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Case Report

Debilitating Bilateral Fibrosing Lumbar Plexopathy in a Patient with Systemic Sclerosis Sine Scleroderma

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Abstract

Systemic sclerosis is an autoimmune fibrotic disease which only rarely affects peripheral nerves. When it occurs, nerve damage is usually mediated by entrapment or small vessel vasculitis. Here we report the first case of bilateral lumbar fibrosing plexopathy in a patient with SSc sine scleroderma, an unusual form of SSc. Neurological symptoms were controlled with high dose prednisone and cyclophosphamide.

ABBREVIATIONS

SSc: Systemic Sclerosis; EMG: Electromyogram; TEP scan: Positron Emission Tomography scan; CRP: C-Reactive Protein

INTRODUCTION

Systemic sclerosis (SSc) is a rare disease characterized by diffuse vasculopathy and immune activation leading to systemic inflammation and sclerosis. Fibroblastic proliferation and subsequent sclerosis may lead to peripheral nerve damage by fibrotic vasculopathy, leading ultimately to ischemia and myelin destruction [1,2]. Plexopathy associated with SSc is fairly rare; only a few cases have been described to date, mostly with cervical plexopathy in the context of limited SSc [3-5].

CASE PRESENTATION

We report the case of a 63 years old woman followed for SSc sine scleroderma. Her SSc manifestations were pulmonary hypertension, Raynaud's syndrome, gastric antral vascular ectasia, gastroesophageal reflux disease and small bowel bacterial overgrowth syndrome. The laboratory tests showed an anti-centromeric ANA and a scleroderma (SD) pattern upon nail fold capillaroscopy. On follow-up, she presented with rapidly progressive bilateral leg weakness with neuropathic pain in absence of an obvious etiology.

Symptoms started with bilateral symmetric proximal leg weakness with marked dysesthesia, transgressing conventional dermatomes and nerve topography. All other SSc symptoms were stable. Her review of systems was not consistent with the development of overlap syndrome, inflammatory myopathies or vasculitis. In particular, no palpable purpura was found. Neurological examination showed prominent proximal muscle weakness (3/5) sparing distal muscles. She had normal CK, HbA_{1C}, TSH and vitamin B12 levels. Her serology for hepatitis B, hepatitis C, HIV, cytomegalovirus, herpes virus and Lyme disease were all negative. At this point, infectious causes were considered unlikely. Inflammatory parameters were slightly elevated but extensive research for other overlapping entities among vasculitides or connective tissus diseases were also all negative. In particular, ANCA, anti-phospholipid antibody, ds-DNA, anti-Ro, anti-La, anti-Sm and anti-Jo were all absent. Complement levels were within normal limits and the blood counts were not informative. Magnetic resonance imaging (MRI) of the thigh showed patchy segmental muscular inflammation of the proximal muscles, while the electromyogram (EMG) was suggestive of discrete inflammatory myopathy with focal necrosis. A primary immune-mediated myopathy was unlikely given the dysesthesia and normal CK levels, which instead pointed towards an immune-mediated neuropathy.Treatment with 1mg/kg prednisone and intravenous immunoglobulin (IVIG) was started. In spite of the immunosuppressants, she rapidly deteriorated with a loss of bilateral patellar and Achilles' tendon reflexes. Her muscle weakness progressed. Her dysesthesic symptoms which diffusely involved the leg now converged below the knee and became more intense with marked hypoesthesia. Pallesthesia and proprioception were also severely affected. A second EMG showed neuropathic and myopathic changes involving both sensitive and motor axonal damage in multiple myotomes of the lower limbs, but paraspinal musculature was spared, thus excluding radicular involvement. The symmetric presentation with extensive nerve involvement argued against mononeuritis multiplex. A contrast enhanced MRI of the spine and lumbar plexus was normal. A

muscle biopsy revealed partial chronic denervation and sural nerve biopsy demonstrated a fibrosing pseudovasculitis of the perineurium without amyloidosis and axonal degeneration. A Positron Emission Tomography (PET) scan excluded malignancy. On the basis of those pathologic findings and the pattern of the EMG, the diagnosis of bilateral lumbar plexopathy was established. Treatment with i.v. methyl-prednisolone 1g/day for 3 consecutive days was initiated followed by 1mg/kg/day of oral prednisone. Concomitantly, a protocol of 600mg/m_2 of intravenous cyclophosphamide every 3 weeks was added. She progressively improved over three months and recovered her muscle strength to 4/5. Pain improved to mild paresthesia and CRP returned to normal levels. IV Cyclophosphamide was maintained for 6 months and prednisone completely tapered.

DISCUSSION

Plexopathies associated with SSc are extremely rare. To our knowledge, only 3 cases of unilateral brachial plexopathy associated with SSc have been reported. The first was in the context of a diffuse oedematous SSc [3] and the other two in a patient with limited SSc [4,5]. Two cases of unilateral lumbar plexopathy associated with limited SSc [6,7] were also reported. Interestingly, one of those cases was in the setting of a necrotising vasculitis [7]. Here, we report the first case of plexopathy associated with SSc sine scleroderma. Moreover, this case was bilateral. Nerve mediated injury in scleroderma could be associated with traditional systemic vasculitis [8] but in this case, the lesion was a fibrosing vasculopathy. Although vasculopathy is a prominent feature of SSc franc vasculitis is rarely observed [9]. The earliest manifestations of immune-mediated vascular dysfunction are upregulation of surface adhesion molecules and hyper-reactivity vasconstrictors such as endothelin-1 leading to chronic ischemia and fibrosis [4,10,11]. Fibrosing vasculopathy has been proposed as one of the pathologic processes underlying mononeuritis multiplex, which falls in the spectrum of plexopathies [12]. In this case, such a vasculopathy may have triggered the patient's symptoms. Interestingly, treatment with prednisone and intravenous immunoglobulin failed to improve her symptoms. She experienced some improvement only with the use of pulsed steroids and cyclophosphamide. Our observation is concordant with another SSc case report where cyclophosphamide halted nerve damage [4], while IVIG did not provide any benefit. More over, the reported ability of cyclophosphamide tomitigate micro vessel damage in SSc may have had a direct impact on the controlling the vasculopathy in our patient [13].

CONCLUSION

In SSc, primary neurological involvement is extremely rare. Here we report the first case of bilateral lumbar plexopathy associated with SSc; moreover, occurring within the rare context of SSc sine scleroderma. In this case, bilateral plexopathy is likely to have arisen from a fibrosing vasculopathy in the perineurium with a minimal inflammatory infiltrate. This condition responded favorably to cyclophosphamide but was unresponsive to IVIG.

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