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Case report

Exquisite response to intravenous immunoglobulin in Susac syndrome during pregnancy

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ABSTRACT

Introduction: From its initial report on two female patients in 1979 by J.O. Susac, Susac syndrome (SuS) or SICRET (small infarctions of cochlear, retinal and encephalic tissue) has persisted as an elusive entity. To date the available evidence for its treatment is based on case reports and case series. The largest systematic review described only 304 reported cases since the 1970s. Here we presented the first reported case to our knowledge in Mexican population and the unusual presentation in a pregnant patient.

Case presentation: A 34-year-old Hispanic woman was brought to the ER in our hospital for apathy and behavioral changes. Upon arrival at the ER, her husband described a one-month history of behavioral changes with apathy, progressive abulia, visuospatial disorientation, and gait deterioration. The initial lab test shows no significance except by a positive qualitative hCG. An MRI was obtained and showed hyperintense periventricular white matter lesions in T2 and FLAIR sequences also involving bilateral basal ganglia and with predominant affection of the corpus callosum, in addition to infratentorial cerebellar lesions. After treatment with intravenous immunoglobulins a marked and prompt clinical and radiological improvement was observed.

Conclusion: SuS is still an elusive disease. To date, no definitive score or clinical feature can predict the outcome of the disease. The presentation during pregnancy is also rare and therefore the optimal treatment and the prognosis is unknown. We hope that this article will serve as a foundation for future research.

1. Introduction

From its initial report on two female patients in 1979 by J.O. Susac, Susac syndrome (SuS) or SICRET (small infarctions of cochlear, retinal and encephalic tissue) has persisted as an elusive entity. To date the available evidence for its treatment is based on case reports and case series. The largest systematic review described only 304 reported cases since the 1970s [1]. Here we presented the first reported case to our knowledge in Mexican population and the unusual presentation in a pregnant patient.

2. Clinical case

A 34-year-old Hispanic woman was brought to the ER in our hospital for apathy and behavioral changes. She had no prior neurological or systemic disease, no exposure to toxic or vascular risk factors, and had suffered a self-limiting (3-days duration) episode of incapacitating vertigo 6 months prior and an episode of right ear tinnitus (2 days of duration) 2 months before hospitalization without receiving any medical care.

Upon arrival at the ER, her husband described a one-month history of behavioral changes with apathy, progressive abulia, visuospatial disorientation, and gait deterioration. Initial exploration revealed a patient with auto-activation apathy, monotonous and dysprosodic speech and bilateral corticospinal involvement with hyperreflexia and Babinski's sign but no weakness.

The initial lab test shows no significance except by a positive qualitative hCG. The patient was unable to answer for any G/O history and her husband was also oblivious about it. An MRI was obtained and showed hyperintense periventricular white matter lesions in T2 and FLAIR sequences also involving bilateral basal ganglia and with predominant affection of the corpus callosum, in addition to infratentorial cerebellar lesions. Lesional restriction of diffusion but no contrast enhancement was observed. T1 weighted images showed hypointense lesions in the same topography (Fig. 1). Due to prominent pericallosal lesions with clinical findings of medial frontal syndrome and bilateral

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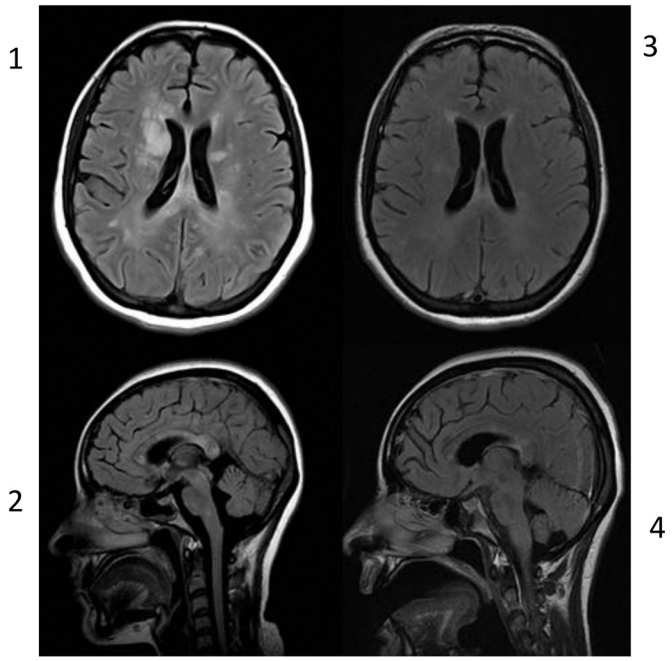

Fig. 1. MRI FLAIR sequence. Part 1 and 2 Pretreatment images shows hyperintense lesions with predominantly pericallosal involvement in the subependymal striatons and the *snowball* lesions. Part 3 and 4 shows IgIV post treatment changes with almost complete disappearance of the previous lesions.

corticospinal involvement of monophasic subacute evolution, primary vs secondary demyelinating disease was suspected. A lumbar puncture was performed resulting and CSF values showed proteins of 77 mg/dl, glucose of 52 mg/dl (serum glucose of 89 mg/dl), and no cells. Anti-AQP4 antibodies and oligoclonal bands were absent in CSF. A comprehensive workup for viral encephalitis and atypical infectious-disease result negative and cultures for fungi and bacteria. Also given the impossibility to further image studies as a complete CT and PET, a workup for paraneoplastic neurologic antibodies was obtained that was also negative Complete rheumatologic workup was negative except for 1: 2560 antinuclear antibodies in a speckled staining fine pattern without any systemic clinical correlate. Obstetric evaluation showed a normal development 15 weeks GA fetus.

Upon admission, 5 pulses of methylprednisolone were administered without obvious clinical improvement. Immunomodulatory treatment was escalated to intravenous immunoglobulin (IVIg) at 0.4 g/kg/day for 5 days. After treatment with IVIg, neuropsychiatric symptoms of medial frontal syndrome remitted, and the patient could cooperate for further study. Ophthalmologic assessment revealed retinal vasculitis corroborated by fluorangiography (FA) (Supplementary Fig. 1). Audiometric testing showed bilateral sensorineural hearing loss. A new MRI showed prior lesions to be smaller or absent, and the patient showed clinical improvement confirmed by neuropsychological testing. Once the diagnosis of SuS was established. The husband decided not to continue further with the pregnancy and a therapeutic abortion was performed, the patient was discharged for further treatment with oral steroids and CCF.

3. Discussion and conclusion

Here we discuss an atypical patient with the unusual diagnosis of Susac syndrome in a Mexican woman who was also in the first trimester of pregnancy. The anatomical basis of the clinical diagnosis as a subacute and evolving frontal syndrome in a young woman guide or workup to focus in autoimmune disorders, demyelinating disorders and structural lesions. The MRI allows to focus on the overview of predominantly callosal disease.

Differential diagnosis of corpus callosum lesions includes demyelinating, non-demyelinating inflammatory lesions, and transient splenial lesions. Demyelinating lesions include MS, neuromyelitis optica and ADEM, all of which were discarded in this patient based on the respective criteria for each one. Non-demyelinating inflammatory lesions include SuS and CNS vasculitis [2]. It is particularly important to differentiate SuS from MS. In SuS, lesions of the corpus callosum are typically centrally located, while the lesions in MS and ADEM involve the undersurface at the septal interface, in MS, these lesions are often extended around the venules of the brain, resulting in a finger-like appearance ("Dawson fingers"), while lesions appear circular in SuS. Typically, these callosal lesions involve the central fibers and spare the periphery [3] MRI reveals widespread abnormalities of the corpus callosum, manifested as small central holes, particularly in the splenium. Linear defects of the corpus callosum can also be detected, the so-called "spokes", representing microinfarctions of obliquely radiating axons [4]. The localization of the lesions is probably explained by the angioarchitecture of the corpus callosum. The inflammation and occlusion of the small precapillary arterioles with a diameter under 100 μm result in infarction of the central portion, but not the undersurface of the corpus callosum [4]. Subsequent documented involvement of retinal vasculitis and vestibulocochlear damage established the diagnosis in our patient.

SuS is currently considered a vasculitis with predominantly endothelial affection of autoimmune origin probably mediated by endothelial cell antibodies (AECA), with subsequent response by complement with C4d deposits, "mummification" phenomena, and endothelial necrosis [5]. Nevertheless, a study showed that in fact only 30% of patients with definite SuS have AECA, suggesting that AECA represent a secondary phenomenon in an etiologically heterogeneous syndrome, with a pathogenesis still far from fully understood [6]. Respecting the other autoantibodies and considering the high titers of ANA in our patients we found that antinuclear autoantibodies have been described in patients with SuS, but do not occur more often than in healthy controls [6].

Diagnosis of SuS is predominantly clinical and based on the evidence of the originally described triad with encephalic, retinal and vestibulocochlear affection. The clinical features include encephalopathy that is characterized by headache that may be migrainous or oppressive. Headache often occurs up to six months before the onset of the other symptoms. It is probably due to an affection of the leptomeningeal vessels. The other symptoms of encephalopathy have a stroke-like or subacute onset, with neuropsychological deficits, bladder disturbance, long tract signs, focal neurological signs, seizures, and often disturbance of consciousness [1]. The hearing loss can be a dramatic and severely disabilitating feature of Susac syndrome. It often occurs overnight and may affect both ears. A loss of the low or middle frequencies is typical, but loss of high frequencies can also occur. The severe hearing loss is often accompanied by vertigo and a roaring tinnitus. The hearing loss is caused by occlusion of the cochlear precapillary arterioles and those of the semicircular canal. Hearing loss is often irreversible and may require cochlear implants or hearing devices for a whole life [7]. Typical findings in patients with SuS include branch retinal artery occlusions (BRAO) detectable on retinal fluorescein angiography, the occlusions may affect the periphery and may not lead to clinical symptoms, but they can also affect the larger branches resulting in visual field deficits. Many patients complain about blurred vision or photopsia [7]. MRI, retinal fluorescein angiography, and audiometry are considered crucial tests to enable diagnosis.

In 2016, specific diagnostic criteria based on a cohort of 32 patients was proposed: Definitive SuS requires involvement of these 3 systems [8]. Being a rare disease, the clinical course and prognosis is largely unknown. Based on empirical stratification [9] the course can be monocyclic, polycyclic and chronic–continuous with a cutoff parameter of 2 years separating the monocyclic course from the other forms.

Many treatment approaches for SuS have been described in case