia (> 120 beats per minute)
10. Fever (temperature > 39 °C)
11. Unexplained anemia
12. Thrombocytopenia (platelet count < 150×10^9/L)

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Chondrodermatitis Nodularis Helicis: Successful Treatment with 2% Nitroglycerin Gel☆

Condrodermatitis *nodularis helicis* tratada con éxito con nitroglicerina al 2% en gel

To the Editor:

Chondrodermatitis nodularis helicis (CNH) is a condition that affects the skin and cartilage of the pinna, manifesting as a single painful nodule on the helix, and less commonly the antihelix. The pathogenesis of CNH is unknown, but has been associated with decreased blood flow caused by prolonged pressure upon the auricular cartilage. Treatment is challenging, with recurrence being common following both conservative treatment and surgery.

We report the case of an 83-year-old woman who presented an erythematous nodule with central ulceration on the helix of the left ear; the nodule had appeared 2 years earlier, was extremely painful to touch, and had not responded to treatment with several courses of topical corticosteroids (Fig. 1) The results of a skin biopsy revealed hyperkeratosis, an acanthotic epidermis with signs of dysplasia, and numerous ectatic capillaries in the upper dermis.

In view of these findings, and after malignancy had been ruled out, the patient was diagnosed with CNH and the lesion was treated topically with a 2% nitroglycerin gel once every 12 hours for 3 months. An improvement was observed in the appearance of the lesion (Fig. 2) and the pain almost completely disappeared. Pain was assessed using a visual analog scale, with 10 corresponding to the worst pain imaginable and 0 to no pain; the patient's score decreased from 8 on the first visit to 1 following 3 months of treatment with nitroglycerin gel. Thus, 4 months after starting treatment (3 months of treatment and 1 of control), a significant improvement in the patient's condition was observed, with no adverse effects.

CNH is an inflammatory condition characterized by a solitary, firm, well-defined, pink or reddish nodule several millimeters in diameter on the helix or, less commonly, the antihelix, sometimes with central ulceration and crusting. Typically, the lesion is extremely painful to touch, a feature that can facilitate differential diagnosis with other entities, such as actinic keratosis, squamous cell carcinoma, and basal cellular carcinoma.[1]

Histologically, CNH is characterized by a hyperkeratotic stratum corneum with areas of parakeratosis, acanthosis, and in some cases the presence of an ulcer covered by a crust. In more advanced stages, degeneration of the dermis is accompanied by an increase in the number of blood vessels and the presence of perivascular inflammatory infiltrate.[2] Cartilage degeneration is also observed in biopsies that include cartilage (approximately 70% of all biopsies).[1]

The pathogenesis of the condition is unknown. It is thought that repeated trauma or prolonged pressure, such as that which occurs during sleep at night, may lead to ischemia of the cartilage and the auricular perichondrium, structures that lack the protection of a thick layer of subcutaneous tissue.[3] Once initiated, ischemia causes necrosis of the cartilage and consequent transepithelial elimination of the

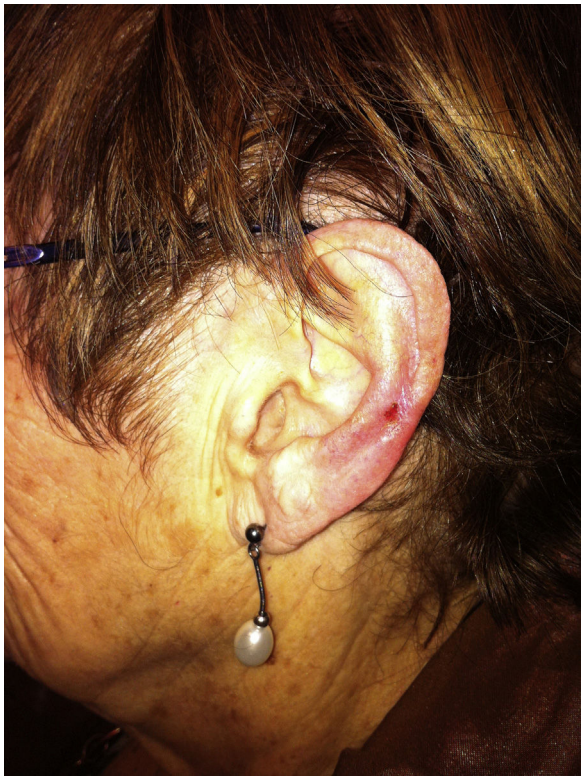

Figure 1 Erythematous ulcer on the helix of the left ear consistent with chondrodermatitis nodularis helicis.

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