CASE REPORT

Susac Syndrome: Retinocochleocerebral Vasculopathy

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Susac syndrome is a rare microangiopathy of cochlea, retina, and brain. We report a case of a 30-year-old man with Susac syndrome. The patient initially suffered from unilateral hearing loss associated with peripheral vestibular syndrome, and followed with recurrent arterial retinal occlusions and encephalopathy. The patient underwent clinical, laboratory, and neuroradiological examination. Laboratory tests were negative for systemic inflammatory or infectious disease. Signs of encephalopathy and vestibular syndrome regressed after 6 weeks, retinal obstructions were partially improved, and deafness remained unchanged. Two unexplained epileptic seizures had been documented 7 years before the development of typical clinical course. The etiology is still unknown and diagnosis was suggested by the clinical triade of bilateral sensorineural hearing loss on low frequency on audiology, recurrent bilateral retinal branch artery occlusions, and small multiple areas of signal hyperintensity in the white and gray matter on brain magnetic resonance T2-weighted images. The clinical course is self-limited and treatment options are not codified. Epileptic seizures, as those in our patient, may extend the clinical spectrum of Susac syndrome. This case also documents the possibility of multiphasic disease course.

Key words: cerebrovascular disorders; hearing loss, sensorineural; microcirculation; retinal artery occlusion

Susac syndrome is a microangiopathy of the cochlear, retinal, and encephalic tissue. Recurrent multiple occlusions of retinal branch artery are observed. In 1979, Susac et al (1) described two young women who presented with multiple bilateral retinal branch artery occlusions, hearing loss, and neurological symptoms without clinical arguments for systemic disease. In 1992, Schwitter proposed the acronym: SICRET syndrome, characterized by small infarcts of cochlear, retinal, and encephalic tissues (2).

Case Report

A 30-year-old man with a past history of two unexplained epileptic seizures of grand mal type, which occurred in 1995 and were followed by antiepileptic treatment for 18 months, suddenly complained of vertigo and unsteady gait in March 2002. On admission, the findings included the vestibular syndrome and right side hearing loss. Brain computed tomography (CT) and laboratory tests showed no abnormality. Treatment consisted of hyperbaric oxygen therapy, vasodilating drugs, and nootropic agents. The family history was uneventful: there were no thrombotic events in younger family members, and the mother had rheumatoid arthritis.

In May 2002, the patient developed visual disturbances, and ophthalmologic examination showed abnormal visual acuity in the left eye and pathological findings in perimetry and fundoscopy. Fluorescein angiography showed multiple retinal arteriolar occlusions of both eyes. Brain magnetic resonance imaging (MRI) demonstrated multiple small subcortical ischemic lesions. A combined therapy with oral corticosteroids (70 mg/day), and cyclosporine A (400 mg/day) was initiated.

In July 2002, the patient suffered from neurological disturbances accompanied by a progression of ophthalmologic signs. Neurological difficulties lasted for seven days and cerebrospinal fluid examination was performed. In August 2002, the patient experienced bilateral hearing worsening. Audiogram revealed severe right perceptive hypacusis and left deafness. In September 2002, he was readmitted to the Department of Neurology with a headache, vestibular syndrome, dysfunction of micturition, blurred vision, and cognitive impairment. Since October 2002, the patient has not had any other symptoms.

The following blood tests showed normal findings: sedimentation rate, VDRL (Venereal Disease Research Laboratory Test), protein C, S, antithrombin III, homocysteine, serum glucose, lipid parameters, renal tests, hepatic tests, uric acid, serum proteins and electrophoresis, autoantibodies to deoxyribonuceloprotein (DNP), antinuclear antibodies (ANA), antibodies to extractable nuclear antigens (ENA), antineutrophil cytoplasmic autoantibodies (ANCA), rheumatoid factor, and antiphospholipid antibodies. Humoral immunity examination showed a slight decrease in IgG concentration (7.7 g/L; reference range, 8-18 g/L) and an increase in the concentration of C3 complement.
(1.97 g/L; reference range, 0.9-1.9 g/L); circulating immune complexes and C-reactive protein were normal. Serologic tests for infectious agents were normal. Blood pressure monitoring showed border arterial hypertension. Electrocardiography (ECG), thorax echocardiography, chest X-ray, and abdominal ultrasound were normal.

Since May 2002, the patient has been continually treated with cyclosporine A (150 mg/day), azathioprine (50 mg/day), and oral corticosteroids (10 mg/day). This immunosuppressive treatment was initially combined with low molecular heparins (2x0.3 mL/day for 9 days), followed by acetylsalicylic acid (100 mg/day). Symptomatic treatment involved nootropic and vasoactive agents. Despite persistent visual deficit and hearing loss, the patient continued his employment. Implantation of a foniatic device is being considered.

**Neurological Symptoms**

In March 2002, during the first relapse of the disease, the patient presented with vestibular and cochlear symptoms. His brain CT was normal. Postcontrast brain MRI demonstrated symmetric multiple small foci of increased T2 signal distributed predominantly subcortically, with severe damage of both temporal lobes. The lesions were described as small ischemic lesions (Fig. 1). In July 2002, dysarthria, lower limbs myalgia, general fatigue, and weight loss appeared. These symptoms lasted 7 days. Cerebrospinal fluid examination showed normal protein content and normal cell count, and cerebrospinal fluid tests for infectious agents were normal. IgG oligoclonal bands were not present, and blood brain barrier indexes showed no abnormalities. Electroencephalogram (EEG) showed nonspecific theta dysrhythmia over temporal channels. Brain Doppler ultrasound confirmed diffuse and increased peripheral resistance in both carotid and vertebrobasilar systems. Visual evoked potentials (VEP) were abnormal on the left eye. In August 2002, brain MRI showed gain in the lesion load and mild cerebellar atrophy. In September 2002, the patient was readmitted to the Department of Neurology for a headache, dizziness, and unsteady gait, imperative micturition, persistently blurred left vision, and poor concentration. Neurological findings indicated pyramidal tract lesion, slight paresis of the right hand, and vestibular ataxia. Paresis and ataxia improved during 3 weeks. In September 2003, control neurological examination revealed slight residual cerebellar syndrome, whereas otiatric and ophthalmological findings were stable. Psychometric tests did not show any intellectual deterioration or cognitive impairment. Control brain MRI showed no further gain in lesion load, and SPECT confirmed normal brain perfusion.

**Ophthalmologic Symptoms**

In May 2002, the second relapse occurred. Ophthalmologic examination showed visual acuity (VA) of 1.0 in the right eye and 0.5 in the left eye. Nasal visual field defect was found in left eye. Fundus examination of the left eye revealed vessel exudates, extensive ischemic retinal edema of the inferior part of macular area, and pallor of the optic disc (Fig. 2). Fundus examination of the right eye showed multiple ischemic areas of the superotemporal retinal artery and inferotemporal vein territory. Optic disc pallor of the right eye was also present (Fig. 3). Fluorescein angiography of the right eye showed multiple vessel occlusions of superotemporal retinal artery and abnormal fluorescein outflow from superotemporal retinal vein (Fig. 4). Fluorescein angiogram of the left eye showed areas of leakage, arterial wall hyperfluorescence of superotemporal retinal artery, and perimacular branch of inferotemporal retinal artery. Retinal arteriolar occlusions were present in inferotemporal retinal artery (Fig. 5). In July 2002, new neurological symptoms appeared, accompanied by visual function worsening. The patient suffered from blurred vision in
both sides and fundoscopy showed progression of atrophic changes of both optic discs. In October 2002, fundus examination of both eyes evidenced persistent multiple retinal arteriolar narrowing, with irregular lumen. Some of the capillary endings were occluded and some showed paravascular exudates (Figs. 6, 7A and 8A). Control fluorescein angiogram showed residual stage, superotemporal and inferotemporal retinal arteriolar occlusions, and dilated veins. Both eyes had abnormal patchlike choriocapillaris and optic disc pallor. Fluorescein angiograms showed equal arteriolar changes in both eyes (Figs. 7B and 8B). Fundus examination findings corresponded to those of fluorescein angiogram. VA of 1.0 in

Figure 2. The patient with Susac syndrome, May 2002. Vessel exudates, extensive ischemic retinal edema of the inferior part of macular area partially involving fovea, and pallor of the optic disc were visible in the fundus of the left eye.

Figure 3. The patient with Susac syndrome, May 2002. A. The fundus of the right eye. B. The fundus of the right eye, red free. Multiple ischemic areas of the superotemporal retinal artery and inferotemporal vein.

Figure 4. The patient with Susac syndrome, May 2002. Fluorescein angiogram of the right eye revealed multiple vessel occlusions, superotemporal retinal arteriolar obstructions, and abnormal fluorescein outflow from superotemporal retinal vein.

Figure 5. The patient with Susac syndrome, May 2002. Fluorescein angiogram of the left eye showed focal areas of arterial wall hyperfluorescence of superotemporal retinal artery and perimacular branch of inferotemporal retinal artery, with inferotemporal retinal arteriolar occlusion.

Figure 6. The patient with Susac syndrome, October 2002. Residual finding of multiple arteriolar narrowing and optic disc pallor visible in the fundus of the left eye.
Figure 7. The patient with Susac syndrome, October 2002. 
A. Residual stage, superotemporal and inferotemporal retinal arteriolar occlusions, dilated veins, and optic disc pallor visible in the fundus (red free) of the right eye. 
B. Fluorescein angiogram of the right eye showed abnormal patchlike choriocapillaris.

Figure 8. The patient with Susac syndrome, October 2002. 
A. Residual stage, superotemporal and inferotemporal retinal arteriolar occlusions, dilated veins, and optic disc pallor visible in the fundus (red free) of the left eye. 
B. Fluorescein angiogram of the left eye revealed abnormal patchlike choriocapillaris.

Figure 9. The patient with Susac syndrome. Automated perimetry. 
A. Right eye: nasal visual field defect, with spared central area. 
B. Left eye: nasal and temporal inferior visual field defect.

Table 1. Comparison between literature data and the presented case

<table>
<thead>
<tr>
<th>Author (reference)</th>
<th>Patient characteristics</th>
<th>Laboratory findings</th>
<th>Clinical findings</th>
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<td>32</td>
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the right eye and 0.6 in the left eye was the last finding. There was temporal pallor of both optic discs with atrophic changes and corresponding nasal visual field defect of the right eye and nasal and inferior temporal visual field defect of the left eye (Fig. 9).

**Auditory Symptoms**

In March 2002, the patient suddenly complained of vertigo, tinnitus, vomiting, and unsteady gait. On admission, he had vestibular syndrome and right side hearing loss, followed with left side hearing disturbance one week later. Audiometry showed right side decrement on the level 30-40 dB, bilateral normal tympanogram type A, and bilateral stapedial reflex absence. In August 2002, patient experienced bilateral hearing worsening. Audiogram confirmed severe hearing loss to all frequencies in the right ear, and left side deafness. Brain MRI showed gain in the lesion load. In March 2004, control audiogram confirmed bilateral deafness. Control tympanogram and stapedial reflex response of both sides were not changed. Brain stem auditory evoked potentials (BAEP) showed bilateral abnormal evoked responses.

**Discussion**

Our patient had a complete form of Susac syndrome, with the clinical triad as detailed in the original description by Susac in 1979 (1). The patient experienced hearing loss associated with peripheral vestibular syndrome as initial feature, followed with recurrent retinal branch artery occlusions and encephalopathy. Dysarthria, slight right upper limb paresis, and Babinski response were found in clinical neurological examination. There was no evidence of any autoimmune, inflammatory, systemic or infectious disease. Hematological parameters showed no abnormalities. There was no evidence of embolic sources. The clinical triade became complete after two months. Disease course involved five relapses of visual, neurological, or auditory symptoms. Fluorescein angiography confirmed multiple bilateral retinal branch artery occlusions. Detection of retinal arteriolar occlusions was the key to the diagnosis of Susac syndrome. Brain MRI as the neuroradiological procedure of choice revealed diffuse subcortical demyelinating lesions. Character and localization of these multiple small foci supported the suggested diagnosis of cerebral microangiopathy.

The duration of the disease is variable: it can remain active from 2 months to 11 years, and the mean duration is 2 years (1,3). There is a tendency towards spontaneous improvement and definite remission of the condition, with no deaths reported so far (1,3,4). The disease has a characteristic fluctuating course, and the patient may have one or more episodes of variable combinations of neurologilcal, ophthalmological, and auditory symptoms. Most case reports have emphasized that the illness tended to be monophasic, with self-limited clinical course. The first case of recurrence of Susac syndrome 18 years after remission was reported by Petty et al (5) in a woman aged 51 years. Our case also documents the possibility of multiphasic disease course. Two epileptic seizures occurred 7 years before the development of characteristic clinical triade. We suppose that it could be the first phase of the disease, caused by cerebral microangiopathy that manifested with an epileptic syndrome. When evaluating patients with a distant history of this syndrome, clinicians should be aware of the possibility of its late recurrence.

The most common manifestations of brain involvement in Susac syndrome are related to cognitive deficit, dizziness, ataxia, and corticospinal tract dysfunction (3,5). As evidenced by our case, epileptic seizures may also be part of the clinical spectrum of Susac syndrome. These symptoms, however, have not been described in association with this syndrome before (Table 1).

Although approximately less than 100 cases of this syndrome have ever been reported, Susac syndrome is probably more common than it is thought (6). It is caused by microangiopathy of unknown origin. Despite the unknown pathogenesis, it is suspected that the disease has an autoimmune basis because some of the patients have nonspecific low-titer of antinuclear antibody or rheumatoid factor tests but no definitive connective tissue disease (1,5). No procoagulant state has been documented consistently. Antiphospholipid antibodies, factor V Leiden mutation, and protein S deficiency were found in rare cases. Some authors postulated that Susac syndrome was a manifestation of the vasospastic syndrome. The onset of the symptoms (pregnancy, or hormone replacement therapy) could also indicate hormonal influence on the pathogenesis, but this could be a coincidence (5).

There is no consensus on the treatment of Susac syndrome. Most patients receive immunosuppressive therapy (3,7-9). Neurologists must be aware of this syndrome in young people in whom multiple sclerosis is the principal differential diagnosis. Early recognition of the syndrome is important because the treatment with immunosuppressants may minimize persistent neurological, visual, and audiologic sequelae. To our knowledge, this is the first report of the patient with Susac syndrome documented in Slovak Republic.

**References**


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