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SHORT COMMUNICATION

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Atypical Vogt–Koyanagi–Harada disease or new uveomeningitic syndrome?

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Abstract *Purpose:* To report on a patient affected by bilateral intermediate uveitis (IU) as the initial sign of an uveomeningitic syndrome. *Methods:* Thorough history, physical examination and ancillary laboratory and radiological testing were performed in this observational case study. *Results:* A 23-year-old Caucasian man developed bilateral IU, primarily diagnosed as "idiopathic" since a detailed etiologic work-up was not indicative of underlying disease. Seven months later, he presented with poliosis and vitiligo. Lumbar puncture revealed cerebrospinal fluid pleocytosis. Optical coherence tomography showed bilateral subclinical macular edema (ME). The visual acuity was still 20/20 in both eyes. Clinical, laboratory and radiological results did not fit into any known syndrome. *Conclusions:* According to all the tests performed, the disease in our patient is a uveomeningitic disease with IU and ME which could be interpreted as an atypical form of Vogt–Koyanagi–Harada disease or a new uveomeningitic syndrome because there is no evidence for any other known disease.

Introduction

Vogt–Koyanagi–Harada (VKH) disease is a chronic, granulomatous, inflammatory disorder affecting the eyes, auditory system, meninges, and skin. It involves a T-lymphocyte-mediated autoimmune process directed primarily against choroidal and other melanocytes, which act both as inducer and as target [4]. Ocular disease therefore usually manifests as choroiditis with multiple exudative retinal lesions, eventually confluent to serous retinal detachment at the early stage and ocular depigmentation or bilateral chronic iridocyclitis at the late stage [6, 8]. We describe herein the case of a patient who primarily presented with intermediate uveitis (IU) and later developed subclinical macular edema (ME), poliosis, vitiligo and subclinical meningitis, evolving to an uveomeningitic syndrome which might be interpreted as an atypical form of VKH disease.

Case report

A 23-year-old Caucasian man presented at our institution complaining of floaters in the right eye for 2 months and in the left eye for 1 month. On examination, he reported an uneventful medical history. He had a Hispanic grandfather. Ophthalmic examination revealed best-corrected visual acuity of 20/20 for both eyes. No clinical signs of anterior segment inflammation were found in either eye. Fundus examination revealed a vitreal inflammation (1+ cells) associated with intravitreal yellowish-white aggregates (snowballs) in the inferior periphery of both eyes. Scleral depression precluded the presence of pars plana exudates. Moreover, we did not find edema of the optic disc or macula, retinal detachment, chorioretinal scars, retinal pigment epithelium clumping or migration, or periphlebitis. Neither fluorescein nor indocyanine green angiography revealed any abnormality (no delay in choroidal perfusion, no pinpoints, no dark dots, no optic nerve staining). Ultrasonography of both eyes was normal. Thus, neither history nor physical (especially neurological) examination allowed a diagnostic affiliation. A broad hematological and serological work-up, in common with radiographic and functional tests, showed no abnormality (Table 1). The HLA typing revealed the following HLA markers: A3, A11, B14, B57, DR7, DR15, DQ2, and DQ6. Intracutaneous tuberculin testing evoked a mild reaction with a palpable lesion of 2 mm diameter, BCG vaccination having being performed a few years previously. The patient declined lumbar puncture. The initial work-up was negative and the patient was diagnosed as having idiopathic IU. Consequently, only topical steroids were prescribed. At regular follow-up examinations, resolution of the inflammatory signs in the left eye and persistence of snowballs in the right eye were observed.

Seven months later, the patient presented with poliosis of cilia on the temporal portions of the left and right upper lids and vitiligo of the left periocular area and the left thigh (Fig. 1). Cerebrospinal fluid analysis revealed pleocytosis (13 cells/mm^3) with a predominance of lymphocytes (93%), normal glucose and protein level (0.29 g/l). Mycobacterial testing of cerebrospinal fluid was negative. Audiometry showed no abnormality. Fluorescein and indocyanine green angiography remained normal. Optical coherence tomography (OCT), performed for the first time, revealed mild subclinical ME (Fig. 2). The visual acuity was still 20/20 in both eyes. From all these findings, our patient was diagnosed as having either VKH disease with atypical ocular signs or an unknown uveomeningitic syndrome. At last examination 27 months after the initial presentation, the findings of ocular examination and OCT as well as the poliosis had remained unchanged.

Table 1 The broad hematological and serological work-up, with radiographic and functional tests, at first presentation: no abnormality was shown

Complete blood count with cell differentiation
Angiotensin-converting enzyme and lysozyme
Serum calcium
Liver enzymes
Fluorescent treponemal antibody absorption
Antinuclear antibodies
Complement proteins
Rheumatoid factor
Bartonella
Toxoplasma
Toxocara
Rickettsia
Brucella
Lyme
Human immunodeficiency virus
Candida antigen titers
Chest X-ray
Lumbosacral spine films
Chest computerized tomography
Pulmonary function tests
Cerebrospinal magnetic resonance imaging
Visual, auditory and somatosensory evoked potentials

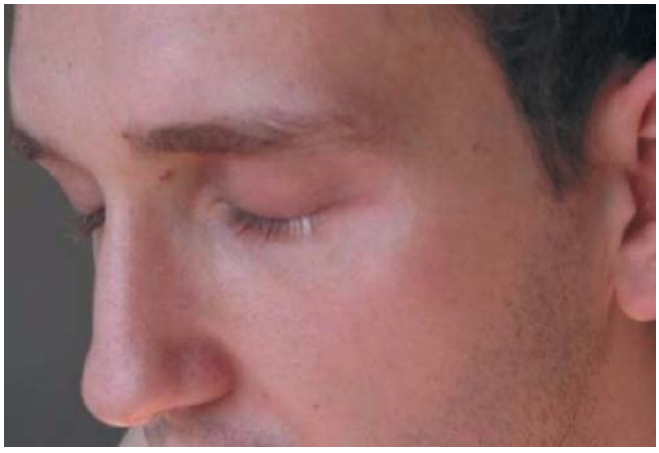

Fig. 1 Periocular vitiligo in a Caucasian patient with suspected VKH syndrome. Note also the temporal poliosis of cilia on the upper lid

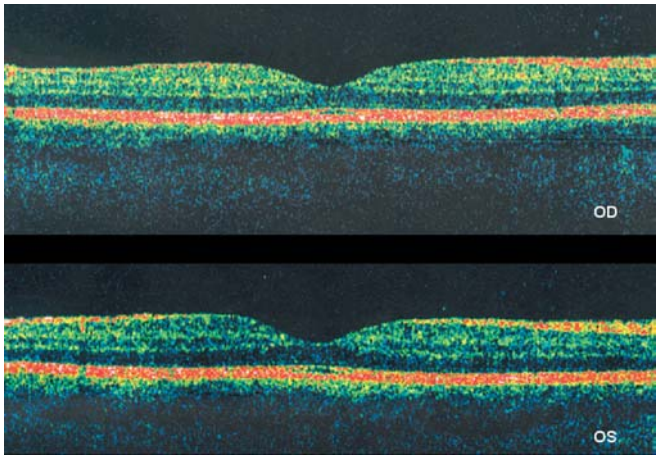

Fig. 2 Optical coherence tomography revealed mild subclinical ME (226 μm OD, 238 μm OS), with the visual acuity still being 20/20 in both eyes

Discussion

The diagnosis of VKH syndrome is based on the association of five diagnostic criteria [4]: no history of penetrating ocular trauma or surgery; no other or underlying ocular disease; bilateral ocular involvement; auditory or neurological findings (cerebrospinal fluid pleocytosis in our case); and typical integumentary changes (poliosis or vitiligo). Based on the presence of these five criteria,

VKH disease has to be assumed in our patient [4]. On the other hand, the ocular signs are unusual, constituted by a bilateral IU with subclinical ME diagnosed by OCT.

ME is relatively rare in VKH disease, but well known in some syndromes of chronic intraocular inflammation, such as pars planitis [5]. It may be the result of leakage from perifoveal retinal capillaries (inner blood–retinal barrier) or at the level of the retinal pigment epithelium (outer blood–retinal barrier) [5]. This ME may correspond to a localized choroiditis with retinal pigment epithelium involvement and a subsequent focal accumulation of subretinal fluid [4]. However, no foci of leakage or other inflammatory choroidal changes were uncovered clinically, by angiography, or by OCT in our patient. In addition, choroiditis has been reported to be diffuse and clinically early manifest in all published case series of VKH disease. Therefore, ME might be explained in our patient by intravitreal inflammatory mediators and breakdown of the inner blood–retinal barrier, the macular area being more vulnerable to edema than the other retinal areas [1].

IU has never been reported in VKH syndrome. And since we still do not have an explanation on the physiopathological level for this manifestation without obvious choroid involvement, we cannot affirm the diagnosis of VKH beyond all doubt. The work-up nevertheless eliminated all other differential diagnoses for IU, including multiple sclerosis, tuberculosis, Lyme disease, syphilis, and cat-scratch disease. Sarcoidosis, the most important differential diagnosis, was ruled out by the normality of serum ACE, lysozyme, calcium, liver enzyme levels, intradermal skin test, chest X-ray, chest CT, and pulmonary function tests. The patient declined biopsy and bronchoalveolar lavage, but these tests were not mandatory for exclusion of the diagnosis given that all previously mentioned tests were negative [7]. Furthermore, the clinical neurological abnormalities normally found in neurosarcoidosis were absent in our patient, and poliosis has never been reported in association with sarcoidosis in the literature.

Even though vitiligo and poliosis have been reported in patients with uveitis but without VKH disease [3], the timing of their occurrence in our patient is in favor of VKH diagnosis. Indeed, in VKH disease integumentary signs never precede the onset of the uveitis [4], in contrast to each of the sufficiently documented cases with non-VKH-associated uveitis described by Nordlund and coworkers [3]. After a thorough follow-up of more than 2 years, no late manifestations of VKH disease were present in our patient, in particular no ocular depigmentation signs; but they are virtually unheard-of in white patients [2, 8].

Until identification of additional, specific clinical features or laboratory abnormalities of VKH disease, the above-cited criteria remain the gold standard for diagnosis [4]. According to these, the disease in our patient might after all be diagnosed as atypical VKH syndrome. We are aware of the originality and singularity of ocular signs in our case, but there is no evidence for any other known uveomeningitic syndrome. If the diagnosis of VKH disease is correct, it may have to be included in the differential diagnosis of IU.

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