CNS Vasculitis as a Manifestation of Systemic Sclerosis

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Neither author has anything to disclose

INTRODUCTION

Systemic sclerosis (or scleroderma) is a connective tissue disease manifested by rapidly progressive fibrosis of the skin, lungs, and other internal organs usually felt to have rare secondary central nervous system (CNS) manifestations. We present a patient with extensive CNS involvement of systemic sclerosis consistent with a diffuse CNS vasculitis. Recent evidence supports a more direct role of the central nervous system in systemic sclerosis.

CASE REPORT

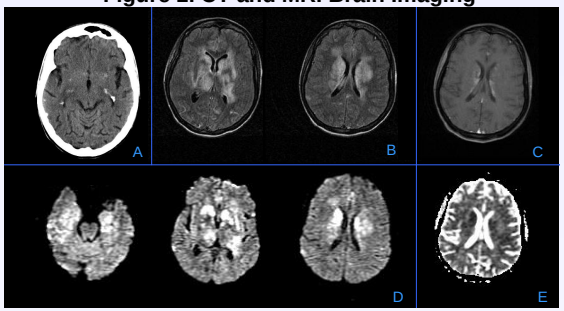
A 24 year-old right-handed woman with a two year history of advanced systemic sclerosis treated with prednisone 10mg daily presented with a week-long history of progressive lethargy and low grade fever without associated focal systemic or neurological symptoms. On exam, she was minimally responsive and not following commands. Her general examination was significant for diffuse signs of systemic sclerosis but no source of infection. Neurologic exam showed pupils were equal and reactive to light with full occulocephalics, normal corneal reflexes bilaterally, no facial droop, and intact gag reflex. She moved spontaneously with good withdrawal to pain in all 4 limbs. Deep tendon reflexes were 3+ in the biceps, brachioradialis, and triceps with 2+ in the patellas and ankles. There was no clonus but plantar responses were extensor bilaterally.

Initial laboratory studies were within normal limits with no leukocytosis. A CT head without contrast demonstrated only multiple parenchymal calcifications throughout the brain, including the bilateral temporal lobes, the insula, and bilateral basal ganglia without evidence of hydrocephalus, edema, or mass effect (Fig 1A). Lumbar puncture showed a normal opening pressure, protein 124, glucose 49, WBC 1 without oligoclonal bands. The IgG synthesis rate was very high at 34.2 but the IgG index was normal. Additional testing including hypercoagulability panels, infectious serologies, and multiple cultures were negative. Initial EEG showed no occipital dominant rhythm with prominent biphasic and triphasic waves.

MRI Brain with and without contrast revealed multiple, confluent, non-hemorrhagic areas of increased FLAIR signal seen in the basal ganglia, thalamus, internal capsule, cerebellum, frontal and temporal lobes (Fig 1B) with some patchy, symmetric, punctate areas of enhancement within these regions (Fig 1C). Most areas were associated with restricted diffusion (Fig 1D-E).

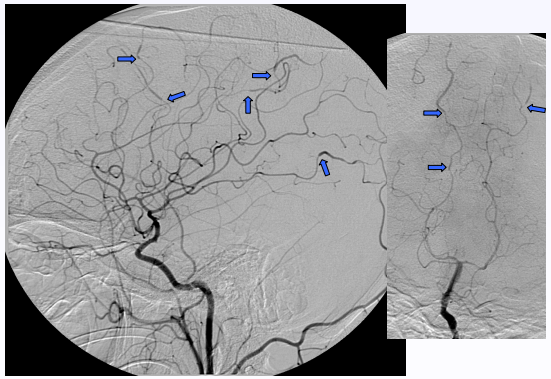
CASE REPORT, cont

Figure 1. CT and MRI Brain Imaging



CT head without contrast (A) shows multiple calcifications. MRI FLAIR (B) shows multiple confluent areas of increased signal with patchy enhancement (C). DWI sequences (D) illustrate many of these areas show restricted diffusion confirmed with ADC (E).

Figure 2. Cerebral Angiogram Results



Carotid (A) and basilar (B) injections with areas of narrowing (Arrows) and beading in all territories.

A 4-vessel angiogram was performed which showed beading and narrowing of all territories, consistent with cerebral vasculitis (Fig 2). The patient was treated with methylprednisolone 1000 mg intravenous daily for 5 days without improvement. The patient deteriorated clinically, with a worsening MRI. The family was not interested in a brain biopsy. She received one dose of intravenous cyclophosphamide. However, she continued to deteriorate and the family elected to withdraw aggressive support. The patient passed away 3 weeks after presentation. An autopsy was not performed.

DISCUSSION

Systemic sclerosis is a connective tissue disease of unknown etiology which causes rapidly progressive fibrosis of the skin, lungs, and other internal organs. Currently, cranial and autonomic neuropathies are widely recognized neurological associations with systemic sclerosis, but central nervous system manifestations are much rarer. This case shows the most extensive involvement of the central nervous system in systemic sclerosis of which we are aware with serologic and imaging evidence of vasculitis.

Previous literature has hypothesized that the CNS involvement in systemic sclerosis is due to a secondary vasculopathy. However, there is argument for a more primary involvement of the central nervous system. Basal ganglia calcifications[1] and white matter hyperintensities[2] have been reported to be more common in systemic sclerosis patients. There have been very few case reports of CNS vasculitis due to systemic sclerosis. One group in 1979 reported a case of encephalopathy associated with right sided hemiparesis, hyperreflexia, and elevated protein on CSF with an associated focal area of narrowing on angiogram that responded to steroids[3]. Other case reports[4,5,6] have demonstrated strokes or subarachnoid hemorrhage, angiograms consistent with vasculitis, but often normal biopsies which have improved with steroids and/or cyclophosphamide.

Given the severe encephalopathy seen in our patient in association with diffuse imaging abnormalities on MRI, elevated protein on CSF, and classic angiogram findings, CNS vasculitis with severe symptomatic involvement needs to be considered as a primary manifestation of systemic sclerosis. Our patient was unresponsive to treatment with steroids or cyclophosphamide, however her course seems more severe than patients previously reported in the literature, which may explain the lack of response.

REFERENCES

1. Héron E, Hernigou A, Fornes P, Chatellier G, Emmerich J, Fiessinger JN. *Ann. Med. Interne.* 2002 153(3): 179-182
2. Sardanelli F, Iozzelli A, Cotticelli B, Losacco C, Cutolo M, Sulli A, Nobili F, Rodriguez G. *Ann Rheum Dis.* 2005 May;64(5):777-9.
3. Estey E, Lieberman A, Pinto R, Meltzer M, Ransohoff J. *Stroke.* 1979 Sep-Oct;10(5):595-7.
4. Ishida K, Kamata T, Tsukagoshi H, Tanizaki Y. J Neurol Neurosurg Psychiatry. 1993 Jun;56(6):720.
5. Lee JE, Haynes JM. *Neurology.* 1967 Jan;17(1):18-22.
6. Lucivero V, Mezzapesa DM, Petruzzellis M, Carella A, Lamberti P, Federico F. *Neurol Sci.* 2004 Oct; 25(4):230-3.