SHORT REPORT

Microangiopathy of the brain and retina with hearing loss in a 50 year old woman: extending the spectrum of Susac’s syndrome


Abstract
A 50 year old woman presented with a subacute onset of vertigo and diplopia followed by an encephalopathy with confusion, spasticity, ataxia, myoclonus, and multiple branch retinal arteriolar occlusions and unilateral sensorineural deafness. Brain biopsy confirmed multiple microinfarcts with no vasculitis. After the procedure she had a right iliofemoral deep vein thrombosis and was found to be heterozygous for the factor V Leiden mutation. She was treated with anticoagulants and made a marked recovery with no relapses 6 months after presentation. This case extends the age range at which Susac’s syndrome can present, and raises the possibility that the condition may be associated with abnormalities of coagulation.

Keywords: Susac’s syndrome; activated protein C resistance

Susac et al first described a syndrome in 1979 in two female patients who presented with encephalopathy, retinal arteriolar branch occlusions, and deafness. Brain biopsy showed multifocal microinfarcts and it was suggested that the condition represented a microangiopathy of the brain, retina, and inner ear. Subsequently there have been 36 cases of Susac’s syndrome reported in the literature and although the condition was initially thought to exclusively involve young women between the ages of 18 and 40 years of age, there have been reports of the condition affecting men. We now describe a 50 year old woman with a clinical picture typical of this disorder with histopathological confirmatory findings who went on to have an extensive iliofemoral deep vein thrombosis and was found to be heterozygous for the factor V Leiden mutation.

Case history
A 50 year old right handed woman presented at the end of August 1996 with a 3 day history of intermittent vertical diplopia followed by worsening vertigo, nausea, vomiting, and a low grade headache. Medical history was unremarkable. She had been a live kidney donor to her son in 1995. She smoked 20 cigarettes a day and had been on hormone replacement therapy for 4 years. Examination on admission showed her to have no systemic abnormalities and she was apyrexial. Neurological examination disclosed jerky nystagmus in all directions of gaze and an extensor right plantar response. Investigations showed a normal haematological and biochemical screen as well as MRI of her brain. Four days after admission she developed worsening dizziness, urinary frequency, and limb and truncal ataxia. She then became intermittently confused and drowsy and developed spasticity in the limbs with hyperreflexia and bilateral extensor plantar responses. She was given a 10 day course of acyclovir and thiamine without any improvement, but a 4 day course of intravenous methylprednisolone (0.5 g/day) followed by a reducing course of oral steroids (60 mg prednisolone) produced an appreciable but short lived improvement in her clinical condition.

Further investigations at this time continued to be either normal or negative and included full blood count, erythrocyte sedimentation rate, urea and electrolytes, liver function tests, glucose, thyroid function tests, C reactive protein, serum angiotensin converting enzyme, calcium, phosphate, autoantibody screen in addition to a normal negative serological screen. Viral, Lyme and an atypical pneumonia screen were all negative. Her CSF was analysed on three occasions and each time had less than 5 white cells/ml, but a raised protein concentration (1.7 g/l) with a normal glucose and lactate concentration. Oligoclonal immunoglobulin bands were detected that were identical in the CSF and serum. Brain MRI was repeated and showed a solitary lesion on the T2 scan in the anterior portion of the left globus pallidus (figure A). Chest radiography and CT of the abdomen and pelvis and chest were all normal, as were her ECG, and transthoracic and transoesophageal echocardiogram. The normality of the echocardiogram test is important given the fact that there has been one reported case of Susac’s syndrome with a patent foramen ovale. Bone marrow biopsy (aspirate and trephine) on two occa-
sions showed only non-specific reactive changes. Her EEG showed diffuse slowing bilaterally and cerebral angiography was unremarkable. Ophthalmological review, however, showed retinal arteriolar narrowing with some occlusions and infarcts (figure B) and on audiometry she had a right sided sensorineural deafness to all frequencies although both her visual evoked responses and brain stem auditory evoked responses were normal.

In view of her continued deterioration and the development of generalised non-stimulus sensitive myoclonic jerks, a right frontal lobe burr hole biopsy was undertaken. Cerebral biopsy showed microinfarcts of varying ages with tiny foci of cosinophilic ischaemic neurons in the cerebral cortex and perivascular rarefaction, breakdown of axons, and accumulation of foamy macrophages in the white matter (figure C, D). Four days after this biopsy, despite being on heparin prophylaxis, she developed a right iliofemoral vein thrombosis established by CT and was subsequently found to be heterozygous for the factor V Leiden mutation. The rest of her clotting screen was normal including the level of protein C and S activity. She was started on intravenous heparin and then oral warfarin, which she continues to take now 6 months after her deep vein thrombosis. At the time of this thrombosis she developed abnormal liver function tests which at their worst showed an alanine transaminase concentration of 141 U/l, a γ-GT concentration of 275 U/l, and an alkaline phosphatase concentration of 191 U/l but with a normal bilirubin. These have subsequently returned to normal.

Over the course of the next 3 months she slowly improved on no treatment other than the anticoagulants. She has some mild cognitive impairments with difficulty walking due to a combination of spasticity and ataxia but her arm function and eye movements are now normal. She still has evidence of previous retinal arteriolar occlusions, but no new lesions have developed over the past 3 months and her sensorineural deafness on the right remains unchanged. An MRI performed 2.5 months into her illness disclosed a few scattered non-specific white lesions on the T2 scan with the previously noted lesion in the globus pallidus persisting.

Discussion

This woman fulfilled the criteria of Susac’s syndrome as detailed in the original description by Susac in 1979. She had a microangio-
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The pathologic process underlying this syndrome is not yet fully understood. The clinical triad—microangiopathy of the brain and retina, hearing loss, and visual disturbances—is often accompanied by other clinical manifestations, such as stroke, peripheral nerve involvement, and thrombosis. The role of anticoagulation in the treatment of Susac's syndrome remains unclear, and further investigation is needed to elucidate the relationship between the disease and the factor V Leiden mutation.

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