

## Susac's syndrome: 2 cases without hearing loss

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### Abstract

**Objectives:** Susac's syndrome is a disease of the microvasculature in the brain, inner ear (cochlea and vestibular apparatus) and retina that consists of a clinical triad of encephalopathy, hearing loss and visual disturbance. It is usually seen in young women. It is first defined by Susac et al. in 1979. Diagnosis is often difficult because the classic triad may take up to 2 years to develop and radiological findings are easily confused with multiple sclerosis. Also, encephalopathy may mask some other findings.

**Case:** We present two cases that we think are particularly instructive because they were male patients, had somewhat unusual presenting symptoms, had no accompanying hearing loss, required relatively less aggressive and less sustained immunosuppression than usual, and followed a relatively short and benign course, without relapse and with excellent outcome.

**Conclusion:** This two case serve as good examples of the apparent efficacy and sufficiency (in their cases) of Intravenous immunoglobulin for Susac's syndrome

**Key words:** Susac's syndrome, Hearing loss

### Introduction

Susac's Syndrome is usually seen in young women and characterized by microvascular occlusion and either microischemia injury or microinfarction in the brain, retina, and inner ear. It can cause a wide spectrum of neuro-psychiatric symptoms, sensorineural hearing loss, vestibular dysfunction, and a spectrum of visual symptoms, including branch retinal arteriolar occlusion (1-5). Susac syndrome appears to represent an autoimmune microvascular endotheliopathy. It is first defined by Susac et al. in 1979 (5). It typically occurs between ages 18 and 50, with a mean age of 25. Female to male ratio is 5 (1-4).

Although presenting symptoms vary, the most common one is headache (6-9). 75% of the patients have cognitive and behavioral symptoms (1,3,4,5,6,8). Because the disease is a microvasculopathy with multiple lesions, the variety of neurological symptoms is wide, according to the affected region. In addition to cognitive dysfunction, ataxia, hemiparesis, paresthesias, brisk deep tendon reflexes, Babinski sign, bladder dysfunction, and seizures may be seen (4,10).

The typical ophthalmological finding is branch retinal artery occlusion (BRAO) with associated visual field deficit (1,2). Fluorescein angiography typically reveals segmental hyperfluorescence and leakage in one or more vessels. The specific audiologic finding is bilateral low frequency sensorineural hearing loss (11-14).

The disease may follow a relapsing and remitting course. However, full and sustained remission after an initial attack has been reported, as have very aggressive forms with frequent attacks and devastating outcome. Relapses may occur despite aggressive immunosuppressive treatment, particularly if treatment is tapered too much, too soon. Moreover, if the treatment is inefficient or delayed; varying degrees of visual, auditory or neurological sequelae can occur. (13-16). Prompt aggressive, and sustained immunosuppressive therapy has been advocated for Susac syndrome, with a realization that there is a spectrum regarding the amount of treatment needed. (14-17).

### Case 1

A 25 year-old male patient was brought to the psychiatry outpatient clinic by family members due to decreased social interaction and change in personality. In addition to acute psychotic behaviors, neurologic findings were evident, and MRI revealed a few plaque-like lesions both in the periventricular region and corpus callosum. These findings prompted admission. He was disoriented, agitated, had increased need for sleep, incoherent speech and mild left central facial paralysis. He had a right ataxia and an extensor Babinski reflex on the right. Remaining neurological examination was inconclusive. CSF analysis revealed no cells, but a protein level of 280 mg/dl (N:15-45 mg/dl).

Oligoclonal band test was negative. Blood tests revealed no evidence of systemic inflammation. ANA, ANCA, ACE were negative or normal.

On the second day of hospitalization, the patient developed right hemiparesis, and repeat cranial MRI revealed an increased number of lesions (with enhancement) in white matter, especially in the corpus callosum, and leptomeningeal enhancement (Fig. 1ABC). EEG showed diffuse slow (theta, delta) waves. A diagnosis of Susac Syndrome was made after seeing many occlusions in FFA (Fig. 1D). He did not cooperate in audiometric examination, but he was not complaining of any auditory symptoms. Ear examination and whispering test were reported as normal. He was initially given methylprednisolone 1 g/day for 5 consecutive days but no improvement was noted. Intravenous immunoglobulin (IVIG), 0.4 g/kg/day was given for the next 5 days.

During these 5 days, his right hemiparesis and central facial paralysis improved, and they vanished after the subsequent week. His speech became meaningful, he became cooperative, more oriented and his ataxia almost disappeared. A repeat MRI (on second week of hospitalization) showed that the supratentorial and infratentorial lesions had significantly decreased in number and size, and there was no longer any leptomeningeal enhancement. After the second week, when the patient was observed as more cooperative and not agitated, audiometric tests were applied and were normal. Also, he was no longer noting visual symptoms, and a repeat FFA showed subsidence of his previous abnormalities. Then he was discharged to continue the monthly IVIG therapy in outpatient setting. One month after discharge examined his neurologic exam was completely normal. His EEG showed a normal wave pattern, with normal amplitudes and rhythm.

This patient has now been followed for one year, during which time he has been asymptomatic and his only treatment has been monthly IVIG (0.4 g/kg/day).

## Case 2

A 22 year-old male patient consulted an ophthalmologist after noticing some dark areas in his visual field when he woke up in the morning. He was complaining of being unable to see the lower halves of objects with his right eye. FFA revealed BRAO (fig. 2AB). The patient was given hyperbaric oxygen therapy for 5 sessions but no alleviation was observed in his complaints.

Neurology consultation was requested and revealed that he had been having a unilateral throbbing headache accompanied with nausea, photophobia and phonophobia for a two months. He had no motor deficits, but had bilateral achilles clonus with 3-4 beats and brisk deep tendon reflexes in both lower extremities. Cranial MRI, revealed gliotic lesions in periventricular area and corpus callosum (fig. 2CD).

His blood tests revealed no evidence of systemic inflammation. CSF analysis revealed no pleocytosis, a negative oligoclonal band test, but a protein level was 170 mg/dl. The distribution of the lesions in cranial MRI, the branch retinal arteriolar occlusions, and the CSF results led to a diagnosis of Susac Syndrome. His audiometric tests were normal. He was treated with methylprednisolone 1 g/day for 7 consecutive days, but his symptoms did not subside and he did not otherwise seem to improve. Then, he received IVIG 0.4 g/kg/day for 5 days, after which his symptoms improved, his headaches fully resolved, and a follow-up MRI (2 weeks later) showed a marked decrease in lesion burden.

Repeat FFA showed some residual zones of infarction. After discharge, he was treated only with monthly IVIG.

He has now been followed for one year and has shown remarkable recovery, with no additional MRI lesions and no evidence of disease relapse. He is still receiving monthly IVIG.

## Discussion

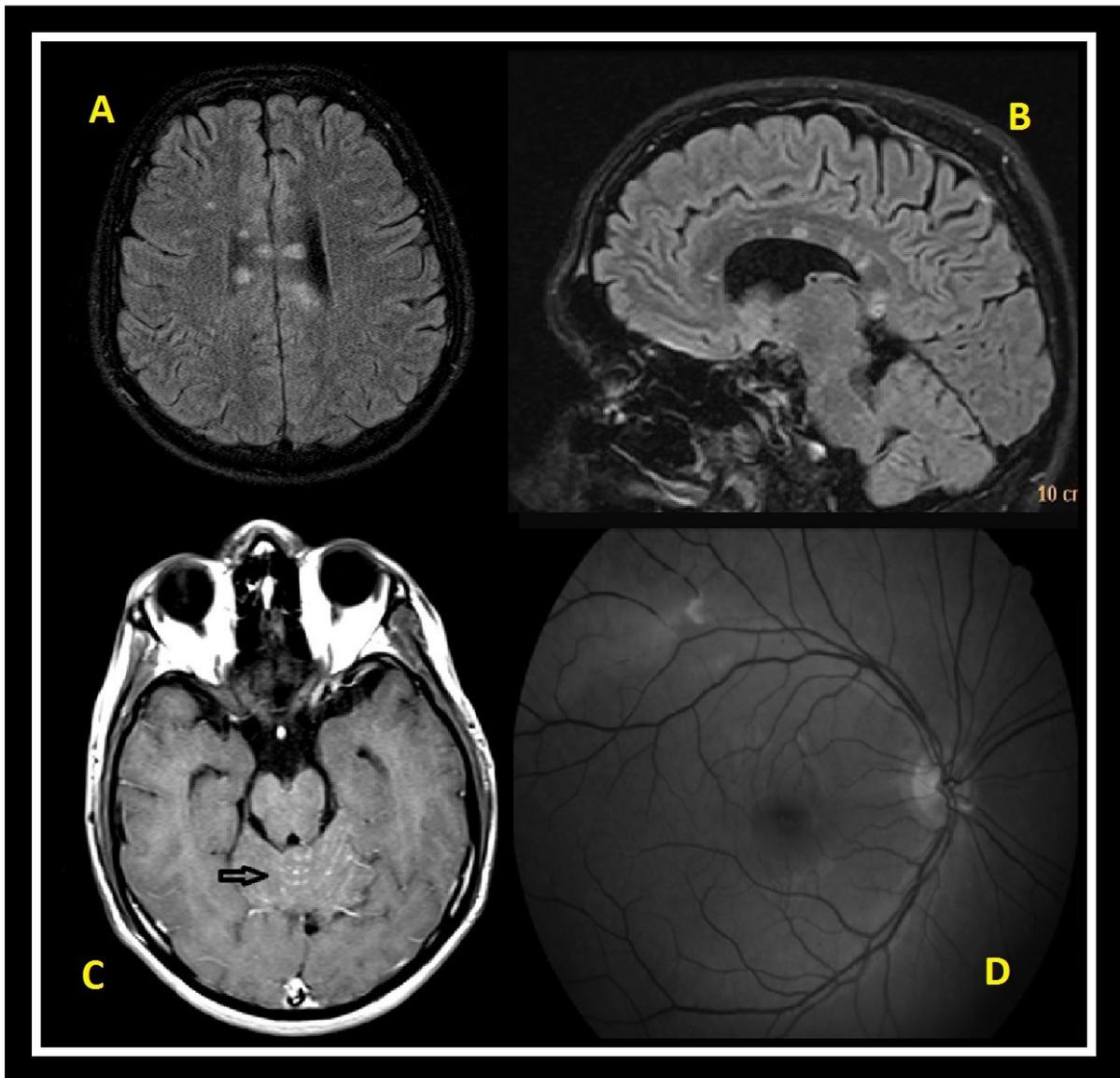
Susac Syndrome is a disease of the microvasculature in the brain, inner ear, and retina, that consists the clinical triad of encephalopathy, hearing loss and visual loss. It is seen most commonly in young women, has a wide variety of clinical manifestations, and is important because it can cause devastating sequelae, is treatable, and is often confused with multiple sclerosis, both clinically and radiologically (1,3,4,5,8,17).

The most common symptom is headache. Visual complaints may mislead the physician to a diagnosis of migraine (1,3,5-9). Moreover, the patients may have psychiatric symptoms, changes in personality and present with encephalopathy. Many patients initially consult a medical doctor because of visual disturbance or hearing loss, or both (2,7,12,13).

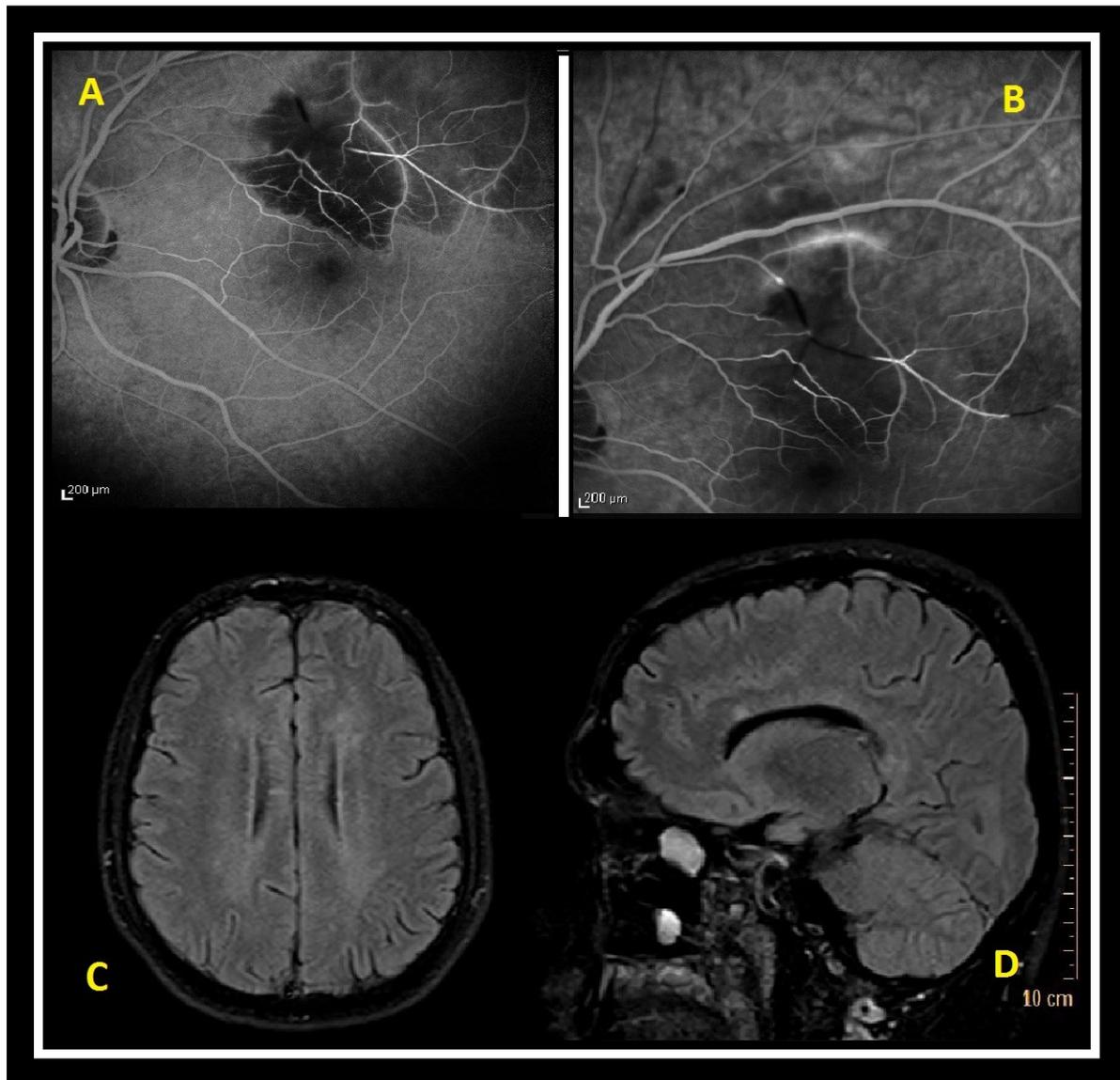
If encephalopathy occurs, it may be hard to evaluate the patient in terms of visual and audiologic examination, which in turn complicates the diagnosis. There have been 2 cases in literature from Turkey (18,19). This may indicate underdiagnosis, but could, conceivably, also be due (at least in part) to a decreased incidence in the Turkish population.

In our cases, the reasons to consult a hospital were the family members' recognition of personality change and increased need for sleep in our first case, and visual loss in the second case. It should be appreciated that patients with encephalopathy or a psychotic condition may have problems with expressing their visual and hearing loss.

The retinal arteriolar occlusions were detected after we suspected Susac Syndrome and ordered a retinal angiography. The typical visual loss in this disease is a segmental visual field loss which is secondary branch retinal artery occlusion.



**Figure 1.** ABC: Leptomeningeal contrast enhancement in inferior fossa in T1 weighted image, Elliptical hyper intense lesions in corpus callosum and white matter in axial FLAIR MRI, Elliptical hyper intense lesions in corpus callosum in sagittal FLAIR MRI. D: Peripheral retinal artery occlusions in FFA



**Figure 2.** AB: Peripheral retinal artery occlusions in the FFA. CD: Lesions in corpus callosum in sagittal FLAIR MRI and elliptical hyperintense lesions in corpus callosum

FFA findings (BRAO and segmental hyperfluorescence and leakage) contribute greatly to our ability to make a diagnosis of Susac syndrome(2,15). Both of our patients had retinal artery occlusions in FFAs and benefited from IVIG therapy, the first patient without retinal sequelae and the second one with mild retinal sequelae. These occlusions are thought to be caused by endothelial injury and swelling, rather than emboli (2).

In Susac syndrome, a low frequency sensorineural hearing loss is most common. It is thought to be due to the microvascular ischemic injury of the apical cochlea, and may not be seen in some cases at the time of diagnosis or during the disease process (10,14). Thus, in our first case, the patient was unable to cooperate with audiometric tests because of encephalopathy, but the whispering test was reported as normal. He had no auditory complaints during the treatment. In the second case, our patient stated that he had had a hearing loss for a short period of time but

had not consulted a physician. He also had no auditory complaints during the follow-ups.

Key MRI characteristics of Susac Syndrome are the typical subcortical white matter lesions, particularly in the corpus callosum. The central part of the corpus callosum is expected to be injured, and as the active lesions resolve, central callosal “holes” may develop. Typically, the callosal lesions consist of round lesions (“snowballs”) of various size, but linear defects (“spokes”) may also be seen in the callosum. These white matter lesions tend to enhance while the disease is active. Lesions may be seen in other subcortical white matter (particularly in periventricular regions) and also in deep grey matter. Leptomeningeal enhancement is common. Our two cases had MRI findings typical of Susac Syndrome. In the first case, some of those lesions were contrast-enhancing. There was leptomeningeal contrast enhancement in the first case, but not in the second. Microinfarction is the fundamental histopathologic pathology in the brain

tissue, and this appears to be due to an ischemic microvascular endotheliopathy, with swollen endothelial cells (6,8,11,14).

In Susac Syndrome, CSF analysis may show high protein levels, pleiocytosis, or both. The oligoclonal band test is expected to be negative (5,6,8,16,14). In fact, high protein levels in CSF and oligoclonal band negativity led us to exclude multiple sclerosis in our cases. Protein levels being this high and oligoclonal band test being negative are important in differential diagnosis with multiple sclerosis (14,16).

A wide spectrum of EEG findings have been reported in susac syndrome, from nonspecific slow wave abnormalities to triphasic wave patterns that are consistent with encephalopathy, (6,10). Our first case had an EEG indicating encephalopathy.

Although Susac syndrome may be monocyclic and self-limited and may fully remit within several months, some patients experience early and/or late relapses, and some patients experience a much more prolonged and severe course of active disease than did our patients.

Because the immunopathogenesis and clinical course of Susac syndrome appear to have much in common with that of juvenile dermatomyositis (both representing autoimmune microvascular endotheliopathies, but affecting different triads of tissues), recommendations for treatment of Susac syndrome have been based on what has been effective and necessary to successfully treat juvenile dermatomyositis (JDM). As with JDM, there is a spectrum of treatment needs for Susac syndrome, due to a spectrum of disease intensity/severity and disease course/duration. As with JDM, a patient whose Susac syndrome is mild in severity and follows a relatively short monocyclic course will not need as aggressive or as prolonged immunosuppression as patients with much more severe and/or much more prolonged and/or relapsing disease. Our two patients were fortunate in that their Susac syndrome, though initially intense, subsided relatively quickly and followed a relatively mild and short course, such that they appeared to require no more than monthly IVIG, after the initial weeks of their illness. Other patients need much more aggressive and much more sustained immunosuppression. For example, it is sometimes difficult to control extremely intense/aggressive Susac syndrome even with a combination of cyclophosphamide, high dose corticosteroid, IVIG, plasma exchange, and rituximab (20).

The long term outcome of Susac syndrome has not yet been well studied (13-,15). Some patients, like our two patients, have an excellent outcome; others experience a devastating outcome, with severe disability and severely diminished quality of life. Much depends on where a given patient's Susac syndrome falls along the spectrum of disease severity. Much depends on how well and how promptly a given patient's treatment needs are recognized and appropriately met.

We considered these cases valuable to present because they were male patients, had somewhat unusual presenting symptoms, had no accompanying hearing loss, required relatively less aggressive and less sustained immunosuppression than usual, and have followed a relatively short and benign course, without relapse and with excellent outcome. They also serve as good examples of the apparent efficacy and sufficiency (in their cases) of IVIG.

### Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The first case was presented as poster presentation at the 16th Congress of the European Federation of Neurological Societies, 8-11 September 2012, Stockholm, Sweden

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