Background: Neurological involvement occurs rarely with systemic sclerosis (SSc). Only a few cases of transverse myelopathy have been reported in the setting of SSc.

Objective: To describe a patient with SSc who developed transverse myelitis that improved during a course of immunosuppression.

Results: A 30-year-old woman with SSc presented with subacute onset of bilateral lower extremity weakness and numbness. Results of magnetic resonance imaging and cerebrospinal fluid studies supported a diagnosis of transverse myelitis. The patient responded favorably to a course of corticosteroids and cyclophosphamide. No overlapping autoimmune disorders were evident. Clinical follow-up showed significant recovery, with resolution of radiological abnormalities.

Conclusion: Transverse myelitis can occur as a rare manifestation of SSc and may respond favorably to immunosuppressive therapy.

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Systemic Sclerosis (SSc) is a multisystem disease that can involve several other organs besides the skin. Reports of neurological involvement have primarily referred to the peripheral nervous system. Central nervous system involvement appears to be rare. We describe a young woman with SSc who presented with lower extremity weakness and numbness. Her evaluation findings were consistent with transverse myelitis. There was no evidence of an overlapping autoimmune disorder or multiple sclerosis.

Report of a Case

A 30-year-old African American woman presented with 3 weeks of low back pain, progressive weakness and numbness of her left leg, followed by similar involvement of her right leg. She also developed urinary urgency, perianal numbness, and left lower facial numbness during that period. Her history was remarkable for recently diagnosed scleroderma, based on the presence of typical skin changes, positive serology, and skin biopsy findings. During the preceding year, she had developed arthralgias, skin changes, Raynaud phenomenon, dyspnea, and dysphagia. Neurological examination at the time of presentation revealed bilateral asymmetric lower extremity weakness. Proximal lower extremity strength, scored with the Medical Research Council scale, was grade 1 to 2 on the left and grade 4 on the right, while distal lower extremity strength was grade 0 to 1 on the left and grade 4 to 5 on the right.

Sensation was decreased to all modalities up to the right knee and the left mid thigh. Saddle anesthesia and reduced rectal tone were noted. Deep tendon reflexes were normal in the upper extremities and increased in the lower extremities. A Babinski sign was present on the left. Skin inspection showed diffuse sclerodermatous changes over the neck, anterior chest wall, dorsum of hands, and shins, along with digital pitting over some finger pads.

Laboratory evaluation findings, including hemogram, routine chemistry, thyroid function, vitamin B12 level, angiotensin-converting enzyme, erythrocyte sedimentation rate, and C-reactive protein, were normal. Hepatitis B and C, Lyme, and human immunodeficiency virus serologic test results were normal. Rheumatologic results included elevated antinuclear antibody at a titer of 1:2560 with a diffuse pattern, positive anti-Scl-70 antibody, and borderline positive ribonucleoprotein. Negative serologies included Ro, La, and Smith antibodies and
double-stranded DNA. Lupus anticoagulant, antiphospholipid profile, and complement levels were normal.

Magnetic resonance imaging (MRI) of the spine revealed increased T1 and T2 signals in the conus medullaris, with mild ring-like gadolinium enhancement (Figure). An MRI scan of the brain and visual evoked potentials were normal. Cerebrospinal fluid (CSF) analysis revealed normal levels of glucose and protein, 197/µL nucleated cells with 96% lymphocytes, and 120/µL red blood cells. Results of routine bacterial, acid-fast bacilli, and fungal studies were negative. The CSF IgG index and synthesis rate, oligoclonal bands, and cytologic findings were also normal. Results of serologic testing for cryptococcus and cytomegalovirus and of polymerase chain reaction testing for herpes simplex were negative. Electrophysiologic testing revealed normal motor and sensory nerve potentials. On needle electromyography, moderately severe active denervation potentials were present in the tibialis anterior, gastrocnemius medialis, and vastus lateralis, suggesting a proximal disorder of the motor nerves, lumbosacral roots or anterior horn cells.

She was initially treated with intravenous methylprednisolone sodium succinate, 1 g/d, for 7 days. She also received empiric antimicrobials and acyclovir sodium until the CSF culture and polymerase chain reaction results for herpes simplex virus returned negative. Despite these measures, weakness continued to progress in the right leg. Repeat MRI of the spine showed a stable appearance of the conus medullaris lesion. She was subsequently treated with intravenous cyclophosphamide at a dose of 700 mg/m². One week later, her left leg strength had improved to Medical Research Council grade 4 proximally and grade 3 distally, while the right leg had regained normal strength. Monthly intravenous cyclophosphamide pulses continued at 700 mg/m² and she was ambulatory with a walker after 2 months. Repeat MRI of the spine performed 2 months later showed complete resolution of the conus lesion (Figure).

Her course was complicated by cellulitis, prompting the cessation of cyclophosphamide for several months. Without immunosuppressive therapy, she experienced a relapse, with increasing weakness in the left leg greater than in the right leg. With reintroduction of monthly cyclophosphamide, her leg strength returned to the prior baseline. Nine months after her initial presentation, the left leg weakness continues to improve slowly.

**COMMENT**

Neurological involvement in SSc is uncommon and usually involves the peripheral nervous system. The most common manifestations are myopathy, present in 17% of patients, and cranial nerve palsies. The various neuropathies reported include trigeminal neuropathy, carpal tunnel syndrome, mononeuritis multiplex, and autonomic and peripheral neuropathy. Central nervous system complications of SSc are rare and usually arise secondary to hypertension and renal or pulmonary dysfunction caused by scleroderma. Isolated cases of cerebral vasculitis, intracerebral calcifications, optic atrophy, tran-
sient ischemic attacks, stroke, subarachnoid hemorrhage, and seizures have been reported.6-10

Spinal cord involvement in SSc may manifest as cord compression secondary to mechanical osteolysis and facet arthropathy or massive calcific deposits.10 Noncompressive transverse myelopathy has been reported in association with SSC, as well as localized scleroderma.11-13 In a retrospective study of 50 patients with SSc, Averbuch-Heller et al11 described 4 patients with myelopathy who had unremarkable findings on metabolic, radiological, and CSF studies. Transverse myelopathy has been described in association with the localized or linear form of scleroderma, in which the neurological symptoms antedated the skin changes.12

The differential diagnosis of transverse myelitis in our patient included infection, demyelinating or inflammatory disease, and a complication of SSc. The investigation for infectious etiologies was unremarkable. Although multiple sclerosis has been described in patients with SSc, ours had normal head MRI, visual evoked potentials, and CSF IgG study findings, making this diagnosis less likely.14,15

Several connective tissue diseases are associated with transverse myelitis, including systemic lupus erythematosus and Sjögren syndrome.16 One could argue that the transverse myelitis in our patient represented an initial manifestation of an overlapping connective tissue disease, such as systemic lupus erythematosus. However, our patient has not developed any defining features of an overlap syndrome to date. Therefore, transverse myelitis in our patient could be an independent event or a manifestation of SSc. To our knowledge, this represents the first case of transverse myelitis associated with SSc in which there were demonstrable CSF and radiological abnormalities.

The underlying pathogenesis of SSc may involve immunologic alterations, vascular endothelial cell activation or injury, and activation of fibroblasts, resulting in production of excessive collagen.17 It has also been suggested that fibrosis, vasculitis, and noninflammatory microangiopathy may contribute singly or in combination to the pathogenesis of neurological lesions in SSc.18 The CSF pleocytosis and neurological recovery associated with immunosuppression in our patient suggest that an immune-mediated process is responsible.

Successful treatment of transverse myelitis has been reported with corticosteroids, cytotoxic agents, and plasmapheresis. Cyclophosphamide has been used successfully in patients with scleroderma associated with transverse myelopathy and alveolitis.13,19 It has also been of fully in patients with scleroderma associated with transverse myelitis has been reported in association with SSC, as well as localized scleroderma.18 The croangiopathy may contribute singly or in combination to the pathogenesis of neurological lesions in SSc.18 The underlying pathogenesis of SSc may involve immunologic alterations, vascular endothelial cell activation or injury, and activation of fibroblasts, resulting in production of excessive collagen.17 It has also been suggested that fibrosis, vasculitis, and noninflammatory microangiopathy may contribute singly or in combination to the pathogenesis of neurological lesions in SSc.18 The CSF pleocytosis and neurological recovery associated with immunosuppression in our patient suggest that an immune-mediated process is responsible.

Successful treatment of transverse myelitis has been reported with corticosteroids, cytotoxic agents, and plasmapheresis. Cyclophosphamide has been used successfully in patients with scleroderma associated with transverse myelopathy and alveolitis.13,19 It has also been of benefit in SSc-related vasculitic neuropathy and central nervous system vasculitis manifesting as cerebral ischemia in a patient with CREST (calcinosis, Raynaud disease, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome.20,21 The combined use of corticosteroids and cyclophosphamide has been successful in a 34-year-old woman with SSc and acute transverse myelopathy,13 as well as in patients with transverse myelitis associated with systemic lupus erythematosus.22

Although our patient’s neurological improvement may have been spontaneous, we believe that immunosuppressive therapy played a key role. Her weakness progressed before initiation of immunosuppression and relapsed when cyclophosphamide was withheld because of an infection several months later. With reinstitution of cyclophosphamide and prednisone, she again improved.

Transverse myelitis is a rare manifestation of SSc and appears to respond favorably to aggressive treatment with immunosuppressive agents. Maintenance therapy may be required for patients with disease relapses.

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REFERENCES