

# Neurological, otolaryngological and ophthalmological implications of Susac syndrome – a case report

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**Abstract.** – Susac syndrome is an endotheliopathy affecting the arterioles of the brain, retina, and inner ear. Many cases of Susac syndrome are underdiagnosed, mainly at the early stages of the disease, while prompt diagnosis enables a speedy recovery. Immediate treatment can halt disease progression and even prevent future disability.

We report a case of Susac syndrome, describe the difficulties in the diagnosis of this case, and include a detailed history of a 35-year-old man via the presentation of extensive laboratory work-up and imaging studies. Audiometry showed sensorineural hearing loss of about 75 dB in the left ear. Ovoid lesions of the corpus callosum in magnetic resonance (MR) were present as were advanced binocular ophthalmological changes in fluorescent angiography. Methylprednisolone with acetylsalicylic acid and intravenous immunoglobulin (IVIg) were implemented with a positive outcome (clinical and audiometric improvement).

Key Words:

Susac syndrome, Imaging studies, Diagnostic implications, Treatment.

## Introduction

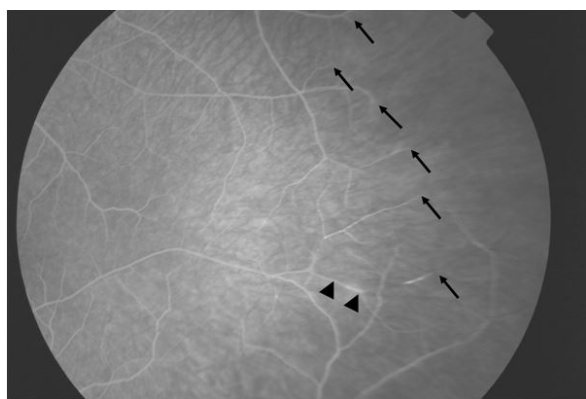
Susac syndrome is a rare neurological disorder described first time in 1979 and named after neurologist J.O. Susac. The characteristic clinical triad of this disease includes encephalopathy, hearing loss, and branch retinal artery occlusions<sup>1-3</sup>. The pathogenesis of this syndrome is unknown, but an autoimmune background is suspected. The mechanisms, which have been already described, include an autoimmune damage and inflammation-related occlusion of the microvessels in brain, retina, and inner ear<sup>1-5</sup>.

## Description of the clinical case

A 35-year-old Caucasian male started to complain of vertigo, fatigue, irritability, drowsiness

during the day, numbness of the tongue and mouth, and a buzzing noise in his ears. Audiometry revealed sensorineural hearing loss of about 75 dB in the left ear (Figure 2). After two months, the symptoms relapsed and unstable balance, problems with short-term memory, and disorientation in time and in space were present. Video-electroencephalography (EEG) revealed numerous irregular theta waves generated in the anterior leads. A small number of delta waves were also present and localized in the temporal region. An elevated level of albumin and an IgG level (increased IgG index) without oligoclonal bands were detected in the cerebrospinal fluid (CSF) and an increased IgG concentration in the serum was identified.

Magnetic resonance imaging showed numerous macular and ovoid lesions in both cerebral hemispheres (Figure 1), most of which ranged from 5 to 6 mm and were localized periventricularly in the frontal and temporal lobes and in the corpus callosum. They were spreading peripherally and were presented as hyperintense lesions (high-signal changes) in T2-weighted images with intravenous contrast and FLAIR (fluid attenuated inversion recovery) sequences. The biggest change was observed in the left lobar of the corpus callosum and amounted to 11 mm. A similar lesion was localised periventricularly in the frontal lobe and was as much as 10 mm. Moreover, on the left hemisphere of the cerebellum a 4 mm lesion was present. After intravenous contrast, pathologic enhancement was not observed. Because of the non-specific MRI finding, multiple sclerosis was suggested. The neoplasm was excluded. Methylprednisolone and mannitol were implemented intravenously with a positive outcome. The patient was discharged from hospital with the diagnosis of viral encephalitis associated with viral cochlear hearing injury.



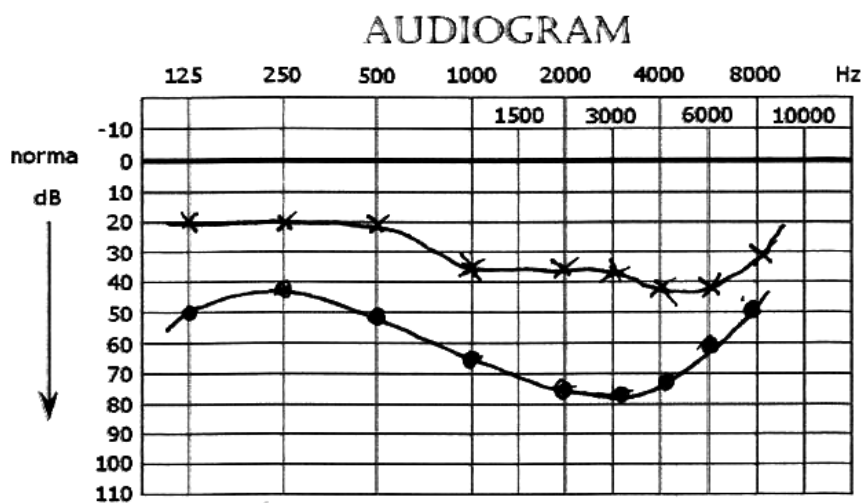
**Figure 1.** Fluorescein angiography, demonstrating the occlusion of a retinal artery (arrows) and leakage of the vessel wall (arrowheads).

Three months later, sudden drowsiness, disorientation, concentration and memory disorders were present and the patient was urgently admitted to the neurological unit. Auto- and allo-psychological disorientation, recent memory disorders, and disinhibition were present. The patient revealed stiffness of the neck, hypoacusia of the left ear, a slight impairment of the coordination of the lower limb. Infectious and immunologic outcomes were negative. Laboratory tests did not reveal HIV, HBV, HCV, *Borrelia burgdorferi* antibodies, *Chlamydia trachomatis* antibodies, antinuclear antibodies, anti- $\beta$ -2 glycoprotein I, anti-cardiolipin, cryoglobulins, pANCA/MPO or cANCA/PR3 in the class of IgG. Fluorescence retinal angiography showed a pattern compatible with resolved branch retinal artery occlusion (BRAO) of both eyes and demonstrated multifocal arteriolar disease in the retinal periphery

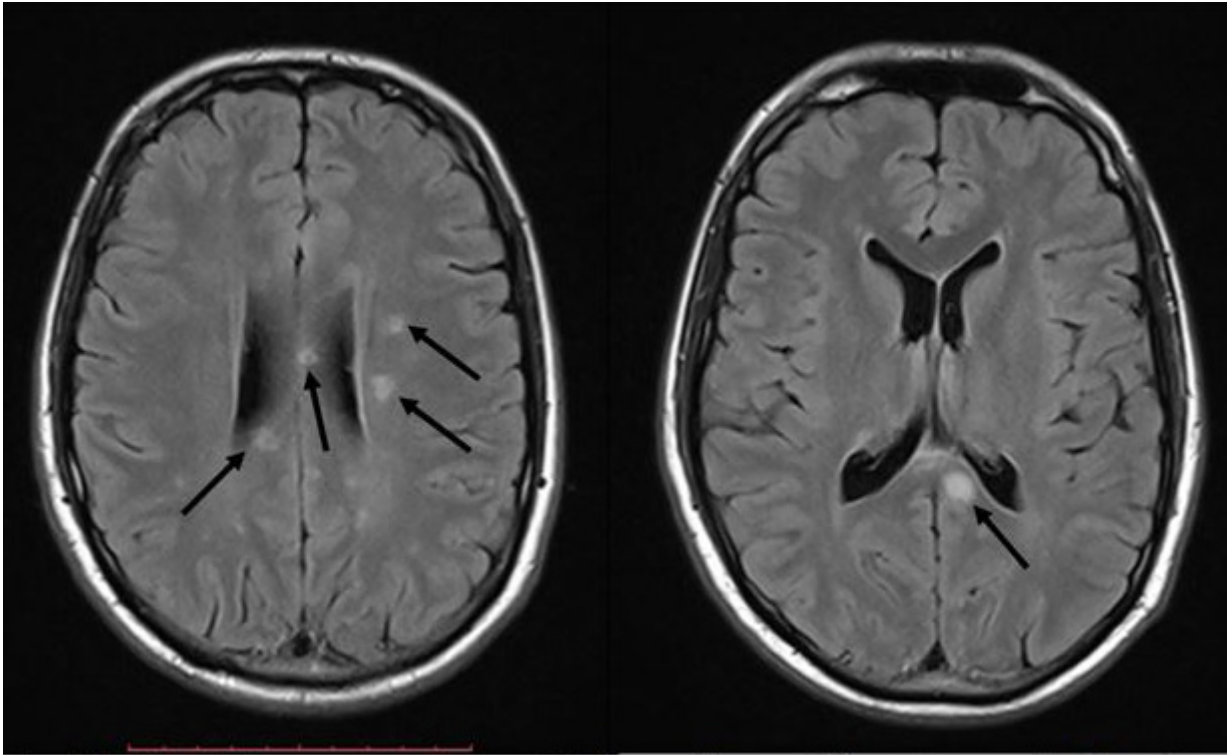
(Figure 1). An audiometric examination revealed a slight (40 dB) sensorineural hearing loss (Figure 2). The presence of clinical signs and imaging outcomes enabled a final diagnosis of Susac syndrome. Immunoglobulin infusions (a total dose of 210 g) were implemented with a good clinical outcome.

## Discussion

The age of the patient in question was characteristic for the development of initial symptoms during the natural course of Susac syndrome. This endotheliopathy is present mainly in young people aged 20-40 years old, predominantly women<sup>3-5</sup>. In this case, at the onset of the disease, mainly otolaryngological symptoms were present such as vertigo, fatigue, irritability, drowsiness, numbness of the tongue and mouth, and a buzzing noise in the ears. Audiometry allowed an assessment of the sensorineural hearing loss at low and mild frequency perception, with an average loss of 75db (in a control examination of 40 dB). The same intensity of hearing lost has been reported in other studies with predominant involvement of the middle and low tones<sup>6</sup>. In Susac syndrome, the hearing disorders are caused by the infarction of the cochlear apex in the vascular territory of small end arteries<sup>3,4,7,8</sup>. The symptoms might be unilateral or bilateral and are usually asymmetric and progressive. The clinical course is usually self-limited, fluctuating, and monophasic<sup>5,9</sup>. Recurrent attacks and spontaneous resolution are occasionally described<sup>1,2,9</sup>. The cranial nerves are not involved in this disease.



**Figure 2.** Audiogram: 75 dB sensorineural lowering of the hearing level with predominant involvement of the middle and low tones; the improvement after treatment (40 dB sensorineural lowering of the hearing level).



**Figure 3.** Axial T1 MR image showing multiple small round hypointense lesions (*arrows*) located in the corpus callosum.

Even electroencephalogram (EEG) contributes little to the diagnosis. This examination is often conducted at the beginning of the neurological evaluation of Susac syndrome. In this case, EEG revealed the presence of numerous theta and delta waves localized in the temporal and parietal regions. In Susac syndrome, a frequently generalized slowing of brain waves (usually attributed to widespread vascular involvement) and intermittent frontal rhythmic delta activity is present (delta waves are suggestive of encephalopathy)<sup>10</sup>.

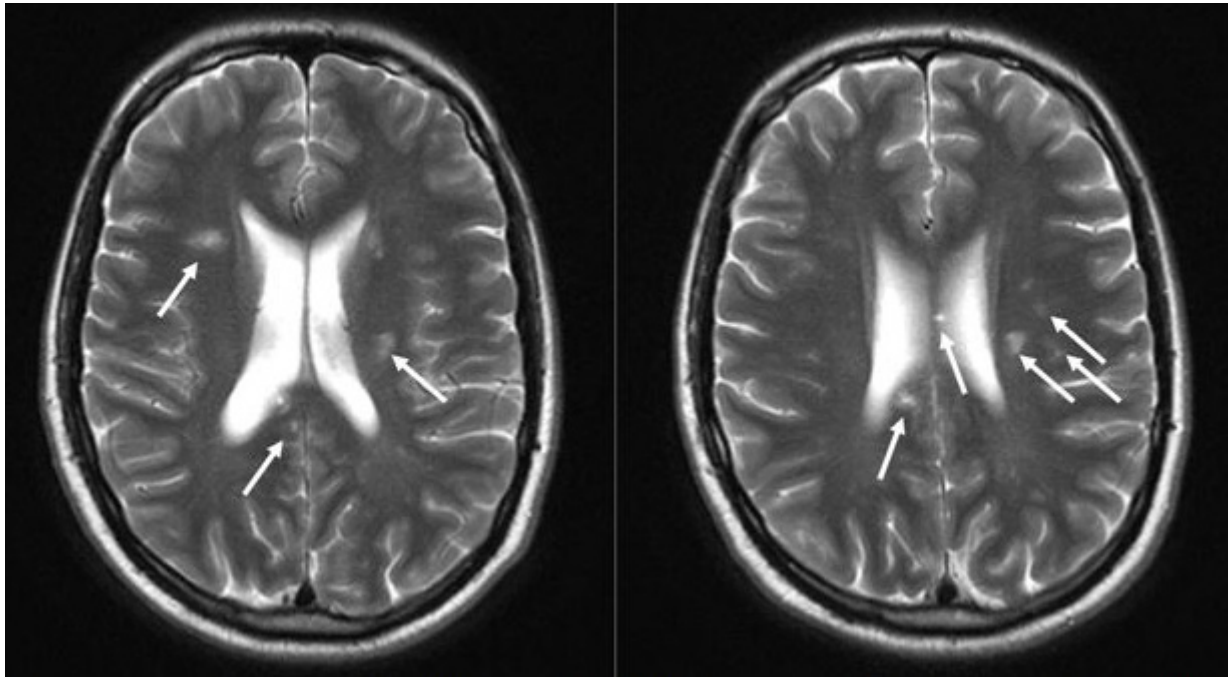
Cerebrospinal fluid (CSF) revealed elevated levels of albumin and IgG level and an increased IgG index  $[(\text{CSF-IgG}/\text{CSF-Albumin})/(\text{Serum-IgG}/\text{Serum-Albumin})]$  without oligoclonal bands. The changes of cerebrospinal fluid are not specific; however, elevated IgG is described in the literature<sup>11</sup>. The other laboratory tests are not characteristic for Susac syndrome and negative viral and bacterial tests are usually reported<sup>12</sup>.

After the short-term recovery, the patient started to complain of unstable balance, disorders connected with orientation in time and in space, and problems of short-term memory. In Susac syndrome, the symptoms usually develop over between several weeks and two years, and patients with this endotheliopathy often do not

exhibit the complete triad at the beginning of the disease<sup>2,9</sup>. Thus, the final diagnosis is delayed for many months or years, whereas immediate treatment can halt disease progression and even prevent future disability<sup>2</sup>.

Magnetic resonance showed the changes characteristic for Susac syndrome (Figures 3 and 4). Callosal ovoid lesions dominated in the central area and the greatest change was also localized there. The changes were in addition present in the peri- and subventricular areas as high-signal changes in T2-weighted images with intravenous contrast and FLAIR sequences (Figure 4). In T1-weighted MR images, hypointense areas were assessed (Figure 3), which are usually present in the subacute or late phase of the disease<sup>8</sup>.

In this case, the patient did not suffer from any of the ophthalmologic disorders, which also hindered the final diagnosis. Nevertheless, fluorescence angiography of the eyes showed typical branch retinal artery occlusions in both eyes, which were localized peripherally and, thus, the acuity and visual field were proper (Figure 1). This examination, together with magnetic resonance and audiometry, enabled the final diagnosis of Susac syndrome. Because encephalopathy is usually present at the onset of this syndrome, it



**Figure 4.** Transverse fast spin-echo T2-weighted MR image of the brain obtained through the level of the corpus callosum showing multiple small hyperintense lesions (arrows) located in the corpus callosum.

should be differentiated from neurological diseases – such as multiple sclerosis, cerebral infarction, acute disseminated encephalomyelitis, migraine, sarcoidosis and CNS infections<sup>9,10,13,14</sup>.

In this case, methylprednisolone with acetylsalicylic acid (75 mg/day) and IVIG (at a total dosage of 210 g) were implemented with a positive outcome. Such treatment enabled a slow tapering off of glucocorticosteroids. In Susac syndrome, the positive effect of immunosuppression is observed; however, the best treatment still needs to be defined (controlled clinical trials). The implementation of glucocorticosteroids in 90% of patients concludes with a diminution of ophthalmological, otolaryngological and neurological symptoms<sup>15</sup>. Moreover, combined treatment with cyclophosphamide or azathioprine is described as very effective in the literature<sup>16</sup>.

#### Conflicts of interest

The authors declare no conflicts of interest.

#### References

- 1) AUBART-COHEN F, KLEIN I, ALEXANDRA JF, BODAGHI B, DOAN S, FARDEAU C, LAVALLÉE P, PIETTE JC, HOANG PL, PAPO T. Longterm outcome in Susac syndrome. *Medicine (Baltimore)* 2007; 86: 93-102.
- 2) GROSS M, ELIASHAR R. Update on Susac's syndrome. *Curr Opin Neurol* 2005; 18: 311-314.
- 3) VALMAGGIA C, SPEISER P, BISCHOFF P, NIEDERBERGER H. Indocyanine green versus fluorescein angiography in the differential diagnosis of arteritic and nonarteritic anterior ischemic optic neuropathy. *Retina* 1999; 19: 131-134.
- 4) RENNEBOHM R, SUSAC JO, EGAN RA, Daroff RB. Susac's syndrome-update. *J Neurol Sci* 2010; 299: 86-91.
- 5) GRYGIEL-GÓRNIAK B, PUSZCZEWICZ M, CZAPLIKA E. Susac syndrome--clinical insight and strategies of therapy. *Eur Rev Med Pharmacol Sci* 2015; 19: 1729-1735.
- 6) MASS M, BOURDETTE D, BERNSTEIN W, HAMMERSTAD J. Retinopathy, encephalopathy, deafness associated microangiopathy (the RED-M syndrome): three new cases. *Neurology* 1988; 38(Suppl): S215.
- 7) ROESER MM, DRISCOLL CL, SHALLOP JK, GIFFORD RH, KASPERBAUER JL, GLUTH MB. Susac syndrome-a report of cochlear implantation and review of otologic manifestations in twenty-three patients. *Otol Neurotol* 2009; 30: 34-40.
- 8) ALLMENDINGER AM, SPEKTOR V, DESTIAN S. CT and MR imaging of Susac syndrome in a young male presenting with acute disorientation. *Clin Imaging* 2010; 34: 138-142.
- 9) PAWATE S, AGARWAL A, MOSES H, SRIRAM S. The spectrum of Susac's syndrome. *Neurol Sci* 2009; 30: 59-64.

- 10) WOOLRIDGE D, STEFANELLI M, HOPPE B. Susac syndrome with frontal intermittent rhythmic delta activity (FIRDA). *Can J Neurol Sci* 2006; 33: 403-406.
- 11) RENNEBOHM RM, LUBOW M, RUSIN J, MARTIN L, GRZYBOWSKI DM, SUSAC JO. Aggressive immunosuppressive treatment of Susac's syndrome in an adolescent: using treatment of dermatomyositis as a model. *Pediatr Rheumatol Online J* 2008; 6: 3.
- 12) GARCÍA-CARRASCO M, JIMÉNEZ-HERNÁNDEZ C, JIMÉNEZ-HERNÁNDEZ M, VOORDUIN-RAMOS S, MENDOZA-PINTO C, RAMOS-ALVAREZ G, MONTIEL-JARQUIN A, ROJAS-RODRÍGUEZ J, CERVERA R. Susac's syndrome: an update. *Autoimmun Rev* 2011; 10: 548-552.
- 13) FARRI A, ENRICO A, FARRI F. Headaches of otolaryngological interest: current status while awaiting revision of classification. Practical considerations and expectations. *Acta Otorhinolaryngol Ital* 2012; 32: 77-86.
- 14) CAMA E, SANTARELLI R, MUZZI E, INCHEI I, CURTOLO S, DI PAOLA F, ARSLAN E, FACCINI E. Sudden hearing loss in sarcoidosis: otoneurological study and neuroradiological correlates. *Acta Otorhinolaryngol Ital* 2011; 31: 235-238.
- 15) TASHIMA K, UYAMA E, HASHIMOTO Y, YONEHARA T, UCHINO M. Susac's syndrome: beneficial effects of corticosteroid therapy in a Japanese case. *Intern Med* 2001; 40: 135-139.
- 16) DÖRR J, RADBRUCH H, BOCK M, WUERFEL J, BRÜGGEMANN A, WANDINGER KP, ZEISE D, PFUELLER CF, ZIPP F, PAUL F. Encephalopathy, visual disturbance and hearing loss-recognizing the symptoms of Susac syndrome. *Nat Rev Neurol* 2009; 5: 683-688.