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SHORT COMMUNICATION

Vogt-Koyanagi-Harada disease after head trauma

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PURPOSE. *To report two cases of Vogt-Koyanagi-Harada disease after closed head trauma.*
METHODS. *Case report.*
RESULTS. *Two patients, one male and one female, developed headache, dysacusis, vertigo, tinnitus, and hair hypersensitivity shortly after a closed head trauma and, 10 and 18 days later, a bilateral uveitis with papillitis and exudative retinal detachment in one and a bilateral mild uveitis with macular exudative detachment in the other. The ocular lesions resolved with intravenous high-dose steroid therapy, but recurred after reduction of the dosages, requiring further steroid therapy. The course of the disease in both patients, with the appearance of fundus depigmentation and pigment clumping, and the occurrence of a concomitant ocular and auditory relapse in one, were typical of Vogt-Koyanagi-Harada disease.*
CONCLUSIONS. *Vogt-Koyanagi-Harada disease may appear after a closed head trauma suggesting that even an indirect trauma in melanocyte-containing tissue may induce an inflammatory response within the eye. (Eur J Ophthalmol 2007; 17: 847-52)*

KEY WORDS. *Vogt-Koyanagi-Harada disease, Head trauma, Uveitis*

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INTRODUCTION

Vogt-Koyanagi-Harada (VKH) disease is a severe bilateral diffuse uveitis with systemic involvement characterized by skin lesions and meningeal and neurologic irritation (1, 2). Its etiology is unknown, although a viral infection hypothesis has been proposed after the isolation by polymerase chain reaction of Epstein-Barr virus genome in the cerebrospinal fluid (3, 4) and after the demonstration of anti-cytomegalovirus antibody production in anterior chamber (5). The most accepted pathogenetic mechanism considers the disease a cellular immune process against melanocytes or against a common antigen expressed and shared by the skin, the eye, meninges, and ear (6-8). A genetic predisposition has also been postulated, with an increased prevalence of the HLA DR4 antigen in patients with VKH disease of different ethnic groups (Chinese, Japanese, Hispanic, Brazilian) (1, 8, 9) and in Italians (10). The clinical course of VKH is usually divided into four stages: prodromal, uveitic, convalescent, and recurrent. The prodromal stage is characterized by the onset of a flu-like syndrome with headache, nausea, vertigo, fever, meningismus, tinnitus, neurosensorial dysacusis, and orbital pain. Up to 80% of patients also showed cerebrospinal fluid lymphocytic pleocytosis, which usually disappeared within 8 weeks (1). Cranial neuropathies, hemiparesis, aphasia, and transverse myelitis have been rarely described (11). Skin involvement in this stage is limited to a particular sensitivity of hair and skin. The uveitic stage (second stage) follows after some days and is characterized by a predominant posterior involvement with multifocal choroiditis, papillitis, and circumscribed retinal edema, usually evolving into exudative retinal detachment. Inflammation eventually involves the anterior segment, with cells and flare in the anterior chamber. The third stage, or convalescence, follows after many weeks, and is characterized by the onset of integumentary (poliosis involving the eyebrows, eyelashes, and scalp hair,

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alopecia, and vitiligo) and choroidal depigmentation. Ophthalmoscopy reveals typical sunset glow-fundus and the appearance of multiple, small well-circumscribed spots of chorioretinal atrophy and retinal pigment epithelium migration. During the recurrent stage, the fourth stage, a panuveitis with a predominant anterior segment involvement not very responsive to steroid therapy is the hallmark. High dose steroid therapy may alter the clinical course of the disease, not allowing the onset of the symptoms of the later stages. According to the revised criteria for the diagnosis of VKH disease (12) the absence of ocular injury is necessary to fit the new diagnostic criteria, in order to differentiate VKH from sympathetic ophthalmia, a similar disease occurring after penetrating injuries of the eye (13). Nevertheless there are some reports on the occurrence of VKH after cutaneous injuries (14), supporting the hypothesis that a sensitization of patients may be induced by trauma on other melanocyte-containing tissues. The aim of this study is to report the clinical course of two patients who presented a typical picture of VKH after a closed head trauma.

Case reports

Case 1

In June 2003, a 69-year-old woman had a car accident, in which her head struck the car windshield. She was immediately examined at an emergency room of a regional hospital and neurologic examination and computed tomography results were normal, thus excluding that a primary cerebral disorder was the cause of the head trauma. Ten days later she complained of headache, dysacusis, vertigo, and visual acuity reduction. She was readmitted to the same hospital and was diagnosed with bilateral uveitis with papillitis and exudative retinal detachment (Fig. 1). The administered therapy was methylprednisolone 1.5 mg/kg/day for 5 days, 0.8 mg/kg/day for 10 days, 0.4 mg/kg/day for 15 days, 0.08 mg/kg/day for 15 days, and then 0.08 mg/kg twice weekly. The patient reported a complete resolution of the signs and symptoms of uveitis and a restoration of visual acuity. Because of the onset of some side effects (fatigue, leg edema) the patient decided to stop the medication in August 2003 and, 1 month later, the uveitis reappeared and the patient was admitted to our department. Clinical examination at that time displayed the following in both eyes: visual acuity 1/10, non-granulomatous keratic precipitates, flare 1+, cell 1+, subcapsular and nuclear cataract, 3+ vitreous cells and 2+ opacities, hyperemia and swelling of the optic disk, pigment clumping in the macular area, and exudative retinal detachment predominantly localized inferiorly. A complete work-up for uveitis was unremarkable. Audiometric examination displayed a neurosensorial hypoacousia. She was administered methylprednisolone 1 g/day for 3 days intravenously in combination with atropine 1% eye drops twice daily, dexamethasone 0.2% eye drops 6 times/day in both eyes. The steroids were then administered orally starting with prednisone 1 mg/kg/day for 4 days, 0.75 mg/kg/day for 14 days, and slowly tapered. Visual acuity was restored to 6/10 and 9/10 in the right and left eye,

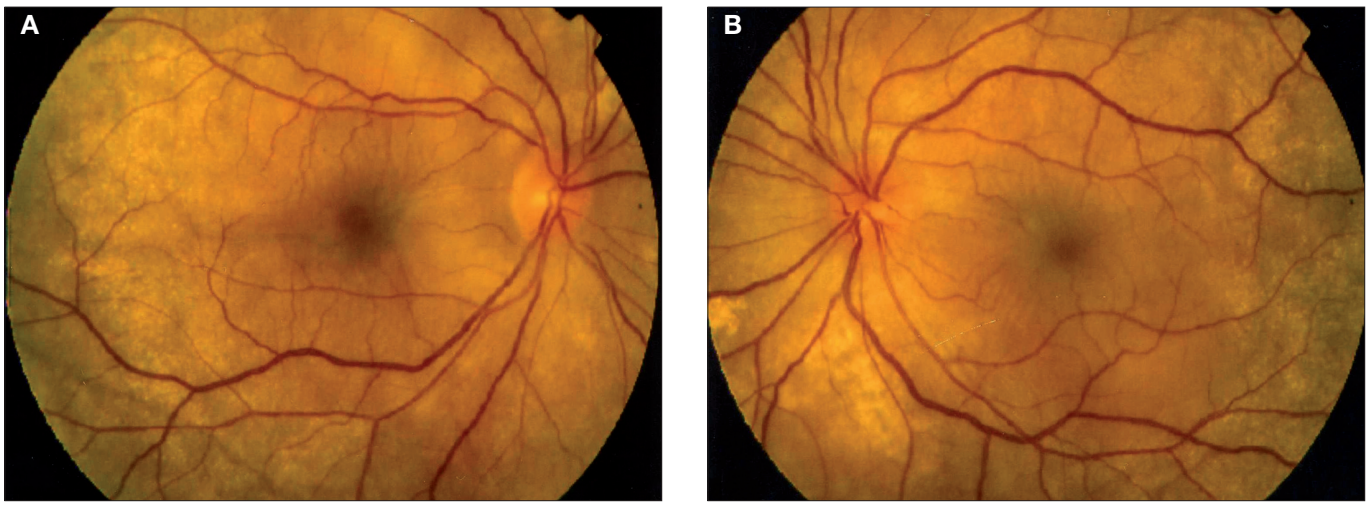

Fig. 1 - *Case 1. Bilateral papillitis and exudative retinal detachment at onset (***A** *= right eye,* **B** *= left eye).*

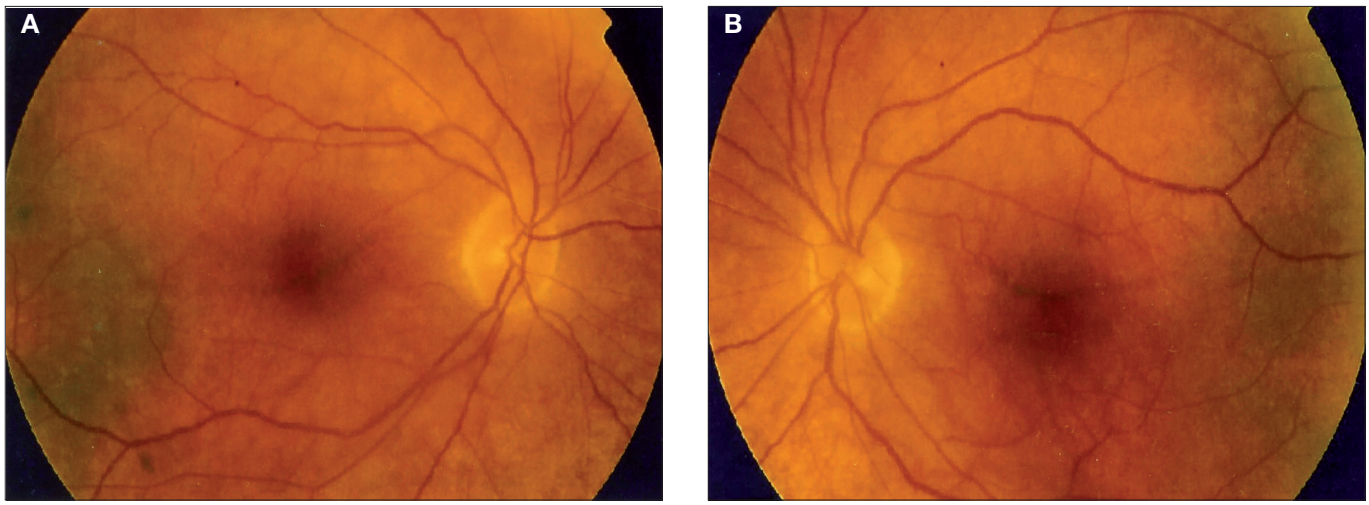

Fig. 2 - *Case 1. Classic pigmentation of the macular area after uveitis and exudative retinal detachment resolution (***A** *= right eye,* **B** *= left eye).*

respectively. No signs of anterior uveitis were detected and the fundus displayed the classic pigmentation clumping in the macular area (Fig. 2). Four months later, while she was taking prednisone 12.5 mg/day, she complained of visual acuity reduction in both eyes. The clinical examination showed a slight macular edema in the right eye (RE). Visual acuity was 6/10 in RE and 8/10 in the left eye (LE). Because of the patient's refusal to increase the steroid therapy appropriately, 17.5 mg/day of prednisone and a peribulbar injection of triamcinolone acetonide 40 mg in RE were administered with complete resolution of the uveitis and visual acuity restoration. In September 2004, while taking prednisone 7.5 mg/day, she again complained of visual acuity reduction in LE. Visual acuity was 3/10 and an anterior uveitis with extensive synechiae in mydriasis and a papillitis were present. Steroids were then given at a dose of 25 mg/day in combination with topical therapy. Visual acuity was restored in 20 days and no further relapses have been detected since October 2005. No changes in the audiometric examination were detected throughout the follow-up, nor the appearance of cutaneous changes. The steroid therapy was slowly tapered and stopped in September 2005.

Case 2

A 48-year-old man had accidental domestic trauma, hitting his head against a door, on December 5, 2003. On December 15, he complained of general malaise, headache, hair hypersensitivity, and tinnitus, and a few days later of bilateral hyperemia and visual acuity reduction. He was examined for the first time by a general ophthalmologist on December 23. The diagnosis was bilateral macular edema and the patient was administered betamethasone 8 mg/day for 4 days and 4 mg/day for 8 days, then deflazacort 6 mg/day, in combination with acetazolamide 500 mg/day. On December 30, optical coherence tomography (OCT) was performed, showing a bilateral exudative macular detachment (Fig. 3). In January 2004, the patient complained of further visual acuity reduction and OCT showed increasing macular edema. The patient received steroid therapy with deflazacort 60 mg/day (approximately 0.75 mg/kg) and any attempted further reduction was followed by a deterioration of visual acuity and increase of auditory symptoms. He was admitted to our service on February 25, 2004. Visual acuity was 10/10 in both eyes with a myopic correction. No anterior uveitis was detectable, but a few cells in the vitreous and a slight macular edema were present. There was also neurosensorial hypoacousia. A complete work-up for uveitis was unremarkable, nuclear magnetic resonance of the brain was normal, and a steroid treatment with methylprednisolone 1 g/day for 3 days was administered. Thereafter oral steroids were given at a loading dose of prednisone 0.5 mg/kg/day for 10 days then decreasing by 5 mg/day every 10 days. Two months later, the visual acuity was 10/10 in both eyes with no correction and no further macular edema was detectable (Fig. 4). In September 2004, the patient complained of tinnitus and hypoacousia. An audiometric examination confirmed the deterioration of neurosensorial

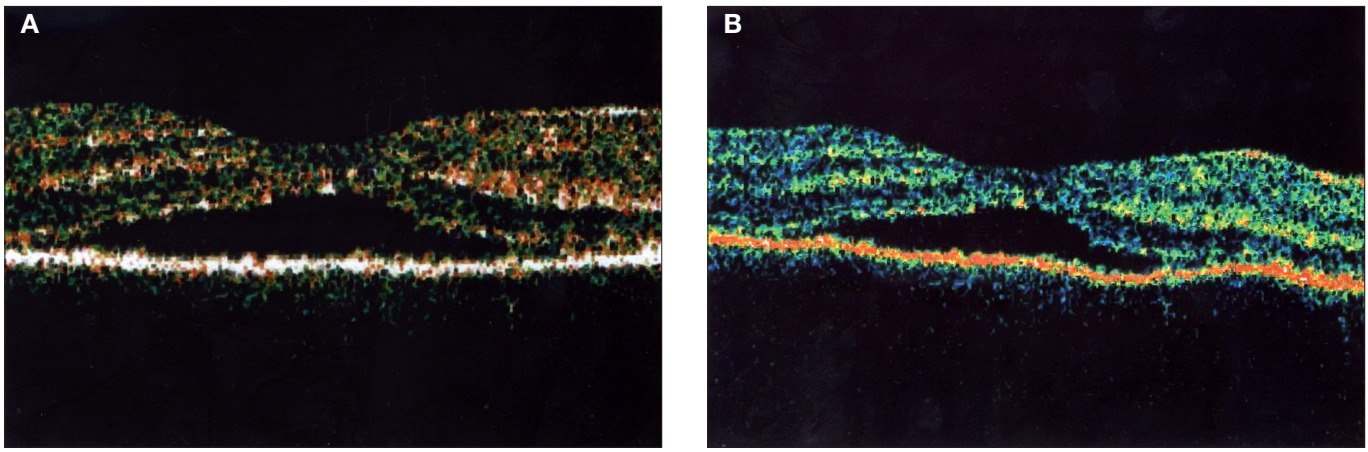

Fig. 3 - *Case 2. Optical coherence tomography scanning of serous retinal detachment 10 days after the onset of ocular symptoms (***A** *= right eye,* **B** *= left eye).*

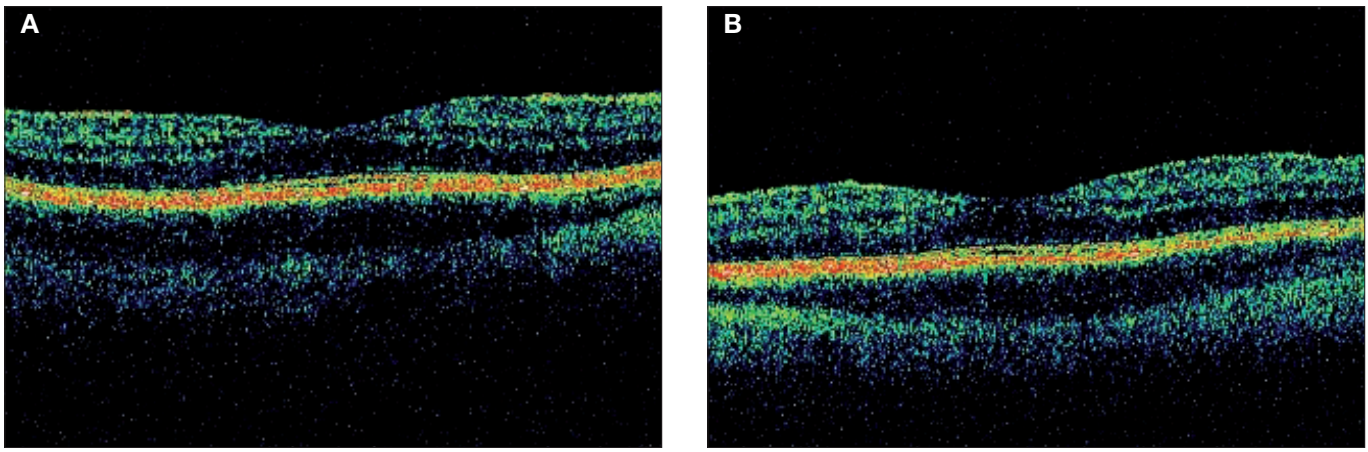

Fig. 4 - *Case 2. Optical coherence tomography scanning of resolution of the macular exudative detachment after steroid therapy (***A** *= right eye,* **B** *= left eye).*

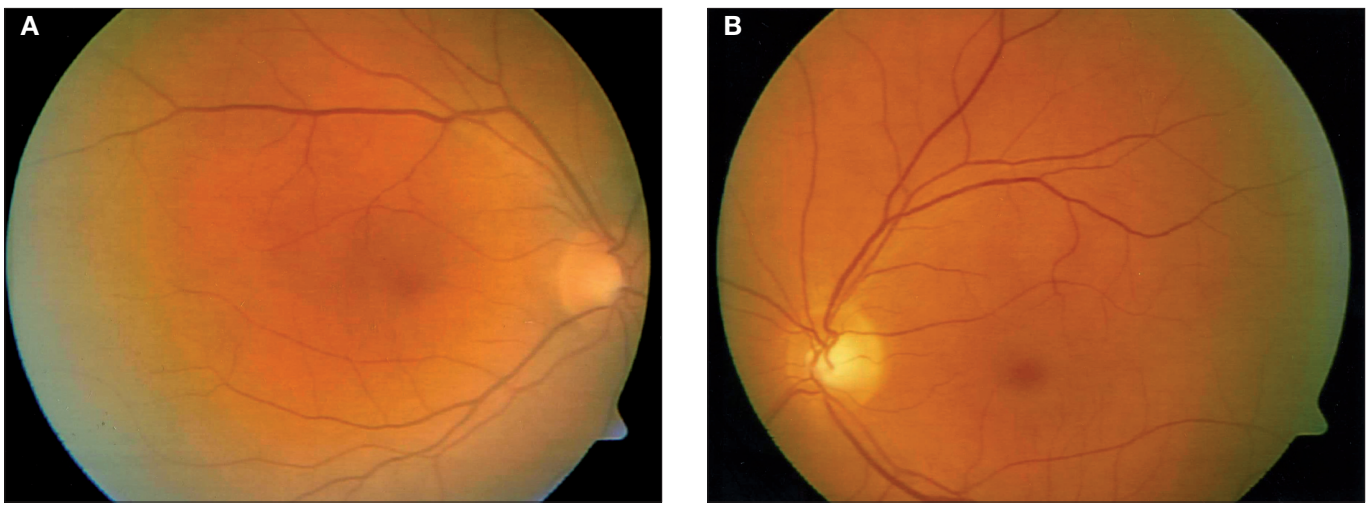

Fig. 5 - *Case 2. Fundus photography in January 2004 (***A** *= right eye,* **B** *= left eye).*

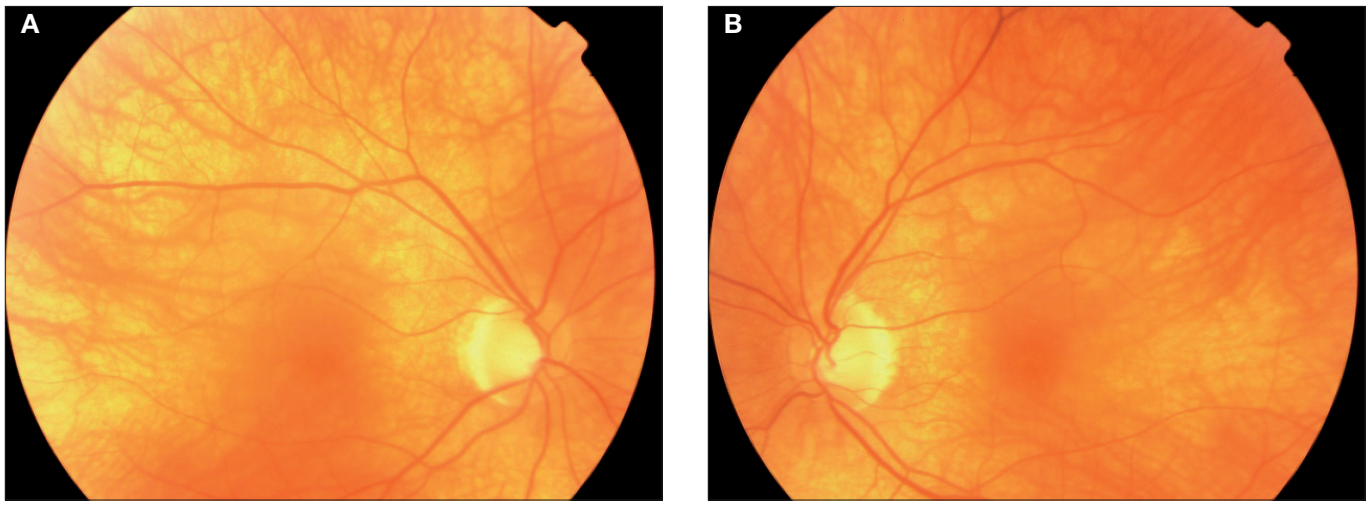

Fig. 6 - *Case 2. Fundus photography in April 2005 (***A** *= right eye,* **B** *= left eye): diffuse depigmentation.*

hypoacousia. Ophthalmic examination also displayed mild anterior uveitis (cells ±, flare ±). The patient was taking prednisone 5 mg on alternate days and therapy with prednisone 25 mg/day in combination with topical treatment for uveitis was restored. Auditory and ocular symptoms resolved in 15 days and then a slow tapering of prednisone therapy was done. Steroid therapy was discontinued in January 2005 and no further uveitis or auditory relapses have been detected. No cutaneous signs of the disease appeared during the follow-up. A progressive depigmentation of the fundus appeared over time in absence of ophthalmoscopic or angiographic findings of ocular relapses (Figs. 5 and 6).

DISCUSSION

VKH disease is a systemic disease of unknown etiology. The pathogenetic mechanism recognizes a cellular immune response against melanocytes (1, 6, 7). Usually there is a prodromal stage characterized by neurologic symptoms (1, 2). In our cases the neurologic symptoms reported at onset were headache, which, unfortunately, was not adequately defined, and neurosensorial hypoacousia. This last finding is usually uncommon after a closed head trauma, being reported in only 16% of 50 children after sustaining head trauma (15). None of our patients had, as shown by computed tomography or nuclear magnetic resonance of the brain, any primary cerebral disorders that may have led to the accidents with the head trauma. The clinical course of the ocular disease is very typical of VKH disease in Patient 1. The other patient might have a much less acceptable diagnosis of VKH at a first instance. Nevertheless we could not disregard the possibility that a prompt and prolonged steroid therapy could have decapitated the natural course of the VKH, allowing a prompt resolution of the ocular lesions as well as preventing further development of extraocular signs (i.e., cutaneous lesions). Nine months after the head trauma and the onset of the ocular symptoms, and while he was taking 5 mg/day of prednisone, the patient developed a concomitant auditory and ocular relapse which respond promptly to an increase of the daily dose of steroids. Furthermore, in the subsequent follow-up, the appearance of a progressive depigmentation of the fundus in absence of ophthalmoscopic and angiographic findings of ocular relapses may stress the possibility that this patient may be diagnosed with VKH. The temporal relationship between the head trauma and the ocular symptoms observed in the two patients (10 and 18 days) may be considered sufficient to allow the onset of an immune reaction against melanocytes, as has been demonstrated in patients with VKH (6, 7). A possible hypothesis is that the head trauma induced, perhaps by concussive mechanisms on melanocytic-containing cells, exposure of the antigen to the immune system and therefore the onset of the disease. Although a coincident onset of VKH disease in patients with head trauma should be considered, other reports of the onset of VKH after trauma in other tissue-containing melanocytes, such as skin injuries fol-

lowed by local vitiligo and some weeks after by the onset of ocular manifestations typical of VKH (14), clearly indicates the possibility that a nonocular trauma may induce a typical VKH disease. The real incidence of VKH after trauma in nonocular sites has never been investigated; neither is a sufficient long-term follow-up of the so-called post-traumatic features available in order to define particular findings of this disease.

In conclusion, these two cases seem clinically to represent typical VKH disease. The temporal relationship with a closed head trauma may suggest that a trauma in melanocyte-containing tissue may induce an inflammatory response within the eye. This possibility, and the other report on VKH occurring after skin injuries, should be further investigated in all patients with a diagnosis of VKH in order to eventually redefine the diagnostic criteria of the disease.

Proprietary interest: None.

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