Microangiopathy of the Brain, Eyes and Ears: A Case Report

Ahmad Mumtaz, MD
Melanie Ward, MD
Muhammad Taimoor Khan, MD
Charleston Area Medical Center.

Corresponding Author: Ahmad Mumtaz, MD, 415 Morris St. Suite 300, Charleston, West Virginia. Email: amdmtz98@gmail.com.

Abstract
Susac syndrome is a neurological condition which affects the brain, the eyes, and the ears, hence presenting with a triad of encephalopathy, sensorineural hearing loss and branch retinal artery occlusion. It is a very rare condition. It is theorized that Susac syndrome has an immunologic basis. This case report sheds light on a Caucasian woman diagnosed with Susac syndrome in West Virginia. The patient presented to the ER with syncope and altered mental status. The MRI showed multiple infarcts involving corpus callosum. Differential diagnoses were ruled out, and she was started on intravenous methylprednisolone and intravenous immunoglobulin to treat her condition.

Case
A 50 year old Caucasian female presented to the emergency room in a confused state with complaints of bilateral hearing loss, gait imbalance and progressive encephalopathy over the course of 2-3 weeks. She had an episode of syncope before the onset of these symptoms. An outpatient magnetic resonance imaging (MRI) was performed after the episode of syncope and revealed multiple punctate bilateral foci of abnormally increased signal intensity on the diffusion-weighted imaging (DWI) sequence with a corresponding signal void on the apparent diffusion coefficient (ADC) map. Some of these lesions involved corpus callosum (figures 1 and 2).

Figure 1. Diffusion-weighted imaging (DWI) on initial brain MRI demonstrating acute infarcts involving the corpus callosum.

Figure 2. FLAIR imaging on initial MRI demonstrating “cannonball” lesion in the corpus callosum. Subsequent MRI performed after 10 days from the first MRI showed progression of the previously found lesions (Figure 3).

There was no enhancing lesion. Outpatient audiology evaluation revealed bilateral hearing loss in a cochlear pattern. The following week, she presented to the emergency department with transient confusion, which resolved during her ED visit. Computed tomography angiography (CTA) of her head and neck were unremarkable at that time. The following week, she developed progressively worsening encephalopathy and gait imbalance. She ultimately re-presented to the ED and was admitted. She denied subjective vision changes.

Subsequent MRI performed after 10 days from the first MRI showed progression of the previously found lesions (Figure 3).

There were numerous foci of increased signal on DWI involving the cerebellar and cerebral hemispheres. Repeat intracranial vessel imaging and transthoracic echocardiogram were unremarkable. Cerebrospinal fluid (CSF) studies revealed markedly elevated protein (192 mg/dL) and slightly elevated glucose (71 mg/dL).

The appearance was nonspecific but suspicious for acute demyelinating process versus ischemic lesions.
Other CSF studies including cell counts, culture, encephalitis panel, angiotensin-converting enzyme, and autoimmune encephalopathy panel were unremarkable. Systemic studies for etiologies of vasculitis including hepatitis panel, HIV serology, ANA, c/p-ANCA, and lupus panel were also unremarkable.

Routine electroencephalogram (EEG) performed after the second MRI manifested a mild degree of encephalopathy of nonspecific etiology. Susac syndrome was felt to be the etiology of her symptoms given her hearing loss, encephalopathy, elevated CSF protein which can be consistent with an inflammatory process, and lack of another more likely diagnosis.

The patient received five days of high dose intravenous methylprednisolone (IVSM) and 2g/Kg of intravenous immunoglobulin (IVIG) during her hospitalization. Maintenance therapy following discharge included monthly IVIG, mycophenolate, and prednisone which was being tapered slowly. The patient reported a significant improvement in her symptoms after initial hospitalization. Outpatient fluorescein angiogram (FA) was subsequently obtained and, despite the patient’s lack of subjective vision changes, revealed extensive ophthalmologic involvement which further supports a diagnosis of Susac syndrome (Figure 4).

Follow-up MRI one month after her initial studies demonstrated improvement and subsequent FA also demonstrated improvement.

Discussion

In 1976, Susac syndrome was first explained by John O Susac. The disease has been called by different self-explanatory names including RED-M (retinopathy, encephalopathy, deafness associated with microangiopathy), SICRET (small infarction of cochlear, retina and encephalitic tissue) and retinocochlear vasculopathy). Several studies have proposed an immune-mediated injury to the small vessels of the brain, retina and inner ear. Vasospastic processes ad coagulopathy has also been pointed out as a possible etiology. It is a rare syndrome, and only around 300 cases have been reported until now. Susac Syndrome is most prevalent among females of 20-40 years of age.

The patient suffering from Susac syndrome might not manifest symptoms indicative of the involvement of all three organ systems at the start. It may take several weeks to 2 years before the involvement of the brain, eyes, and ears is expressed. This patient is an excellent example of how symptoms in Susac may evolve, as initially, she had only hearing changes and MRI abnormalities, followed by the development of encephalopathy, and no subjective vision complaints despite subsequent confirmation of extensive eye involvement.

John Susac observed the onset of personality change before the onset of other symptoms in patients suffering from this order. The patient at hand suffered an attack of syncope that brought her to seek medical attention and subsequent changes in her hearing, gait, and personality. A headache is the most common symptom suggestive of encephalopathy. Other symptoms include cognitive changes, loss of memory, confusion, difficulty speaking, strange behavior and change in personality.

Retinal Involvement can be seen in the form of branch retinal artery occlusion. It can be seen before, during or after the development of encephalopathy. Retinal involvement can cause scotomas or photopsias. The presence of Gass plaques in the mid-segment of an arteriole suggests focal disruption of the endothelium. Fluorescein angiography is an

Figure 3. DWI imaging on repeat MRI 10 days after initial presentation, demonstrating an increased number of acute infarcts, again with some involving the corpus callosum.

Figure 4. Fluorescein Angiography showing Branch Retinal Artery Occlusion
appropriate diagnostic study to demonstrate the hyperfluorescence of the arteriole wall at the site of the lesion. The lack of intraocular inflammation coupled with occlusion of retinal arterioles and a normal choroidal vasculature is very suggestive of Susac syndrome.

Hearing impairment can either be unilateral or bilateral sensorineural hearing loss. In the majority of cases, it is noted to be asymmetrical impairment for low and mid frequencies. Hearing impairment can be seen in addition to vestibular symptoms and tinnitus.

A combination of sensitive diagnostic tests and specific findings allows a clinician to diagnose Susac syndrome accurately. MRI is considered the gold standard to diagnose this condition. Presence of lesions in the central portion of the corpus callosum, which is always affected, is highly indicative of Susac syndrome. Susac syndrome can also inflict radiological changes in other structures of the brain including the cerebellum, cerebellar peduncles, brain stem and thalamus. Small infarctions and microbleeds can also be seen in the white matter in the periventricular and pericallosal areas. However, specificity of white matter lesions is low.

Biopsy shows inflammation with mononuclear infiltrate of the perivascular area. The absence of necrosis points at the vasculopathy instead of vasculitis. CSF analysis reveals an elevated protein in the range of 100-790 mg% and a minimal pleocytosis. EEG is diffusely slow.

The rarity of the disease makes it incumbent to rule out the differential diagnosis. The differential diagnosis includes SLE, Vasculitis, sarcoidosis, dermatomyositis, Sjogren syndrome, cryoglobulinemia, cerebral angiitis.

### Table 1: General features of Susac Syndrome

<table>
<thead>
<tr>
<th>Affected organ</th>
<th>Signs/ Symptoms</th>
<th>Diagnostic tests</th>
<th>Findings on diagnostic tests</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>Headache cognitive changes, loss of memory, confusion, difficulty speaking, strange behavior and change in personality.</td>
<td>MRI, EEG and CSF analysis</td>
<td>Lesions in the central portion of corpus callosum, small infarctions and microbleeds can also be seen in the white matter in the periventricular and pericallosal areas, T2 FLAIR shows typical “snowballs” lesions in the central portions of corpus callosum, T1 weighted MRI shows numerous central callosal “holes”, “strings of pearls” in the internal capsule and various lesions in the genu and splenium of the corpus callosum can be viewed on DWI, increased protein and pleocytosis in CSF and diffusely slow EEG.</td>
<td>Prednisone, Intravenous methylprednisolone, Intravenous immunoglobulin (IVIG), Cyclophosphamide, Mycophenolate mofetil, Azathioprine and Biological therapies</td>
</tr>
<tr>
<td>Eyes</td>
<td>Blurring of vision, painless loss of vision, dark spots (scotomas), flashing lights (photopsias), and sensation of curtain being drawn over a portion of vision.</td>
<td>Fluorescein Angiography</td>
<td>Branch retinal artery occlusion, Gass plaques and hyperfluorescence of the arteriole wall.</td>
<td>Same as above</td>
</tr>
<tr>
<td>Ears</td>
<td>Unilateral or bilateral hearing loss, tinnitus and vertigo.</td>
<td>Audiogram</td>
<td>Unilateral or bilateral sensorineural hearing loss.</td>
<td>Same as above</td>
</tr>
</tbody>
</table>
In order to rule out differential diagnosis the following diagnostic tests should be considered: HIV, herpes simplex virus, hepatitis B and C, Rose Bengal staining, EBV serology, CMV, VZV, Lyme, Mycoplasma, Campylobacter jejuni, Chlamydia, antinuclear antibodies, anti dsDNA, anti-SSA and SSB, anti-beta2 glycoprotein I, IgG, antiphospholipid, anti-thyroglobulin and anti-thyroxin peroxidase antibodies, ENA, anti-Ro, anti-La, anti-RNP, and rheumatoid factor.  

Immunomodulation is the mainstay of treatment. High-dose steroids are initial treatment of choice. Common additional immunomodulation includes mycophenolate and IVIG, but multiple other treatment options including rituximab, cyclophosphamide, and tacrolimus have been suggested. Recent publications propose guidelines for management of Susac syndrome based upon severity. Although a rare disease, prompt diagnosis, and management of Susac syndrome is imperative. Susac syndrome should be considered in the differential diagnosis for patients presenting with encephalopathy especially when associated with hearing or vision changes and concerning MRI findings.

**Conclusion**

Susac syndrome is a rare disorder. Its rarity makes it difficult for less experienced physicians to diagnose the condition and treat it effectively. The multisystem involvement in Susac syndrome makes this disorder of interest to many specialties. The involvement of any system in a manner that Susac syndrome affects the organs should raise suspicion for this disorder. Timely intervention can help to decrease the impairment and morbidity associated with this disorder.

**References**
