CASE REPORT

Susac's syndrome: an immune mediated endotheliopathy laden with challenges and controversies

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The case was presented as a poster in the ANZAN (Australia New Zealand Association of Neurology) ASM 2011 at Hobart.

SUMMARY

Susac's syndrome is a microangiopathy of the retina, inner ear and brain manifesting as a triad of encephalopathy, hearing loss and branch retinal artery occlusion. The pathological mechanism is thought to be an immune-mediated small vessel vasculitis with some pathophysiological similarity to dermatomyositis. Awareness and early recognition of this syndrome is important as early treatment with immunosuppression can minimise cognitive, audiological and visual sequelae. We report a case of a 33-year-old woman who presented with the characteristic syndrome. She was treated with immunomodulatory therapy and remains well 2 years postpresentation with no new events.

BACKGROUND

Susac's syndrome (SS) is a rare but important condition. It is a differential diagnosis of multiple sclerosis (MS) and other white matter diseases like acute demyelinating encephalomyelitis (ADEM) and central nervous system (CNS) vasculitis. Failure to diagnose it and to institute prompt treatment with immunosuppressant therapy may lead serious adverse outcomes.

CASE PRESENTATION

A 33-year-old woman presented in early December 2010, with an intermittent bilateral throbbing headache and blurred vision and photopsia. The initial neurological examination was unremarkable apart from visual field testing demonstrating a right inferior quadrantanopia. She had no significant medical or family history and did not smoke. The MRI of brain performed at that time was reported as being unremarkable. A possibility of migraine was considered.

Given the increased frequency of the headaches, she was started on valproate (for migraine prophylaxis). However, she developed bilateral hearing loss and this was initially thought to be due to valproate and was changed to topiramate.

Within a fortnight she developed an encephalopathy and represented to hospital in late December 2010 with a 3-day history of drowsiness and confusion. She was afebrile but disoriented to place/person/time. Headache and hearing loss had persisted. The remainder of her neurological examination was unremarkable.

INVESTIGATIONS

Fluorescein angiography of the retina showed branched retinal artery occlusion (figure 1). An MRI

of brain was repeated and it revealed the characteristic multifocal supratentorial white matter lesions with involvement of corpus callosum (figure 2) seen in SS. Pure tone audiometry revealed bilateral sensorineural hearing loss (figure 3).

The vasculitis and thrombophilia screen were unremarkable except for a positive antinuclear antibodies with a titre of 1:160 (homogeneous pattern). A lumbar puncture revealed one mononuclear cell and a protein of 1.2 g/L. Cerebrospinal fluid microscopy, culture and sensitivity/cytology/herpes simplex virus PCR were unremarkable and the oligoclonal bands were absent.

DIFFERENTIAL DIAGNOSIS

The diagnosis of SS was made based on the classical triad of encephalopathy, hearing loss and branch retinal artery occlusion (BRAO). This was supported by the evidence on imaging.

The differential diagnosis includes conditions that cause white matter changes on MRI including MS, cerebral lupus, vasculitis including primary cerebral vasculitis, ADEM and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). Cogan's syndrome with its auditory-vestibular dysfunction is also a differential. Distinguishing from other conditions is important as management differs.

TREATMENT

The patient had a good initial response to intravenous methylprednisolone and intravenous

Figure 1 Fluorescein angiogram of retina showing the branch retinal artery occlusion.

To cite: Malhotra A, Reyneke E, Needham M. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-008390

Figure 2 (A) Sagittal fluid-attenuated inversion recovery (FLAIR), (B) axial FLAIR and (C and D) diffusion-weighted imaging (DWI): numerous callosal, hemispheric and posterior fossa white matter lesions. These are associated with several sites of acute small vessel ischaemic change as evidenced by restricted diffusion on the DWI.

immunoglobulin (IVIG). Within 3 weeks of beginning treatment, her mental status improved from being drowsy and disoriented to only mild memory deficits on the Cognistat standardised testing. Other cognitive domains, including orientation, attention, language, construction and reasoning, were within average range. However, on formal neuropsychiatry assessment a week later, she was found to have mild to moderate executive dysfunction and mild to moderate deficits with verbal and visual memory.

She was later started on monthly pulsed intravenous cyclophosphamide and oral steroids. She was discharged to rehabilitation, after more than a month of acute inpatient stay.

OUTCOME AND FOLLOW-UP

The patient is now almost 2-year postattack with no further clinical events and is functionally independent. She has completed six cycles of cyclophosphamide, and continued four weekly IVIG with oral steroids for 2 years. She did tolerate azathioprine and declined rituximab.

DISCUSSION

SS is an immune mediated vascular endotheliopathy characterised by a triad of encephalopathy due to CNS ischaemia, visual changes due to BRAO and sensorineural hearing loss due to cochlear ischaemia. Rarely, vertigo from semicircular canal ischaemia can also be a feature.

More common in young women, the natural history is not well known with only a limited number of cases described in medical literature. Treatment with various immune modulators has been used in this condition with good results, including corticosteroids (first-line of treatment), IVIG, cyclophosphamide, mycophenolate, azathioprine, methotrexate, rituximab and plasmapheresis. Despite the gamut of treatment available for SS, there still are challenges and controversies.

Diagnostically it can be mistaken for multiple other conditions. These include CNS lupus, vasculitides including primary cerebral vasculitis, MS, ADEM, Cogan's syndrome and CADASIL. In our patient, it was initially misdiagnosed as a migraine before the clinical triad and MRI changes became

Figure 3 Pure tone audiometry showing mild to moderate sensorineural hearing loss on the left and moderate to moderately-severe sensorineural hearing loss on the right.

apparent. Headache, often severe and sometimes migrainous in character, is an almost constant problem and may be the major presenting feature.¹ MRI always shows corpus callosum involvement in SS and may be misidentified as demyelination/MS. However, unlike MS the callosal lesions in SS typically involve the central fibres with relative sparing of the periphery.¹

Although some believe SS is mainly self-limited, however, aggressive and prolonged immunosuppression is recommended to prevent complications.^{2–3} It can be fatal.⁴ However, the exact duration of therapy, choice of agent and method of monitoring of disease activity remains uncertain. Gonadal function preservation with gonadotropin-releasing hormone analogues or other fertility preservation methods prior to starting cytotoxic therapy (eg, cyclophosphamide) should be considered in women of childbearing age.⁵ Cochlear implants may be considered when there is severe bilateral hearing loss due to cochlear dysfunction.

Ideally, randomised controlled trials for therapy would be useful but may not be possible due to the rarity of the condition. The SS International Collaborative Study and International Disease Registry set up by Rennebohm et al may help answer some of the dilemmas and provide more insight into this intriguing condition.⁶

Learning points

- ▶ Consider Susac's syndrome as a differential diagnosis in patients who present with an encephalopathy and are found to have white matter lesions on MRI.
- ▶ Diagnosis is made by the presence of the triad of encephalopathy, branch retinal artery occlusion and sensorineural hearing loss.
- ▶ The corpus callosum is usually involved but unlike multiple sclerosis, there is involvement of central fibres which is common with relative sparing of peripheral fibres.
- ▶ Immunosuppressive therapy is recommended and prompt treatment may prevent serious sequelae.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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