

Case Report

Systemic sclerosis associated with colliquative necrosis in the cerebellum

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Abstract

Background: The scleroderma is a complex autoimmune collagen disorder that can affect many organs simultaneously, as it occurs in the systemic sclerosis (SS), or only the skin, as it occurs in the localized scleroderma (LS). The neurological presentation is extremely uncommon, and even more uncommon are the symptoms of the scleroderma in the cerebellum.

Case Description: We report the case of a 56-year-old male with cerebellar lesions mimicking a brain abscess. After surgical excision, the histopathological diagnosis deposited for an ischemic necrosis caused by a vasculopathy. All the bacteriological and viral exams were negative, whereas the rheumatologic tests were compatible with the scleroderma pattern.

Conclusion: Up to now, the literature has described only 5 cases of scleroderma in the posterior cranial fossa. The authors report a case of SS causing colliquative necrosis in the cerebellum. Pathogenetic mechanisms, clinical aspects, and radiological features are discussed along with the pertinent literature.

Key Words: Cerebellum, colliquative necrosis, posterior cranial fossa, scleroderma

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INTRODUCTION

The term “scleroderma” literally means “hard skin,”^[18] however generally, this term includes disease processes that can affect only the skin in the localized scleroderma (LS) or can develop progressive multiple organ disorders in the systemic sclerosis (SS).^[8] The annual incidence of scleroderma is 6–12 patients per million population with a female predominance.^[15]

In general, the neurological presentation is extremely rare.^[15] This is probably due to the lack of adventitial fibrous tissues in the central nervous system (CNS).^[8] Only a few case reports have described the potential symptoms

of scleroderma in the cerebellum, and in no one of them, surgery has been reported to be necessary.

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The authors report the first case of ischemic necrosis of the cerebellum in a patient with SS mimicking a brain abscess. Clinical aspects, radiological features, surgical treatment, and operative findings are discussed along with a review of the pertinent literature.

CASE REPORT

A 56-year-old male was admitted to our Institute with a sudden headache and dizziness accompanied by nausea and vomiting. The patient had been in good health until this event, except for a history of skin thickening, a Raynaud's phenomenon with acrocyanosis to the fingers from 1 year and arthralgia from 3 years. Other sclerotic lesions were observed on the knees and elbows.

On admission, his blood pressure, pulse, body temperature, and respiration were normal. The neurological examination showed dysmetria, nystagmus, and dizziness. There were neither sensory nor motor deficits and cranial nerves abnormality. The results of the routine hematologic tests showed only neutrophilic leukocytosis with relative lymphocytopenia. The initial brain computerized tomography (CT) scan and the subsequent magnetic resonance imaging (MRI) showed a lesion with fluid collection, measuring 1.5×3.5 cm in the right cerebellar hemisphere [Figure 1]. The CT of the total body did not detect lesions of the internal organs. A right suboccipital craniotomy was performed, the fluid collection was free-hand evacuated, and the wall of the lesion was resected [Figure 2]. The bacteriological exams of the fluid collection and of the blood cultures were negative. The echocardiogram showed no pathological lesions. The histopathological diagnosis of the wall of the lesion deposited for ischemic necrosis caused by a vasculitis [Figure 3]. The post-operative MRI showed no residual lesions [Figure 4].

Further investigations tested positive for antinuclear antibody (ANA) $>1:160$ and Scl-70 (16.3 UA/mL), whereas other tests for rheumatology and infectious diseases tested negative (antiphospholipid anticentromere and anticardiolipin antibodies, Lupus-like anticoagulant, anti-DNA autoantibodies, perinuclear antineutrophil antibodies (P-ANCA), cytoplasmic antineutrophil antibodies (C-ANCA), Anti-Smith antibodies (Anti-Sm), Anti-Sjögren's-syndrome-related antigen A/B (Anti-SSA/B), Antibodies against antigen Ro52 (Anti-Ro52), antibodies histidyl-tRNA synthetase Jo-1 (Anti-Jo1), major centromere autoantigen B (CENP-B), Nucleosomes, Ribosomal P- Protein, Anti-Ribonuclear Protein (Anti-U1RNP), Histones, Protein S Factor V Leiden, Hepatitis B surface antigen (HBs-Ag), Hepatitis C Core antibodies (HCV-Ab), antibodies Human Immunodeficiency Virus (HIV-Ab), Venereal Disease Research Laboratory). In addition to this, it was found an increase of circulating immune complexes (38 $\mu\text{g/ml}$), α 1-acid-glycoprotein (208 mg/dl) and C-reactive protein

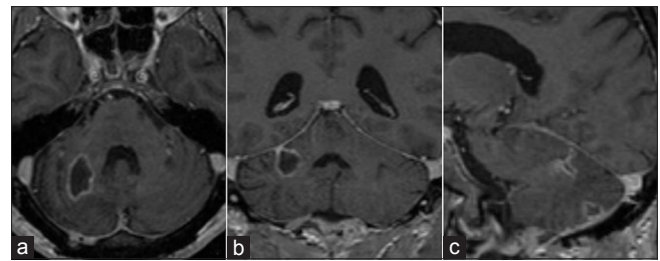


Figure 1: Preoperative magnetic resonance image in axial, coronal, and sagittal view showing a lesion with fluid collection, measuring 1.5×3.5 cm, localized in the right cerebellar hemisphere (a-c)

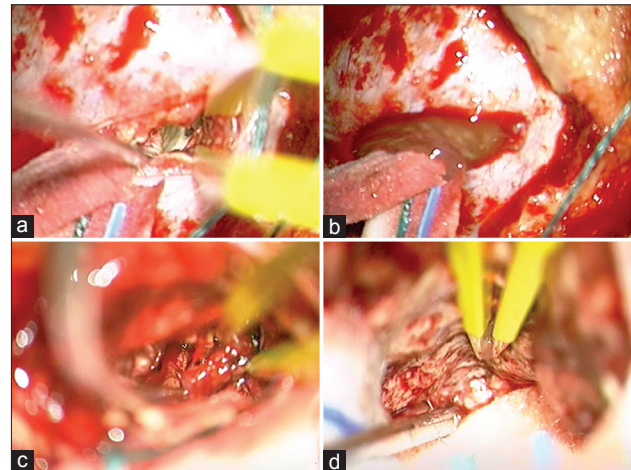


Figure 2: After suboccipital craniotomy, the intraoperative visualization showed a subcortical colliquative necrosis (a and b). The wall of the lesion was resected (c) and the fluid collection was completely free-hand evacuated (d)

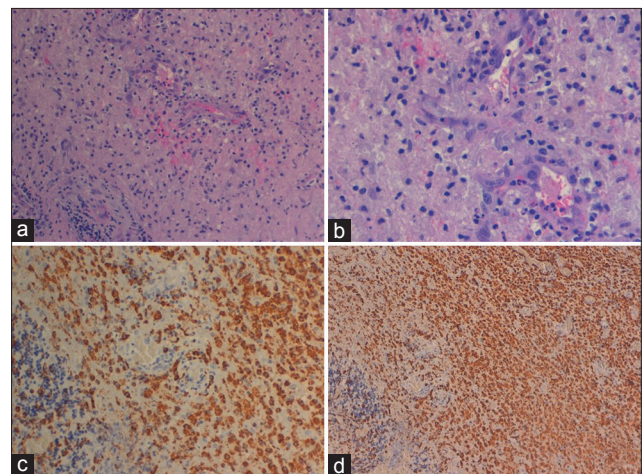


Figure 3: Imaging in hematoxylin and eosin and original magnification $\times 20$ and $\times 40$ showed cerebellar necrosis associated with microparenchymal hemorrhage, leukocytoclastic vasculitis, and swollen endothelial cells (a and b). Immunohistochemistry imaging (CD 68 +) showed massive macrophages infiltration in the cerebellar parenchyma (c and d)

(0.80 mg/dl). The capillaroscopy in the periungual area showed slight disorganization of the capillary architecture, numerous giant capillaries and microhemorrhages,

moderate capillary loss, and few ramified capillaries with initial neoangiogenesis. The skin biopsy confirmed a focal extension of dermal collagen in the subcutaneous tissue. All these conditions were compatible with a scleroderma pattern. The patient was sent to our rheumatology reference center to start a specific therapy. At 1-year follow-up there were no other complications.

DISCUSSION

In general, the scleroderma represents a complex autoimmune collagen disorder.^[10] The etiology remains obscure and the course is unpredictable.^[18] It can be a multisystemic disease affecting the skin, lungs, kidneys, vascular system, myocardium, nervous system, and gastrointestinal tract,^[12] or affecting only the skin.^[8] In both the SS and LS, the CNS lesions are considered an uncommon symptom. Even more uncommon are the lesions of the scleroderma localized only in the cerebellum.^[8,12]

Currently, only 5 cases have been described in literature.^[1,3,9,13,15] The average age of the reported patients is 35 years, however, in one case, the patient was 5 years old. There is a female prevalence (4:1). In most of these

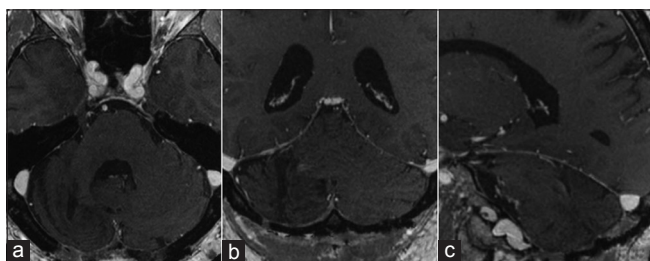


Figure 4: Postoperative magnetic resonance in axial, coronal, and sagittal view showing the complete resection of the lesion (a-c)

cases, the cerebellar lesions are secondary to the vascular effects of the scleroderma. In 3 cases, the lesions were caused by the SS, whereas in 2 cases, they were caused by the LS. Raynaud's phenomenon was present only in the SS. The presence of the Anti-Scl-70 and Anti-U1RNP antibody was not always reported. Hypertension was reported in only 2 cases of SS. Surgical treatment was not considered to be necessary, except for our case. We have not found previous reports of cerebellar ischemia with colliquative necrosis associated with the SS [Table 1].

In literature, no studies have correlated the posterior circulation and cerebellum with SS, whereas several theories have been proposed to explain the mechanism of a vascular damage caused by the SS in CNS. Some authors think that the pathogenic mechanism is caused both by the cell-mediated activity and autoantibody production responsible for a chronic inflammation. This determines a progressive fibrosis of the visceral organs and vascular damage, including the intracranial vessels.^[2]

Other studies have shown that the vasculopathy in the SS is caused by an obliterative vasculopathy rather than by the classical atherosclerosis.^[17] In addition, in the early stages of SS, an onset of endothelial dysfunction has been demonstrated, progressively followed by more severe endothelial damages, such as necrosis and devascularization.^[2,14] The endothelial dysfunction has been correlated with an increased risk of acute ischemic stroke.^[2,16] Another possible pathogenetic mechanism is an increased vasospasm in patients with SS.^[2,6]

In general, the cerebral angiopathy in the scleroderma is associated with the presence of malignant hypertension or renal disease,^[4,5] however, in our case, as well as in a few cases present in literature,^[4,5,12] these are not present.

Table 1: Review of the literature on cerebellar lesions in patients with scleroderma

Authors and year	Pt. age (year) and sex	Type of cerebellar lesions	Raynaud's phenomenon	Neurological deficits	Anti-SCL-70-antibodies	Anti-U1RNP-antibodies	Type of Scleroderma	Malignant hypertension or renal disease
Kawano H 1990	72, F	Hemorrhagic infarction	Yes	Vertigo	Not reported	Not reported	Systemic Scleroderma	Yes
Pinheiro L 2004	46, F	Atrophy	Yes	Unsteadiness, ataxia	Negative	Negative	Systemic Scleroderma	Not reported
Poursadegh Fard M 2012	37, F	Infarction	Yes	Slurred speech, Right-sided clumsiness	Positive	Negative	Systemic Scleroderma	Yes
Choi EJ 2012	17, F	Calcified parenchymal lesions	Not reported	Dizziness, nausea, vomiting	Not reported	Not reported	Linear Scleroderma	Not reported
Allmendinger AM 2015	5, M	Micro-hemorrhages	No	Not reported	Not reported	Not reported	Linear Scleroderma	Not reported
Ricci A 2016	56, M	Colliquative necrosis	Yes	Dizziness, nausea, vomiting	Positive	Negative	Systemic Scleroderma	No

Other rare CNS abnormalities described include encephalopathy, subarachnoid hemorrhage, psychosis, anxiety, and trigeminal neuropathy.^[4,5,12]

There are few reports on the possible associations of different autoantibodies with neurological manifestations of scleroderma.^[7] According to Hietarinta *et al.*,^[7] the positivity for anti-U1RNP and anti-Scl-70 antibodies in patients with SS could be related with the pathogenesis of the microangiopathy. Furthermore, on the basis of their study, these patients are more prone to developing neurological symptoms.^[7]

We think that the involvement of the CNS is unpredictable, and according to Mohammed *et al.*,^[11] the use of the MRI might allow an early detection of CNS involvement in patients with SS.

CONCLUSION

We believe that in our case the cerebellar lesion was caused by microangiopathy of the posterior circulation secondary to a high activity of the SS. The pathogenetic mechanism that causes the colliquative necrosis might be generated by microglia and macrophages surrounding the cerebellar vessels. In response to inflammatory stimuli, secondary to the scleroderma effect on the microcirculation, the microglia rapidly transform into an activated phenotype, elaborating both neurotoxic and neurotrophic factors responsible for the formation of a colliquative collection.

In our case, the first manifestation of the scleroderma is cerebellar, and therefore, in the presence of a brain lesion similar to an abscess, it is recommended to include autoimmune diseases such as the scleroderma among the diagnostic hypotheses.

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Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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