Case report
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Unusual flare up of Susac syndrome

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Introduction. Spinal cord involvement as a flare-up of Susac syndrome (SuS) is rarely reported in the literature. The pathogenesis of SuS includes multiple occlusions in micro vessels mediated by an autoimmune response to unknown antigens. This condition is characterized by a triad: central nervous system (CNS) dysfunction with a frequent involvement of the corpus callosum in brain MRI, visual disturbances due to branch retinal artery occlusion, and sensorineural hearing impairment.

Case report. A 50-year-old man presented in December 2019 symptoms associating gait instability, diplopia and hypoacusis. A year later, he developed a vesical-sphincter disorder and a hypoesthesia in his right lower limb. Neurological examination identified a medullary syndrome, cerebellar ataxia and hypoacusis. We performed a brain and spinal MRI showing supratentorial and infratentorial white matter lesions, and gadolinium enhancing cervical lesions. Lumbar puncture with isoelectric focusing results was normal. Screening for differential diagnosis such as other inflammatory central nervous system diseases other than multiple sclerosis was performed considering this atypical presentation of the disease; workup of serological, immunological, angiotensin converting enzyme, and tumor markers was negative. A bilateral hearing deficit was confirmed with an audiogram. Retinal angiography showed ischemic retinal vasculitis. We diagnosed the patient with SuS and treated him with intravenous corticosteroids in transition to oral corticosteroids. We noticed a partial regression of his symptoms. Therefore, we highlight the importance of an early diagnosis for SuS to avoid a prognostic turnover of the disease. Spinal cord involvement should not rule out the diagnosis of SuS.

Keywords: Susac syndrome, retinal artery occlusion, hearing loss, spinal cord involvement

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Poussée singulière du syndrome de Susac

Introduction. L'atteinte de la moelle épinière en tant que poussée du syndrome de Susac (SuS) est rarement rapportée dans la littérature. La pathogenèse du SuS comprend des occlusions multiples dans les micro-vaisseaux médiées par une réponse auto-immune à des antigènes inconnus. Cette affection est caractérisée par une triade : un dysfonctionnement du système nerveux central (SNC) avec une implication fréquente du corps calleux à l'IRM cérébrale, des troubles visuels dus à l'occlusion d'une artère rétinienne ramifiée et une déficience auditive neurosensorielle.

Étude de cas. Un homme de 50 ans a présenté en décembre 2019 des symptômes associant une instabilité de la marche, une diplopie et une hypoacousie. Un an plus tard, il a développé un trouble vésico-sphinctérien et une hypoesthésie du membre inférieur droit. L'examen neurologique a révélé un syndrome médullaire, une ataxie cérébelleuse et une hypoacousie. Nous avons réalisé une IRM cérébrale et rachidienne montrant des lésions de la substance blanche supratentorielle et infratentorielle, et des lésions cervicales rehaussées de gadolinium. La ponction lombaire avec les résultats de la focalisation isoélectrique était normale. Un dépistage des diagnostics différentiels tels que d'autres maladies inflammatoires du système nerveux central autres que la sclérose en plaques a été effectué compte tenu de cette présentation atypique de la maladie ; le bilan sérologique, immunologique, de l'enzyme de conversion de l'angiotensine et des marqueurs tumoraux était négatif. Un déficit auditif bilatéral a été confirmé par un audiogramme. L'angiographie rétinienne a montré une vasculite rétinienne ischémique. Nous avons diagnostiqué un SuS chez le patient et l'avons traité avec des corticostéroïdes intraveineux en transition vers des corticostéroïdes oraux. Nous avons constaté une régression partielle de ses symptômes. Par conséquent, nous soulignons l'importance d'un diagnostic précoce pour le SuS afin d'éviter que le pronostic de la maladie évolue défavorablement. L'atteinte de la moelle épinière ne doit pas exclure le diagnostic de SuS.

Mots-clés : syndrome de Susac, occlusion artérielle rétinienne, perte d'audition, atteinte médullaire

Abbreviations

MRI: magnetic resonance imaging
CNS: central nervous system
BRAO: branch retinal artery occlusion
AECA: anti-endothelial cell antibodies
SuS: Susac syndrome

1. Introduction

Susac syndrome (SuS) is a rare condition caused by autoimmune-mediated occlusions of micro-vessels in the brain, retina, and inner ear. These occlusions lead to a characteristic triad of central nervous system dysfunction, visual disturbances due to branch retinal artery occlusions (BRAO), and hearing deficits. We report the case of a 50-year-old male who has a rare spinal presentation of SuS.

2. Case report

A 50-year-old man with no prior medical history presented in December 2019 symptoms associating gait instability, diplopia and acute hypoacusis. Neurological examination identified truncal and limb cerebellar ataxia and hypoacusis. Cranial nerves and oculomotor nerves examination was normal. A brain and spinal MRI was performed, showing supratentorial and infratentorial white matter lesions, and gadolinium enhancing cervical lesions. Using the McDonald's 2017 criteria, we initially suspected a multiple sclerosis and treated the patient with intravenous corticosteroids during 5 days. We noticed a partial regression of his symptoms. Chronic treatment of multiple sclerosis was not introduced because the first manifestations and brain imaging were atypical. A year later, the patient developed a vesical-sphincter disorder and a hypoesthesia in his right lower limb, and his ataxia worsened. He received intravenous corticosteroids. Workup, including serological, immunological, angiotensin converting enzyme and tumor markers were negative (Table 1). An audiogram confirmed a bilateral hearing deficit. Retinal angiography showed ischemic retinal vasculitis (Figure 1). Brain and spinal cord control MRI were performed, showing corpus callosum typical snowball lesions of SuS (Figure 2). Lumbar puncture with isoelectric focusing results was normal. We diagnosed the patient with SuS in front of the typical triad associating central nervous system dysfunction, visual disturbances due to BRAO, and hearing deficit. The patient was treated with acetylsalicylic acid 100 mg/day and oral corticosteroids 1 mg/Kg/day with a progressive degression of 5 mg each 15 days. We had a favourable outcome regarding the cerebellar ataxia, and a partial improvement of his hypoacusis and vesical sphincter disorders. Visual function assessment with repeated fluorescein angiography and ophthalmologic examination revealed a partial improvement of the initially observed vasculitis. Control brain MRI showed a reduction in contrast enhancement of the cerebral lesions. After a one-year follow-up, no recurrence of neurological symptoms was observed. The patient is now taking 2.5 mg of prednisolone and is considered in remission without complications. The patient has given his informed consent.

3. Discussion

SuS is an immune-mediated, ischemia-producing, occlusive micro-vascular endothelium pathology that affects three systems: the brain, the retina, and the inner ear [1-4]. In its most usual form, it is characterized by a clinical triad (encephalopathy, BRAO, and low-frequency sensorineural hearing loss). Brain MRI shows distinctive "snowball" lesions in the corpus callosum. According to the SuS diagnostic criteria, in our case, the diagnosis is definite, including the clinical

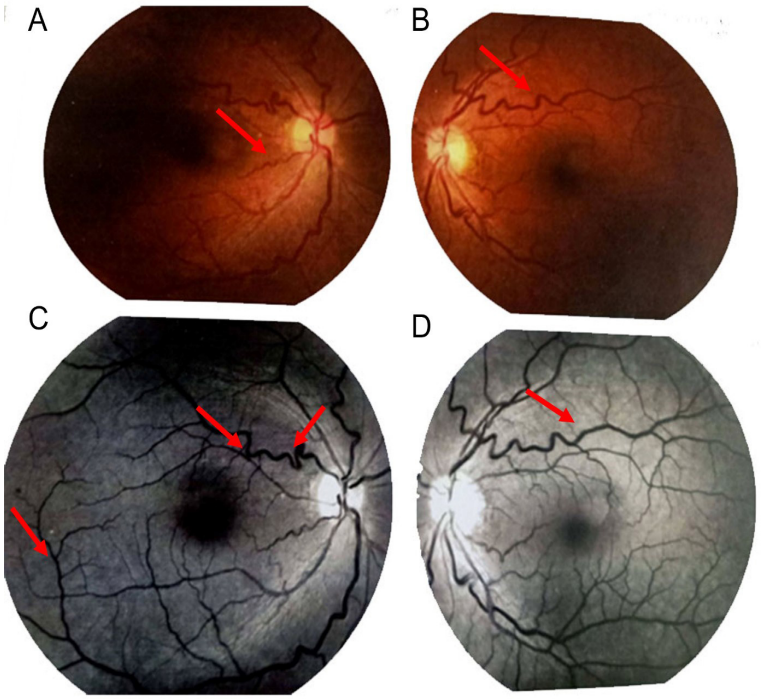

Figure 1. Fluorescein angiography showing ischemic occlusion in some small vessels: retinal vasculitis. Fundus of the right (A) and left (B) eye. Fluorescein angiography of the right (C) and left (D) eye.

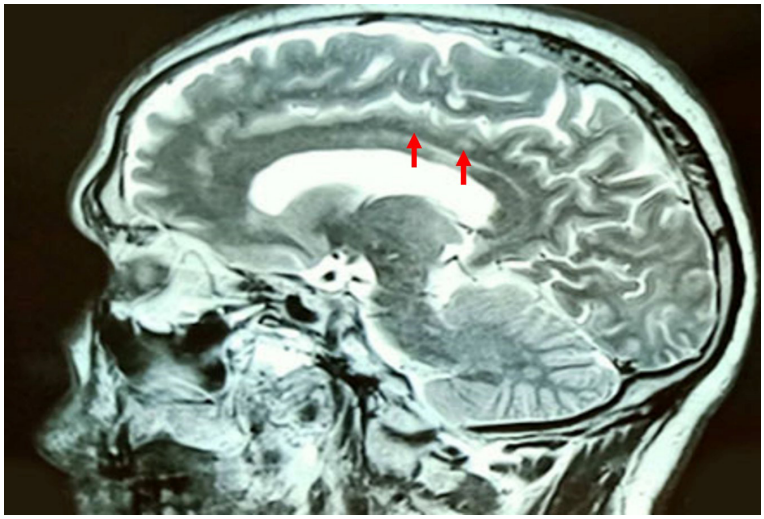

Figure 2. Brain MRI of a 50-year-old man showing characteristic "snowball" lesions in the corpus callosum on sagittal T2.

triad (neurological deficits, retinal vasculopathy, bilateral hearing loss) and snowball lesions in the corpus callosum found on brain MRI. Disease onset often occurs between the age of 20 and 40. Our patient was 49 years old at the onset of his symptoms. The female-to-male ratio is 3:1, so the representation of a SuS in a male patient is rare and may be more severe, as we observed in our case. Brain MRI showed multiple white matter lesions with snowball lesions in the corpus callosum, as described in the literature. Recently-proposed diagnostic criteria provide definitions of definite, probable, and possible SuS and offer guidance regarding diagnostic evaluation. There is a great variability regarding the clinical presentation of the disease. At the time of first medical evaluation, less than 20% of patients exhibit the full clinical triad. Any of the triad components may be the first and only manifestation, with the other components developing weeks or months after the initial symptom. This delay in development of second and third components may delay the diagnosis.

In our patient, ataxia and hypoacusis were the first manifestations, followed by spinal cord symptoms. In fact, ataxia is one of the clinical findings described in patients with SuS. It was reported in seven cases among 13 patients in a review of literature [3,5,6]. Spinal cord involvement is extremely rare [8,9]. SuS has many forms according to the disease's severity: extremely severe, severe, moderate and mild. The urinary dysfunction accounts for 9% of cases and sensory disturbance for 24% of cases.

The clinical manifestations of SuS can occur at first onset and during disease. In several series of literature, only 13% of patients with available data had a typical clinical triad of SuS at disease's onset. The average delay between the first symptoms and completeness of the triad was 21 weeks. The assumption that the presence of the triad is needed for a

Table 1. Tests and results.

Tests	Results
Lumbar puncture	Proteins = 0.45 g/L, glucose = 1.2 g/L, CSF white cell count=4
Serum and urine calcium	Serum calcium = 2.4, urine calcium = 2.5 mmol/24h
Serum and urine phosphorus	Serum phosphorus = 0.8 mmol/L, urine phosphorus = 30 mmol/24h
Tuberculin test	Negative
Quantiferon test	Negative
Carbohydrate antigen 19-9	20 U/mL
Alpha-fetoprotein	15 U/mL
Prostatic specific antigen	5 ng/mL
Carcinoembryonic antigen	2 ng/mL
Serum angiotensin converting enzyme	62 units/mL (normal value: 12-68)

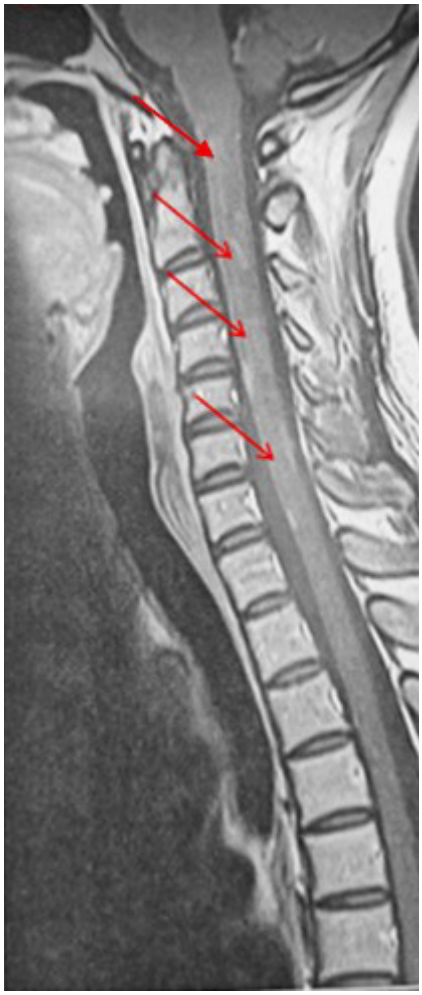

Figure 3. Spinal cord MRI shows gadolinium enhancing cervical lesions.

definitive diagnosis of SuS is a major cause of misdiagnosis [6], and this is mainly because of the absence of specific serological markers for SuS. Antinuclear autoantibodies positivity was observed in patients with SuS, however it wasn't more frequent than the positivity observed in healthy control subjects. A role of anti-endothelial cell antibodies (AECAs) in SuS's pathogenesis has been repeatedly discussed. Although mean AECA levels were significantly higher in patients with SuS than in healthy controls, recent studies showed AECA levels above 1/100 in only 25% of patients with SuS [3,6,7]. Treatment studies on immunosuppressive therapy in SuS are scarce. Though such studies are important, they are difficult to carry out because of the rarity of the disease, the variability of its presentation, its prognostic severity, and the absence of adequate biomarkers of its activity. The absence of prospective trials made it difficult to develop a precise treatment for SuS. The easy damage of the brain, retina, and cochlea made it even more challenging, requiring most of the time a rapid management to achieve an optimal therapeutic outcome and avoid sequelae [3,7].

4. Conclusions

Spinal cord involvement is rare and should not rule out the possibility of an underlying SuS. A better understanding of this disease is crucial so as to provide patients with the appropriate treatment and care.

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