

Diagnosing Susac Syndrome Despite Incomplete Clinical Triad: A Case Report of Convergent Atypical Neuroimaging and Inflammatory Cerebrospinal Fluid Findings: Case Report

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Case Report

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Abstract

Background

Susac syndrome (SuS) is a rare autoimmune endotheliopathy involving the brain, retina, and inner ear. Because patients frequently present without the complete clinical triad of encephalopathy, branch retinal artery occlusions (BRAO), and sensorineural hearing loss (SNHL), diagnosis can be challenging. The European Susac Consortium (EuSaC) criteria classify SuS according to objective involvement of the brain, retinal, and vestibulocochlear domains; however, many patients do not fulfill criteria for probable or definite disease at initial presentation. Furthermore, neuroimaging and cerebrospinal fluid (CSF) findings may overlap with inflammatory demyelinating disorders such as multiple sclerosis (MS). We report a case where EuSaC criteria was not met, however there was strong clinical and radiographic evidence to support the diagnosis of SuS. This case brings to question whether strict fulfillment of EuSaC criteria is needed to initiate early inpatient treatment to prevent irreversible neurological deficits.

Case presentation

We report the case of a woman in her early forties with hypertension, hyperlipidemia, chronic kidney disease, recurrent ischemic strokes, and an unspecified hypercoagulable disorder who presented with progressive gait instability, dizziness, and bilateral lower extremity weakness. Brain magnetic resonance imaging (MRI) demonstrated characteristic central corpus callosum “snowball” lesions and cerebellar leptomeningeal enhancement. CSF analysis revealed elevated immunoglobulin G (IgG) index, elevated IgG synthesis rate, and markedly elevated myelin basic protein (MBP) in the absence of oligoclonal bands (OCB). At the time of presentation, only the brain domain of the EuSaC criteria was objectively fulfilled, and the patient therefore did not meet criteria for probable or definite SuS. Nevertheless, the characteristic neuroimaging phenotype, inflammatory CSF profile without oligoclonal bands, and absence of typical MS features strongly favored SuS and prompted treatment with high dose steroids and further diagnostic evaluation.

Conclusions

This case demonstrates that strict fulfillment of EuSaC criteria may not be required to recognize SuS when characteristic neuroradiographic findings and supportive clinical features are present. Recognition of central corpus callosum “snowball” lesions and cerebellar leptomeningeal enhancement may facilitate earlier diagnosis and treatment, potentially reducing irreversible neurologic, retinal, and auditory morbidity.

Introduction

Susac syndrome (SuS) is a rare autoimmune endotheliopathy characterized by immune mediated injury of the precapillary arterioles supplying the brain, retina, and inner ear [6]. The disorder is classically described as a triad of encephalopathy, branch retinal artery occlusions (BRAO), and sensorineural hearing loss (SNHL). However, fewer than one third of patients demonstrate the complete triad at presentation [6], resulting in frequent diagnostic delays and misclassification as multiple sclerosis (MS), ischemic strokes, or central nervous system vasculitis.

The EuSaC diagnostic criteria classify SuS as definite when objective evidence exists for all three domains (brain, retina, and inner ear), probable when two domains are satisfied, and possible when only one domain is objectively demonstrated [2]. Because formal retinal and audiometric evaluation is not always available at the time of initial presentation, especially in research poorer settings, clinicians must often rely on the convergence of characteristic neuroimaging findings, supportive cerebrospinal fluid (CSF) profiles, and clinical suspicion to arrive at the correct diagnosis before the full triad becomes apparent [3].

Distinguishing SuS from MS is particularly important because both disorders may present with multifocal white matter lesions and inflammatory CSF abnormalities [8]. Nevertheless, SuS possesses several distinguishing radiographic features, including centrally located corpus callosum lesions, leptomeningeal and vestibulochlear enhancement [5]. Additionally, cerebrospinal fluid oligoclonal bands, a hallmark of MS, are typically absent in SuS [7].

We report a case in which only the brain domain of the EuSaC criteria was objectively satisfied at presentation. Despite this, the combination of a pathognomonic neuroimaging phenotype, atypical CSF findings, and exclusion of classic demyelinating disease supported a diagnosis of SuS.

Patient Information

A woman in her early forties with hypertension, hyperlipidemia, stage III chronic kidney disease, recurrent ischemic strokes, and an unspecified hypercoagulable disorder treated with warfarin presented with acute on chronic gait instability, dizziness, and bilateral lower extremity weakness as a stroke alert. She reported that her gait dysfunction had begun in November 2025 and was gradually worsening. One month prior, she had been hospitalized for an ischemic stroke and finished inpatient rehabilitation (IPR) though she noted persistent mild dizziness since that event. The patient was uninsured and had poor family support as both her father and brother suffered from financial instability and were unable to provide significant medical support.

Clinical Findings

On arrival, blood pressure was 170/82 mmHg, serum glucose was 151 mg/dL, and the National Institutes of Health Stroke Scale score was 4 for chronic deficits. Neurologic examination demonstrated an alert and oriented patient with fluent speech and intact comprehension. Cranial nerve examination revealed a right inferior homonymous quadrantanopia consistent with a prior left occipital infarction.

Bedside Weber and Rinne testing raised suspicion for right sided SNHL though the patient herself did not notice any hearing changes. Motor examination showed mild weakness of right hip flexion and chronic right foot drop, with otherwise preserved strength. Coordination testing demonstrated subtle overshoot during finger pursuit, and gait assessment revealed marked truncal instability (Table 1).

Timeline

Table 1. Timeline of patient's presentation, hospital course, and follow up.

Diagnostic Assessment

Computed tomography of the head (CTH) demonstrated bilateral cerebellar and left occipital encephalomalacia. Computed tomography angiography of the head and neck (CTA H/N) revealed no significant vascular abnormalities. MRI of the brain demonstrated a chronic left occipital infarction and multifocal T2/FLAIR hyperintense lesions involving the periventricular and juxtacortical white matter. Of particular interest were lesions involving the genu and body of the corpus callosum, including multiple lesions with a characteristic "snowball" appearance (Fig. 1).

Additional confluent cerebellar T2 hyperintensities with associated leptomeningeal enhancement were identified (Fig. 2). MRI of the cervical and thoracic spine demonstrated no intramedullary cord lesions or abnormal enhancement. MRI of the orbits showed no evidence of active or prior optic neuritis.

Lumbar puncture revealed CSF without pleocytosis and with normal protein concentration. Additional studies demonstrated an elevated IgG index (0.8), elevated IgG synthesis rate (5.1), and markedly elevated myelin basic protein (15 ng/mL). Oligoclonal bands were absent. Serum and CSF aquaporin-4 antibodies were negative, and autoimmune serologic studies including antinuclear antibody and rheumatoid factor were unrevealing (Table 2).

Table 2

Cerebrospinal fluid (CSF) and serum results. H, high; L, low; RBCs, Red Blood Cells; WBCs, White Blood Cells; Ig, immunoglobulin; ANA, antinuclear antibody; RF, Rheumatoid Factor; Ab, Antibodies; EBV, Epstein Bar Virus; TB, Tuberculosis; ACE, Angiotensin Converting Enzyme; AQP4, Aquaporin 4 antibody

CSF Studies	Result / Interpretation	Serum Studies	Result / Interpretation
Appearance	Hazy (Tubes 1 and 4)	IgG	1208 mg/dL
RBCs	4919 mm ³ (Tube 1) 254/mm ³ (Tube 4)	IgA	361 mg/dL (H)
Protein	43.6 mg/dL	IgM	85 mg/dL
Glucose	254 mg/dL (H)	Immunofixation	No monoclonal immunoglobulin detected; Hypoalbuminemia pattern; increased α2 globulins may reflect inflammation or nephropathy
WBCs	0 (Tube 1) 0 (Tube 4)	Albumin	3.5 g/dL (L)
Oligoclonal bands (OCBs)	0 (absent)	Rheumatoid factor	Negative
CSF IgG (absolute)	4.4 mg/dL	ANA	Negative
CSF IgG Local Synthesis Rate	5.1 (H)	EBV Nuclear Antigen IgG	8 (H)
CSF IgG/albumin index	0.28 (H)	Hepatitis A IgM Ab, Hepatitis Bs Antigen, Hepatitis B Core IgM Ab, Hepatitis C Ab	Negative
CSF albumin/serum albumin index	5	QuantiFERON-TB Gold Plus	Negative
Myelin Basic Protein	15 (H)	ACE	37
AQP4 Antibody (Cell-Based IFA)	Negative	AQP4 Antibody (Cell-Based IFA)	Negative

At the time of initial evaluation, the patient did not fulfill the EuSaC criteria for definite or probable SuS based on available objective findings. Only the brain domain was definitively satisfied, as evidenced by new neurological deficits (progressive gait instability and dizziness) and characteristic MRI findings (central corpus callosum snowball lesions and cerebellar leptomeningeal enhancement). The retinal

domain had not yet been objectively evaluated because fluorescein angiography was pending and was not available inpatient. Similarly, the inner ear domain was not yet formally confirmed because audiometric testing had not been completed, although bedside examination raised suspicion for unilateral sensorineural hearing loss.

Nevertheless, the convergence of several atypical and supportive findings strongly favored SuS over alternative diagnoses such as multiple sclerosis, Neuromyelitis Optica, or Myelin Oligodendrocyte Glycoprotein Antibody associated disease.

Therapeutic Intervention

Due to high suspicions for SuS, patient was treated with 3 days of high dose intravenous methylprednisolone 1000 mg once daily with plans to follow patient in clinic for further consideration of immunologics based on pending CSF studies.

Follow-up and Outcomes

Patient reported subjective improvement on subsequent days following treatment with high dose intravenous methylprednisolone. However, objectively patient's clinical exam did not demonstrate any significant change. Patient did not have any adverse effects to steroid treatment. Unfortunately, the patient did not follow up in our clinic in the setting of her uninsured status and poor social support to arrange accommodations.

Discussion

At presentation, the only objectively fulfilled European Susac Consortium (EuSaC) domain was the brain domain [2]. The patient demonstrated progressive vestibulocerebellar dysfunction, and brain MRI revealed two hallmark neuroradiographic features of Susac syndrome: central corpus callosum lesions and posterior fossa leptomeningeal enhancement. Central corpus callosum involvement is among the most distinctive imaging findings in SuS, producing characteristic “snowball,” “spoke,” and “punched-out” lesions that preferentially affect the central callosal fibers [1]. This pattern contrasts with multiple sclerosis (MS), which more commonly involves the inferior corpus callosum and calloseptal interface. Additional MRI findings, including confluent cerebellar T2 hyperintensities and associated leptomeningeal enhancement; leptomeningeal enhancement is increasingly recognized as a characteristic manifestation of SuS related to endothelial dysfunction and microvascular injury and is not considered a typical feature of MS [5].

Cerebrospinal fluid (CSF) findings initially complicated the diagnostic evaluation. Elevated IgG index, increased IgG synthesis rate, and markedly elevated MBP suggested active CNS immune mediated injury and raised concern for a demyelinating disorder such as MS. However, several features argued against classic MS. Although elevated MBP reflects active myelin injury, it is nonspecific and may occur in

inflammatory, ischemic, and autoimmune CNS disorders; moreover, MBP elevations in MS relapses are typically modest. More importantly, oligoclonal bands were absent, whereas they are present in the majority of patients with MS [7]. In contrast, oligoclonal bands are typically absent or only transiently detected in SuS.

Additional investigations further reduced the likelihood of MS. There were no convincing cervical or thoracic spinal cord lesions and no evidence of active optic neuritis or optic nerve thinning on orbital MRI. Formal fluorescein retinal angiography, the gold standard for detecting branch retinal artery occlusions, had not been performed, and formal audiometric testing was still pending, although bedside examination raised suspicion for right-sided sensorineural hearing loss. This suspicion was further supported by the patient's demographic profile, as she was a 40-year-old woman, consistent with the most commonly affected population by SuS [1].

This case was particularly challenging because the patient had a history of recurrent ischemic strokes and an underlying hypercoagulable disorder requiring long term anticoagulation, making recurrent strokes a plausible explanation for her progressive neurological decline.

Nevertheless, the characteristic neuroimaging phenotype served as the diagnostic anchor. When considered alongside the absence of oligoclonal bands, spinal cord lesions, and optic nerve involvement, the markedly elevated MBP, and the clinical suspicion for vestibulocochlear dysfunction, the overall pattern was substantially more consistent with SuS than with MS. Although the patient did not meet EuSaC criteria for definite or even probable SuS at the time of initial evaluation because objective evidence of the retinal and vestibulocochlear domains was unavailable, the characteristic neuroradiographic findings, supportive ancillary data, compatible demographic features, and evolving clinical presentation appropriately prompted consideration of SuS despite its incomplete clinical expression. This case highlights the importance of recognizing the characteristic MRI signature of SuS and maintaining a high index of suspicion in patients who present with only a partial manifestation of the classic triad [3], as early diagnosis may facilitate timely treatment and potentially reduce irreversible neurologic, retinal, and cochlear injury.

Conclusion

This case highlights the diagnostic challenges of SuS in a patient with recurrent ischemic strokes and an underlying hypercoagulable disorder who presented with progressive vestibulocerebellar dysfunction and multifocal white matter abnormalities initially suspected to represent multiple sclerosis. However, several features were atypical for MS, including central corpus callosum “snowball” lesions, cerebellar leptomeningeal enhancement, absence of oligoclonal bands, lack of spinal cord lesions or optic neuritis, and clinical suspicion for sensorineural hearing loss. The characteristic neuroimaging pattern ultimately served as the principal diagnostic clue and established a phenotype more consistent with SuS despite incomplete objective fulfillment of the EuSaC criteria at the time of presentation. This case underscores the importance of recognizing the distinctive radiographic features of SuS and maintaining a high index

of suspicion when the classic triad is only partially expressed. Early recognition based on characteristic imaging findings may facilitate timely treatment and help prevent irreversible neurologic, retinal, and auditory disability.

Patient Perspective

The patient and her father were grateful to the teams for acknowledging her symptoms and finding a possible diagnosis as she had previously been to multiple hospitals with similar symptoms without a clear etiology or diagnosis. She subjectively felt some improvement after steroid treatment; however objectively her clinical exam was unchanged. Patient and her father also expressed disappointment in the lack of financial resources available to assist with inpatient rehabilitation placement.

Abbreviations

ACE
Angiotensin-converting enzyme
ANA
antinuclear antibody
AQP4
aquaporin-4
BRAO
branch retinal artery occlusion
CNS
central nervous system
CSF
cerebrospinal fluid
EuSaC
European Susac Consortium
FLAIR
fluid-attenuated inversion recovery
MBP
myelin basic protein
MRI
magnetic resonance imaging
MS
multiple sclerosis
OCBs
oligoclonal bands
SNHL
sensorineural hearing loss

SuS

Susac syndrome.

Declarations

Ethics approval and consent to participate

Institutional review board approval was not required for this single patient case report, in accordance with institutional policy.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. A copy of the completed consent form would be available on request for review by the Editor in Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

JL conceived the report, collected and reviewed the clinical data, performed the literature review, and drafted and revised the manuscript. EG, SF, CM and MS contributed to the literature review, clinical interpretation and critically revised the manuscript. AL provided senior supervision and clinical oversight and critically revised the manuscript. All authors read and approved the final manuscript. JL is the guarantor of this work, accepts full responsibility for the integrity of the work and the accuracy of the data presented, and made the decision to submit for publication.

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Availability of data and materials

All data generated or analyzed during this case are included in this published article. No additional unpublished data are available.

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Table

Table 1 is available in the Supplementary Files section.

Figures

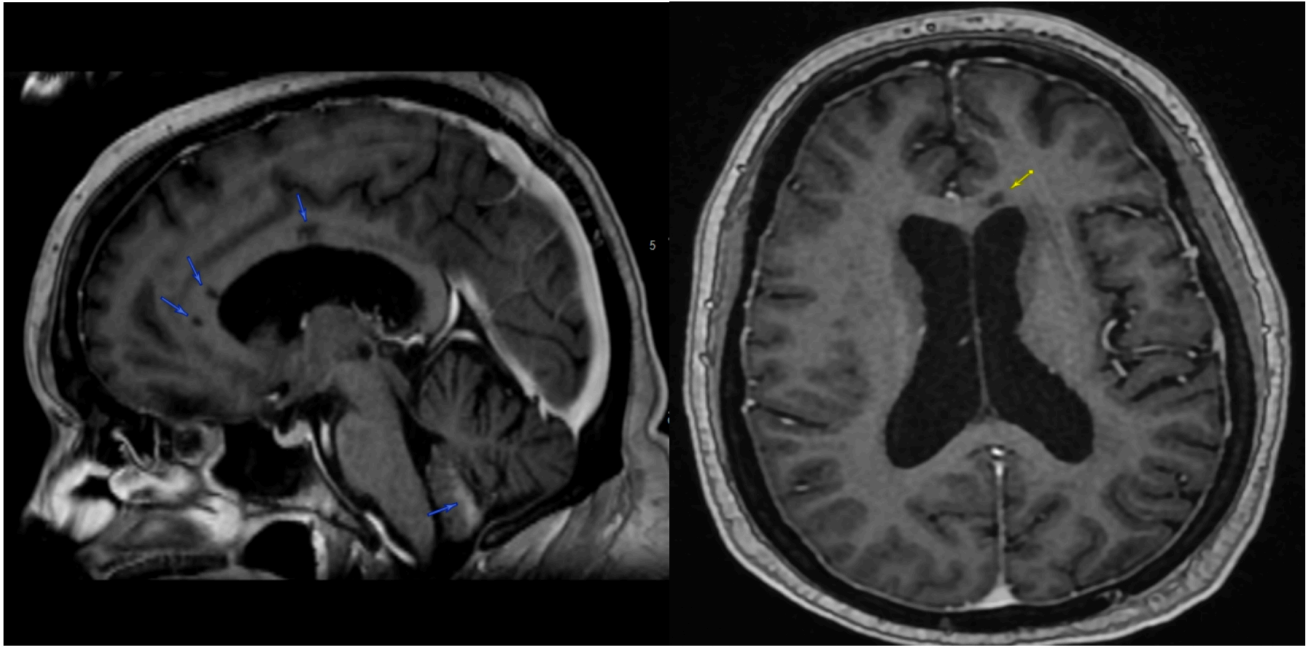


Figure 1

MRI Brain demonstrating classic “snowball” appearing lesions in the corpus callosum on both post contrast sagittal (blue arrows) post contrast T1 weighted imaging and axial T1 weighted imaging (yellow arrow). In the sagittal post contrast T1 MRI Brain leptomeningeal enhancement can be seen involving the inferior cerebellum (blue arrow.)

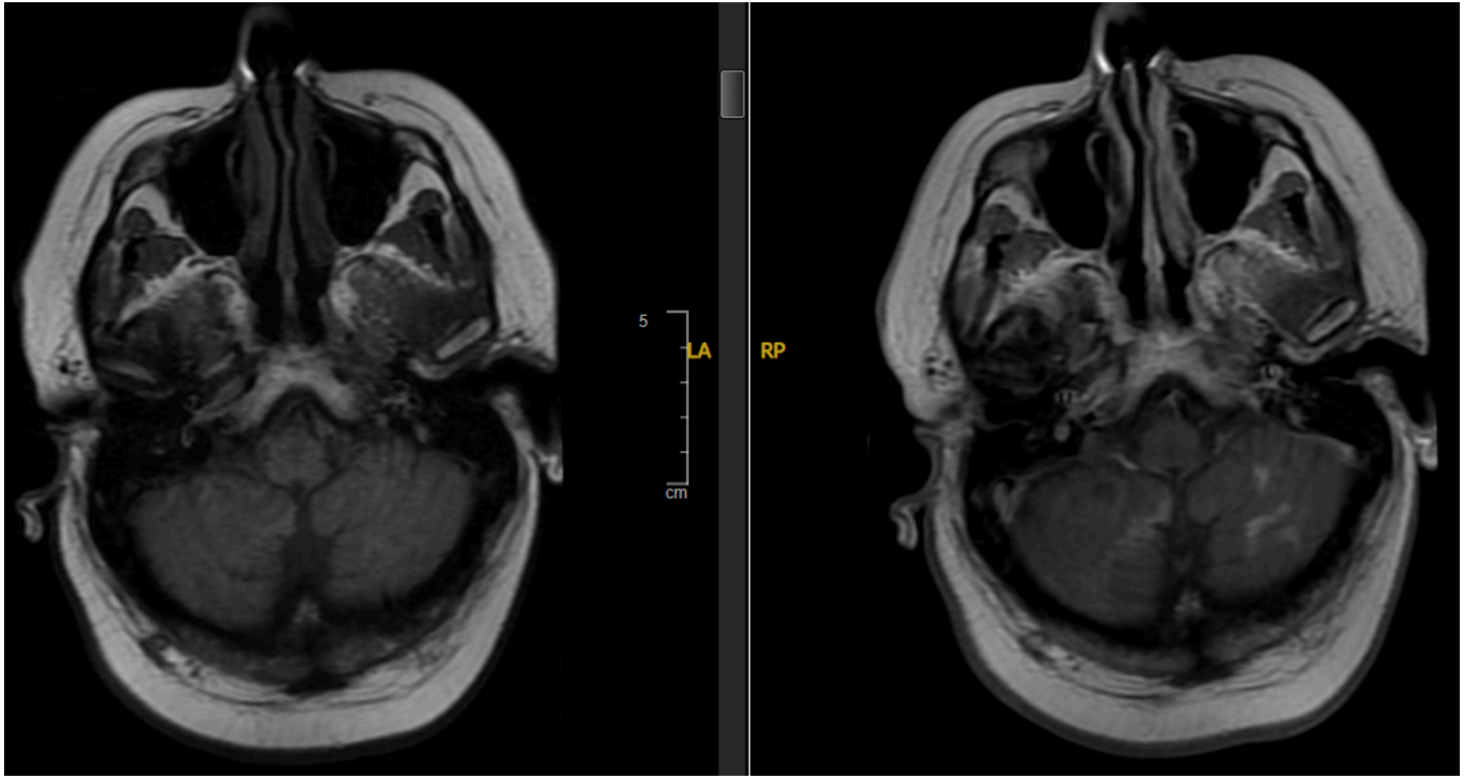


Figure 2

Pre and post contrast axial MRI T1 weighted imaging demonstrating confluent patchy leptomeningeal enhancement of the bilateral cerebellum.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.docx](#)
- [CAREChecklistSusac.pdf](#)