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CLINICAL VIGNETTE

A Case of Mononeuritis Multiplex as a Presenting Symptom of Wegener's Granulomatosis

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Objective

To present a case of GPA who presented with a chief complaint of bilateral lower extremity weakness and numbness, with EMG showing mononeuritis multiplex of the lower extremities.

Case Report

A 54-year-old female with a history of Raynaud's phenomenon and chronic rhinitis presented to the hospital with three weeks of progressively worsening bilateral lower extremity weakness and numbness. She initially noticed severe sharp shooting pain on the bottom of her right foot, which improved with NSAID use. Two days later the pain started to involve her left foot, and eventually transitioned to numbness and tingling bilaterally. Over the course of the next three weeks, the pain, paresthesias, and loss of sensation progressively worsened, and ascended symmetrically up to her knees. The patient also endorsed distal weakness of her legs with some difficulty ambulating. The patient denied any arthralgias, erythema, swelling, or visible changes in the lower extremities.

Over this same time period, the patient had seen multiple doctors for other concurrent symptoms. Three weeks prior to presentation, the patient experienced left ear pain, epistaxis, and a cough with trace hemoptysis. She went to an otolaryngologist and was prescribed oral low-dose prednisone, nasal steroid spray, and antibiotics for presumed sinusitis. After failing to improve on this regimen, the patient was referred to an immunologist. The immunologist initiated a full autoimmune disease work-up, which revealed a positive ANA (1:1280) and c-ANCA (1:160). Additionally, the patient was referred by her primary care doctor to a pulmonologist, after two weeks of unremitting cough. A chest CT revealed three irregular shaped nodular lung parenchymal lesions. No biopsy was done at that time, and the patient was started on nebulizers. Shortly thereafter, due to her progressive lower

extremity pain, weakness and numbness, she was referred to a neurologist. MRI showed no spinal cord pathology to account for her current symptoms. Two days later, her symptoms progressed to the point where the patient could no longer ambulate unassisted. She therefore presented to the UCLA emergency room for further work-up and management.

The patient's medical history included undifferentiated connective tissue disease, Raynaud's phenomenon, and history of positive PPD status post treatment. She emigrated from Columbia several years ago and was working as a medical lab technician. She reported no recent alcohol intake, smoking history, or use of drugs. Current medications included Prednisone 40 mg (started <1 week prior), tramadol for pain, and inhaled budesonide and albuterol for her known reactive airway disease. The patient had no history of allergy to any medications.

Physical examination in the ED revealed a thin, middle-aged female, in no acute distress. She was afebrile, with a blood pressure of 142/67, a pulse of 75, and O2 saturation of 99% on room air. Head and neck exam were only significant for dry mucous membranes of the oropharynx. Cardiac and pulmonary exam did not reveal any abnormalities. She had small punctate hemorrhages on several of the pads of her fingers (see figure 1).

There was no effusion or erythema around her joints or any joint tenderness. Neurological exam demonstrated decreased sensation to temperature, proprioception, and light touch bilaterally and symmetrically on the dorsum and plantar surfaces of her feet, as well as the lateral aspects of her lower legs up to her knees with sparing of the medial calves. Dorsiflexion and plantarflexion were 2/5 on the right and 4/5 on the left. Knee extension and flexion were 4/5 bilaterally. Reflexes were symmetric and 1-2+ throughout.

The patient could not ambulate independently due to weakness.

Laboratory workup revealed a C-ANCA titer of 1:160, elevated Proteinase-3 antibody of 133 (normal <21), anti-centromere titer of 1:1280, borderline DRVVT and a urinalysis with 19 RBCs and an elevated WBC to 19. Infectious workup was completely negative and patient had no B12 or folate deficiency to account for her neuropathy. A biopsy of a right lower lobe nodule was performed and showed "scattered multinucleated giant cells in a background of predominantly acute inflammation with focal necrosis and vasculitis, compatible with Wegener's granulomatosis." Additionally, echocardiography showed a circumferential medium size pericardial effusion with no tamponade physiology.

Electromyogram and nerve conduction studies of her lower extremities concluded "evidence of sensorimotor polyneuropathy with predominantly axonal features consistent with mononeuritis multiplex." GPA often presents as a polyneuritis but less commonly as a mononeuritis multiplex. Nonetheless, the patient was started on pulse-dose steroids for three days, followed by rituximab. The patient's cough, hemoptysis, and epistaxis resolved, and she regained some strength and sensation in her lower extremities, as well as her ability to walk unaided before discharge.

Discussion

Granulomatosis with polyangiitis (GPA), also known as Wegener's granulomatosis, is a rare antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis of small to medium-sized vessels. The incidence is 10 per million per year, with over 90% affected being Caucasian¹. According to the American College of Rheumatology, a patient must have two of the following four criteria to be diagnosed with GPA: nasal or oral inflammation; abnormal chest x-ray showing nodules, fixed infiltrates or cavities; microscopic hematuria; and granulomatous inflammation on biopsy of an artery or perivascular area². In addition to the effects on the upper and lower respiratory system and kidneys, GPA can cause arthritis, skin lesions, polyneuropathy, and (rarely) cardiac and gastrointestinal symptoms. Treatment consists of steroids and immunosuppressive medications, such as cyclophosphamide, azathioprine, methotrexate, and rituximab¹.

This case demonstrates several important points about the diagnosis, pathogenesis, and co-morbidities

associated with GPA. The initial presentation of GPA can be very dynamic and often complex. This patient in particular had chronic sinusitis, which is a common medical condition seen independently of GPA, but likely was one of the presenting symptoms of her diagnosis of GPA. Additionally, because of its multi-system involvement, there were several specialized physicians involved in her care including a Pulmonologist, Neurologist, Immunologist and Rheumatologist. The patient also had a past medical history that included undifferentiated connective tissue disease with features of limited scleroderma based on Raynaud's disease and repeatedly positive anti-centromere ANA pattern, further clouding the picture. Therefore, several months had passed before a unifying diagnosis was made.

Interestingly, this patient presented to UCLA with a chief complaint of bilateral loss of sensation and weakness of the lower extremities developing over a three-week time course. EMG was consistent with mononeuritis multiplex, a condition in which there is simultaneous inflammation of noncontiguous nerve branches, in this case, likely the peroneal nerves. The differential for such a neuropathy would include diabetes mellitus, inflammatory demyelinating polyneuropathy, multiple nerve entrapments, infections such as Lyme disease, and nerve infiltration (e.g., lymphoma, sarcoid, leukemia, or other forms of vasculitis and connective tissue disease). We believe the most likely cause of this neuropathy is a vasculitis of the vasa nervosum causing tissue ischemia³ secondary to GPA. The occurrence of symptoms late in the course of a disease suggests ischemia resulting from healed, scarred vessels as well as from those that are acutely inflamed³. Symmetric mononeuritis multiplex is an uncommon reason for admission and initial presentation of GPA. More frequently, cases of symmetric polyneuropathy occur and there have been several described cases of cranial involvement secondary to GPA.

There are only a few reported cases of vasculitic neuropathy in relation to GPA³. There is one case report in American literature showing mononeuritis multiplex as a presenting feature of GPA⁴. DeGroot et al. in 2001, presented an evaluation of 128 patients with GPA⁵. About half of these patients had neurological involvement of their vasculitic disease. Of these 64 patients, 56 had a peripheral neuropathy, 31 patients showed a distal symmetrical polyneuropathy, and 25 demonstrated a mononeuritis multiplex. In an earlier series of GPA patients in the Mayo clinic, eight out of 324 patients had presenting features of mononeuritis multiplex⁶.

It is important to recognize mononeuritis multiplex and other neurological complications of GPA to avoid delay in diagnosis and treatment. Our patient had neurological symptoms early in the course of her disease and had this been recognized earlier and correlated with her symptom of chronic sinusitis and CT evidence of pulmonary nodules, earlier intervention may have limited progression of her bilateral lower extremity weakness and sensory loss.

FIGURES



Figure 1-Small punctate hemorrhages on the pads of patient's fingers.

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