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Diagnostic implications and effective treatment of Susac syndrome with thrombophilia

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Abstract

Susac syndrome is an uncommon autoimmune microangiopathy characterized by a combination of encephalopathy, branch retinal artery occlusions (BRAO), and hearing loss. In this report, we present a detailed history of a 31-year-old man with Susac syndrome with thrombophilia. The diagnosis was based on clinical signs and neurological, otolaryngological and ocular examination. Fluorescence retinal angiography showed right BRAO. A slight (30 dB) sensorineural lowering of the hearing level was observed in the audiogram. Numerous ovoid lesions in the corpus callosum were detected in magnetic resonance (MR). The applied treatment included glucocorticosteroids, disease-modifying antirheumatic drugs, anticoagulant treatment and immunoglobulin infusions. After treatment, ophthalmologic symptoms receded, the recanalization of BRAO was detected in angiography, and the lesions in the corpus callosum were reduced in control MR. To date, this is the first report showing the effective treatment of Susac syndrome, which was confirmed simultaneously in MR and fluorescein angiography in a case of Susac syndrome with thrombophilia.

Key words: Susac syndrome, microangiopathy, diagnosis and treatment, thrombophilia.

Introduction

Susac syndrome is an autoimmune-mediated endotheliopathy characterized mainly by neurological disorders [1, 2]. This syndrome is caused by a microangiopathy affecting the precapillary arterioles of the brain, retina, and inner ear, and in consequence encephalopathy, hearing loss, and branch retinal artery occlusions are present [3, 4]. In the early stages of this disease, headache, visual or hearing disturbances and non-specific neurological disorders are present. Later, fully developed encephalopathy usually occurs and neuropsychiatric symptoms may dominate in as many as 75% of patients [5]. Unfortunately, many cases are underdiagnosed, because the symptoms are not specific and the characteristic triad is not present at the onset of this disease [6].

Case report

A 31-year-old Caucasian man suffered at the beginning of the overt disease from intermitted unilateral hearing loss that resolved after 24 hours. After three months, the patient was suffering from headache, vertigo and nystagmus that disappeared within three hours. The neurologic examination did not reveal any disorders, and computed tomography of the brain did not show any pathologic changes. From this time onwards, regular incidents of blurred vision kept recurring.

One year after the first symptoms, the patient started to complain of sudden visual field loss in the right eye affecting the inferior nasal visual quadrant, which was preceded by retrobulbar pain. Fundoscopic examination showed cotton wool spots in the right eye with signs of branch retinal arteriolar occlusion. Fluorescence

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retinal angiography revealed a pattern compatible with resolved branch retinal artery occlusion in the right eye and demonstrated multifocal arteriolar disease in the retinal periphery (Fig. 1).

The vision disorders were associated with transient hearing loss. An audiogram revealed a slight (30 dB) sensorineural lowering of the hearing level with predominant involvement of the middle and low tones (Fig. 2).

Two months after the sudden visual field loss, the patient complained of numbness in the right side of the face, hand and thorax. Magnetic resonance imaging showed numerous macular, ovoid, periventricular lesions in the corpus callosum (Fig. 3A). These disorders were also manifested as high-signal changes in PD (proton density), T1- and T2-weighted images with intravenous contrast and STIR (short TI inversion recovery) sequences. Although the MRI findings were initially thought to represent atypical multiple sclerosis, the central location of the corpus callosal lesions and the enhancement of branch retinal artery occlusion associated with the hearing loss enabled a final diagnosis of Susac syndrome. At this time, high doses of oral methylprednisolone (64 mg/day), low-molecular-weight heparin (80 mg subcutaneous injection twice a day) and acetylsalicylic acid (75 mg/day) were implemented. Glucocorticosteroids were used and provided fast recovery; however, the trial of tapering them was unsuccessful and the visual disorders recurred. Intravenous immunoglobulin infusions (IVIG) were administered at a total dose of 198.0 g with a high level of tolerance and temporary subsidence of visual and hearing disorders. The coagulogram showed a significant increase in factor VIII, and thrombophilia

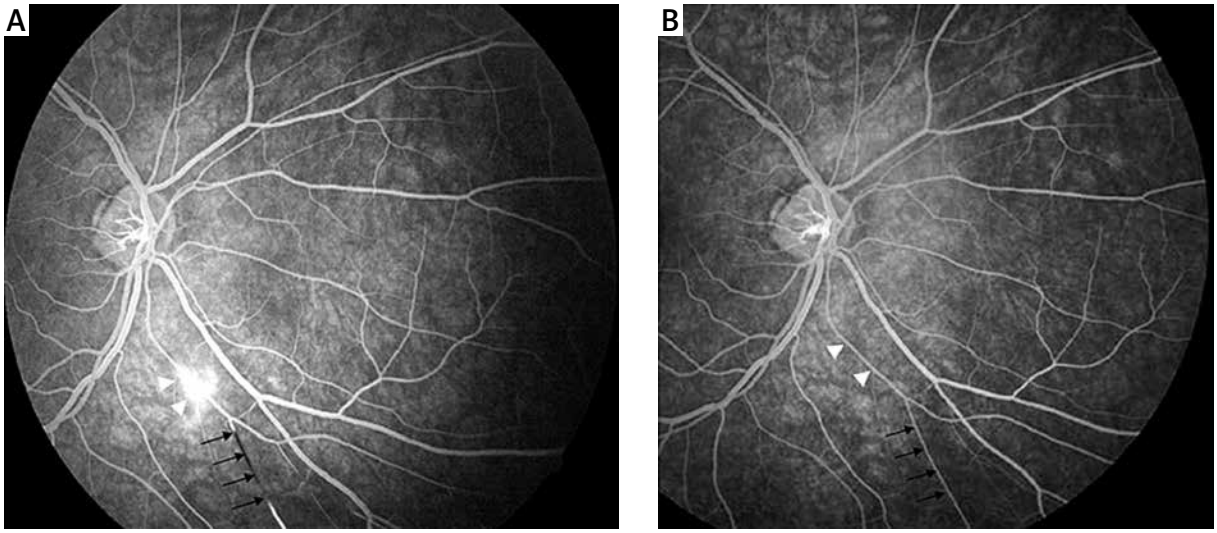

Fig. 1. Fluorescein angiography: an occlusion of a retinal artery (arrows) and leakage of the vessel wall (arrowheads) (A); Fluorescein angiography: the recanalization of a retinal artery (arrows) and healed vessel wall (arrowheads) (B).

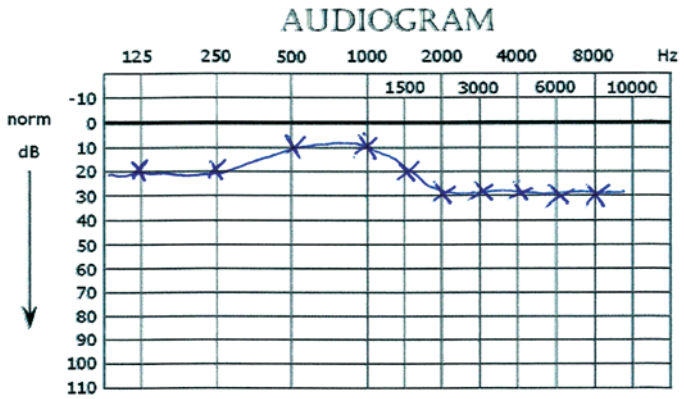

Fig. 2. Audiogram: 30 dB sensorineural lowering of the hearing level with predominant involvement of the middle and low tones.

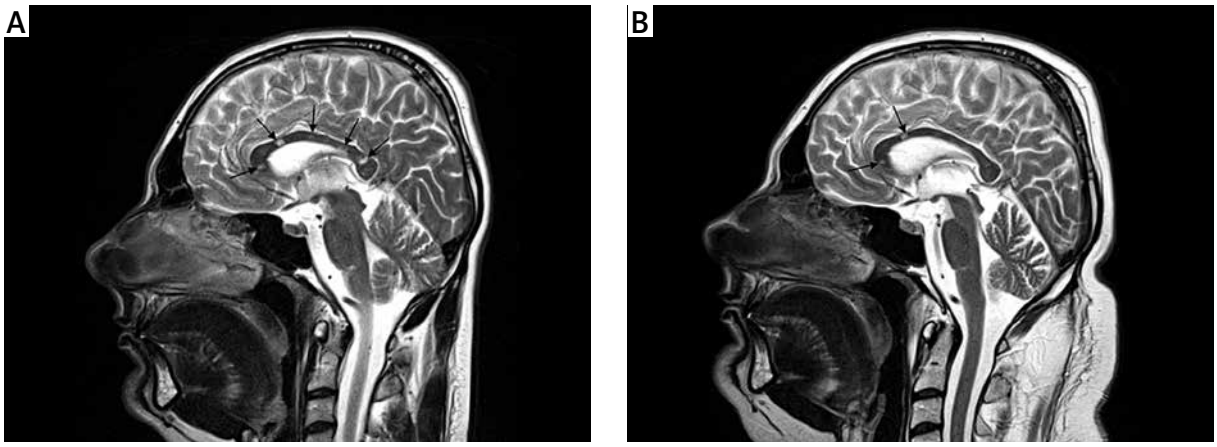

Fig. 3. Midline sagittal unenhanced T1-weighted MRI: multiple hypointense lesions (arrowheads) in corpus callosum (A); Midline sagittal unenhanced T1-weighted MRI: decreased size and number of hypointense lesions in corpus callosum (arrowheads) (B).

was diagnosed. The acetylsalicylic acid was replaced by clopidogrel, azathioprine was applied (100 mg/day) and glucocorticosteroids were ceased. After the treatment, clinical improvement was observed (ophthalmologic symptoms and nystagmus receded), and in fluorescein angiography the recanalization of a retinal artery and the subsidence of inflammation were observed (Fig. 1B). Moreover, in the control MR the lesions localized in the corpus callosum were diminished compared with the previous imaging study (Fig. 3B).

Discussion

In this report, we described the case of a 31-year-old man with Susac syndrome. This microangiopathy affects mainly young women aged 20–40 years old (the female to male ratio is 3 to 1) [1, 5, 7]. At the beginning, the patient reported a headache, which is usually present in more than half of the patients at the onset of Susac syndrome. Audiometry revealed sensorineural hearing loss at low and mild frequency perception, with an average loss of 30 dB (Fig. 2). These data corresponded with other studies which described a 40 dB sensorineural hearing loss with predominant involvement of the middle and low tones [4, 8]. The loss of hearing and the presence of vertigo are caused by the infarction of the cochlear apex in the vascular territory of small end arteries [7, 8], while the nystagmus may indicate infarction of the membranous labyrinth [5–7].

Because of sudden visual disorders in the right eye and the pain in the posterior area of the right eyeball, fluorescence angiography of the eyes was implemented and showed typical branch retinal artery occlusions in the peripheral areas (Fig. 1A). This examination evoked Susac syndrome, and magnetic resonance was ordered to confirm the brain disorders. We observed typical changes of the corpus callosum in the MR imaging (Fig. 2A). The callosal ovoid lesions were present mainly in the central area, which is very suggestive of Susac syndrome [6]. The observed lesions were sparing peripherally, and T1-weighted images revealed typically multifocal small hypointense foci in periventricular areas, the pons of the cerebellum and the middle cerebellar peduncles. Differential diagnoses based on MR findings should include thromboembolic stroke, multiple sclerosis, encephalitis, lupus erythematosus, Ménière's disease, migraine, and schizophrenia [6, 8, 9].

Susac syndrome has also been suggested to represent an autoimmune coagulopathy similar to catastrophic antiphospholipid syndrome [8]. In this case, the anticardiolipin antibodies (ACA) and anti-β-2-glycoprotein I were negative, but we observed an elevated level of factor VIII. In an analysis of 10 cases of retinocochleocerebral vasculopathy, Petty et al. also described elevated factor VIII levels [4]; however, concomitant thrombophilia has not been mentioned in any previous reports.

In this case the symptoms fully developed after 2 years. Unfortunately, the insidious onset and slow development of Susac syndrome cause diagnostic problems [5]. Glucocorticosteroid therapy usually is successful; nevertheless, the sudden tapering of methylprednisolone leads to relapse. In the literature, the simultaneous implementation of IVIG, cyclophosphamide, azathioprine, dipyridamole, and acetylsalicylic acid is also reported to have good outcomes [10].

In this case, after the diagnosis of thrombophilia, treatment with methylprednisolone was ceased and an oral anticoagulant and azathioprine (100 mg/day) were implemented. The immunoglobulins were applied with good results and diminished changes were shown in

fluorescein angiography (Fig. 1B) and MR compared to previous examinations (Fig. 3B).

Summary

To date, this is the first report showing the changes in MR and fluorescein angiography after the effective treatment of Susac syndrome.

The authors declare no conflict of interest.

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