CASE REPORT

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Ulnar Claw Hand as Presenting Feature in Systemic Lupus Erythematosus with Sjögren's Disease

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Abstract

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with diverse clinical presentations, including neurological manifestations predominantly affecting the central nervous system. Peripheral nervous system involvement, although less common, significantly impacts patient morbidity and quality-of-life. This case report describes a 35-year-old woman with SLE who presented with acute peripheral neuropathy characterised by burning pain, weakness, claw hand deformity and sensory loss in the distal extremities, alongside purpuric rashes. Initial diagnostic challenges arose due to the overlapping symptoms of mixed connective tissue disease. Comprehensive evaluation, including nerve conduction studies, serological findings, elevated antinuclear antibodies, specific autoantibodies, and skin biopsy, confirmed axonal sensorimotor neuropathy secondary to vasculitis associated with SLE. The patient was treated with pulse steroids and cyclophosphamide due to the severity of her neurological symptoms. This case underscores the necessity of considering SLE in patients presenting with peripheral neuropathy, as it can occur early in the disease course and requires prompt diagnosis and management to mitigate its profound impact on quality-of-life.

Key words: Systemic lupus erythematosus (SLE), vasculitis, peripheral neuropathy.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that involves one or several organ systems over time, with damage mediated by autoantibodies and immune complexes. An estimated 37% to 90% of SLE patients have neurological symptoms, which are primarily related to the central nervous system[1,2]. In contrast, peripheral nervous system involvement in SLE is comparatively less common, occurring in about 2 - 27% of cases[3-5].

Patients with SLE who have peripheral nervous system involvement have a significantly higher risk of morbidity and a lower quality-of-life. Even though SLE has a major impact on a patient's quality-of-life, peripheral nervous system complications have not received much attention.

Sjögren's disease, characterised by the sicca complex of xerophthalmia, xerostomia, and dryness of other mucous membranes, can independently be associated with neuropathy. Patients commonly present with axonal sensorimotor neuropathy, while pure small fiber neuropathy or cranial neuropathy involving trigeminal nerve can also be seen. Sjögren's disease is also associated with sensory ganglionopathy. It is rarely associated with necrotizing vasculitis, but nonspecific perivascular inflammation may be present.

Mixed connective tissue disease (MCTD) is also associated with mild distal axonal sensorimotor neuropathy in 10% of patients.

A case of peripheral neuropathy attributed to SLE with Sjögren's disease, which initially caused a diagnostic conundrum between SLE and MCTD, is reported here.

Case

A 35-year-old woman presented with burning pain with numbness in hands and feet for 12 days, weakness of hand grip for 10 days, inability to walk for 10 days, and purpuric rash over the front of the ankle for 10 days. The patient also complained of fatigue for the past 25 days, which had progressively increased to limit her daily activities. The numbness progressed to the wrist in the upper limbs and ankle in the lower limbs. Initially, the patient had difficulty in holding slippers, and gradually, it progressed to complete loss of weight bearing on her feet with twisting of her ankle upon attempted weight-bearing. The patient; however, could walk with support, get up from a squatting position with support, and lift her legs while changing trousers. The patient simultaneously struggled to grip objects tightly, which progressed to a complete loss of ability to hold onto objects such as cups, utensils, opening taps, and buttoning or unbuttoning her shirt. The patient did not have any difficulty lifting her hand above the head.

There was no history of fever, headache, altered consciousness, vertigo, dizziness, hearing loss, blurring vision, double vision, dysphagia, dysarthria, or deviation of mouth.

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The patient also developed a rash over the bilateral ankle for the past 10 days, which was purplish, painless, and non-pruritic.

There was no history of joint pain, discoloration of fingers, tightening of the skin, photosensitivity, hair fall, oral ulcers, recurrent pregnancy loss, or any drug intake. The patient had regular menstruation with normal flow. She had three children, all born by full-term normal uneventful delivery at the hospital.

There was no history of diabetes, tuberculosis, or any other chronic disorder. There was no history of any toxin exposure or chronic drug intake. She was a vegetarian by diet, with a regular sleep pattern and had no history of chronic alcohol intake or any other addiction.

On examination, the patient was conscious and oriented to time, place, and person. Her vitals were within normal limits. On head-to-toe examination, there was visible wasting of small muscles of the hand and significant wasting in leg muscles. Local examination revealed multiple purpuric rashes over the anterolateral aspect of both ankles, with the largest measuring 7 x 2 cm (Fig.1). No other skin lesions suggestive of leprosy or thickening of nerves was present.

On neurological examination, she had claw hand deformity

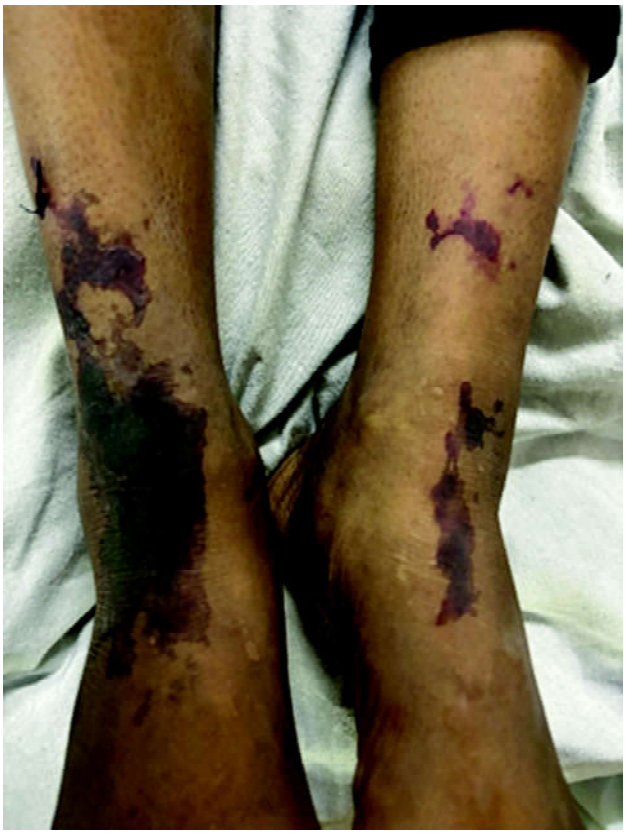

Fig 1: *Purpuric rash over the anterior aspect of both ankles.*

(Fig. 2) in both hands with atrophy of hypothenar muscles. Motor examination showed decreased power of MRC grade 1/5 at the wrist joint and ankle joint. On testing individual hand muscles, there were weak lumbricals, palmar interossei, dorsal interossei, abductor pollicis, adductor pollicis, flexor pollicis, and opponens pollicis in both hands. Deep tendon reflexes were normal except for finger flexion and ankle reflex, which were absent. On sensory examination, there was decreased sensation of all modalities in hands bilaterally up to the wrist joints and bilateral feet up to the ankle joints along the dermatomal distribution of the median and ulnar nerves. On examination of the respiratory system, there were decreased breath sounds in bilateral infrascapular regions. Other systemic examination was normal.

Laboratory examination revealed normocytic normochromic anemia, Hb 8.6 g/dL, total leukocyte count 7,700/mm^3, and platelet count 3,65,000/mm^3. ABG analysis showed pH - 7.48, pCO2 - 38 mmHg, Po2 - 98 mmHg Lactate - 1.2 mmol/L Hct of 29%, Na - 136 mmol/L, K - 3.8 mmol/L, Glucose - 87 mg/dL, HCO_3 - 28.33 mmol/L. Urine routine microscopy showed no protein. UACR levels were less than 30 mg/g. Total serum protein was 6.8g/dL (albumin - 3.5 g/dL, globulin - 3.3 g/dL). Other biochemical parameters such as serum electrolytes, serum calcium, renal function tests, and liver function tests, were normal.

Chest X-ray showed blunting of bilateral costophrenic angles suggestive of bilateral mild pleural effusion.

The cerebral spinal fluid (CSF) analysis was normal. Normal levels of CSF biochemistry were observed (protein - 40 mg/dL, Sugar - 43 mg/dL, Total cells 2/mm^3) with no cytoalbuminological dissociation. CSF Venereal Disease Research Laboratory test (CSF VDRL) was also negative. An MRI of the entire spine and brain showed no signs of acute pathology. ESR and CRP levels were significantly raised (65 mm Ist hour and 133 mg/L, respectively).

A fine-speckled antinuclear antibody pattern at a diution of 1:640 was found in the first serological analysis. The complete ENA profile later revealed positive Smith antibody (1+), positive SS-A and Ro52 kd antibody (3+), positive Ku antibody (1+), positive nucleosomes (1+), positive RNP (3+). C3 level was 72 mg/dL, and C4 level was 6 mg/dL. Anti MPO - 0.20 (Negative) and anti proteinase 3 antibodies - <0.01 (Negative). Serology for HIV, hepatitis B, and hepatitis C was negative. The levels of vitamin B12 and thyroid-stimulating hormone (TSH) were within normal limits. The laboratory investigations are summarised in Table I.

The nerve conduction study supported the presence of axonal sensorimotor neuropathy.

Skin biopsy was taken from the site of purpuric rash, which revealed proliferation of small to medium-sized blood

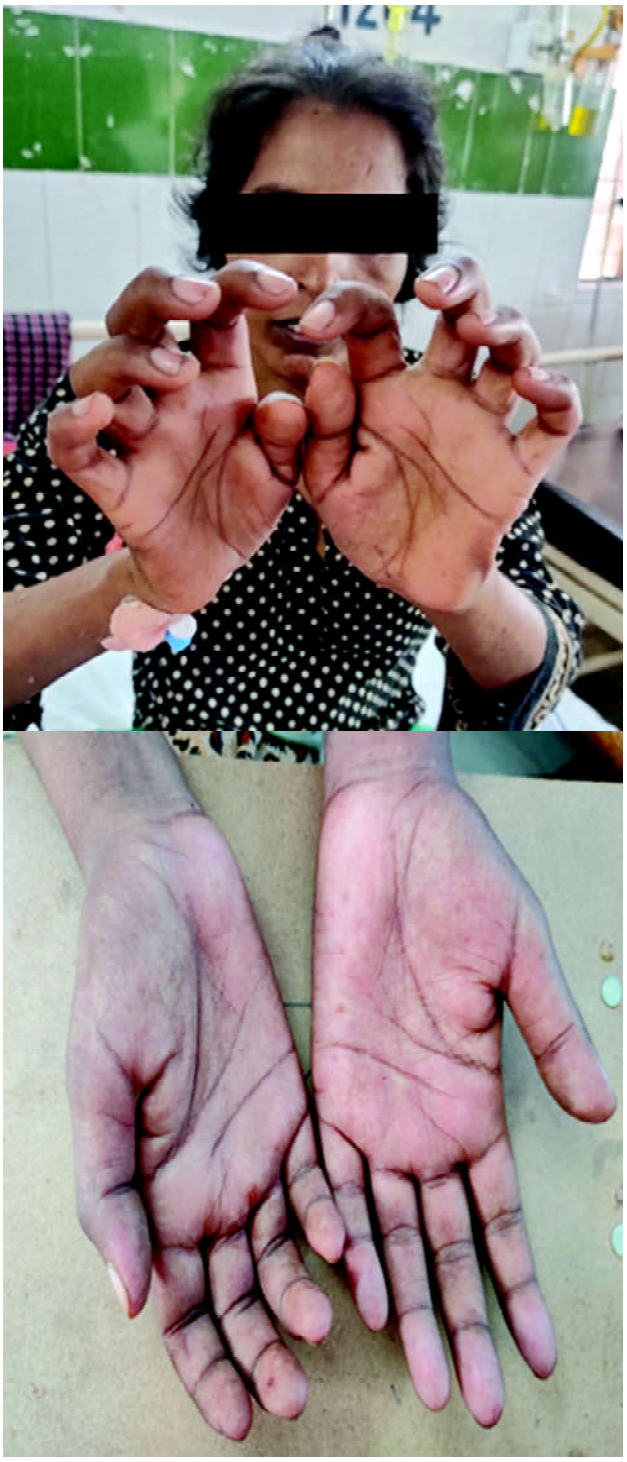

Fig. 2: *Ulnar claw hand with wasting of thenar and hypothenar muscles.*

vessels with perivascular infiltration of neutrophils. Focal destruction of blood vessels, extravastion of RBCs, and fibrinoid necrosis was also seen. These findings were consistent with cutaneous small vessel vasculitis (Fig. 3).

Nerve biopsy was also planned in our patient due to high suspicion for vasculitis. However, as it would have added little to what we already knew from clinical, biochemical and histopathological findings of skin biopsy, we deferred this procedure.

The patient also complained of dry eyes and dry mouth. Schirmer's test was also done, which showed a tear film up to 4 mm in both eyes. Tear filar breakup time was 20 seconds in both eyes.

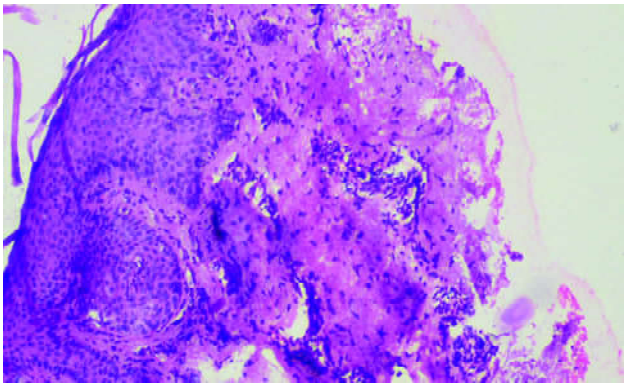

Fig. 3: *Examined section of skin biopsy slide in H & E staining showing perivascular inflammatory infiltrates consistent with vasculitis.*

Table I: Investigations

Total leukocyte count	7700/mm^3
Haemoglobin	8.6 g/dL
Platelet count	3,65,000/mm^3
BUN	13 mg/dL
S. creatinine	0.8 mg/dL
S. sodium	136 meq/L
S. potassium	4.2 meq/L
AST	31U/L
ALT	15 U/L
ALP	95 U/L
Urine routine microscopy	No protein
ANA (Indirect Immunofluorescence)	**1:640 (fine speckled)**
Anti smith	1+
Anti U1 RNP	**3+ (>200 U/mL)**
Anti-SSA	**3+**
Anti-SSB	**3+**
Anti-dsDna	**Negative**
ESR	65 mm Ist hour
CRP	133 mg/L
C3	72 mg/dL (90 - 180 mg/dL)
C4	6 mg/dL (10 - 40 mg/dL)

Differential Diagnosis

The patient presented with acute onset weakness and numbness in all four limbs involving predominantly distal muscles. History of dragging of feet, slipping of slippers, weakness of handgrip along with burning sensation and numbness in all four limbs since 10 days was suggestive of symmetric sensorimotor neuropathy or polyradiculopathy. Neuropathies with acute and subacute presentations include demyelinating neuropathy like Guillain Barré syndrome (GBS), vascultitis, radiculopathies related to diabetes, infective pathology like leprosy, lyme disease, Syphilis or any toxin exposure. The possibility of metabolic causes like vitamin B_{12} deficiency and niacin deficiency were also kept. The pattern was symmetrical, predominantly distal weakness associated with sensory loss. There was no history suggestive of any toxin or drug exposure. Acute motor sensory axonal neuropathy (AMSAN) variant of GBS was ruled out by the presened of deep tendon reflexes and absence of cytoalbuminological dissociation in CSF analysis. The patient also did not have any evidence of skin lesions or thickening of nerves suggestive of leprosy, neither any evidence of leprosy was found in skin biopsy. Metabolic causes were ruled out by normal vitamin B_{12} level and absence of clinical manifestation of niacin deficiency. Diabetic neuropathy was ruled out by normoglycaemia. MRI spine also did not show any features of radiculopathy.

The ANA profile report was strongly positive with a fine-speckled antinuclear antibody pattren (1:640) along with raised ESR and CRP levels.

The patient's presentation of polyneuropathy with vasculitic rash, lab results indicating antinuclear antibody (ANA) and anti-Smith Ab positivity, low complement level, electrodiagnostic studies revealing axonal sensorimotor neuropathy, and biopsy showing changes of vasculitis led to the diagnosis of severe sensorimotor polyneuropathy secondary to vasculitis associated with SLE.

Treatment

The patient was administered pulse intravenous steroids and an induction regimen of cyclophosphamide, given the organ-threatening complication of polyneuropathy. She was discharged on prednisone 40 mg, gabapentin, and nortriptyline for pain.

Discussion

Peripheral neuropathy is a known and underestimated complication in SLE, which may take several different forms. Patients usually present with generalised sensory or sensorimotor polyneuropathy. Some patients may present with burning pain and paraesthesiae with normal reflexes, suggesting small fiber neuropathy. In contrast, other patients may present with less common syndromes, including multiple mononeuropathies and acute or chronic demyelinating polyradiculopathy[6]. In our case, the patient presented with weakness of distal muscles and sensory loss of both upper limbs and lower limbs, which was consistent with symmetrical sensorimotor polyneuropathy.

Histopathological studies of the peripheral nerves in SLE have revealed axonal degeneration, inflammatory changes, and vasculitis. The primary characteristic of SLE vasculitic neuropathy is blood vessel wall inflammation, which leads to ischaemic nerve damage and axonal loss. According to Mawrin *et al*, vessel wall damage may be linked to the upregulation of matrix metalloproteinase-3[7] and matrix metalloproteinase-9 in the pathophysiology of peripheral neuropathy in SLE, leading to a chronic combined axonal and demyelinating type of SLE-PN.

In our case, we diagnosed vasculitic neuropathy based on skin biopsy and nerve conduction study findings, as nerve biopsy would be invasive and may lead to neurological complications. Histological findings of nerve biopsy would have been helpful only in difficult circumstances where nerve conduction studies and other non-diagnostic investigations were non-diagnostic.

Meanwhile, the clinical and laboratory manifestations of the patient also satisfied the ACR-EULAR 2016 classification criteria for Sjögren's disease with a score of 4 (Schirmer's test <5 mm and positive anti-SSA/SSB antibodies). Sjögren's disease can also be complicated by neuropathy most commonly axonal sensorimotor neuropathy followed by ganglionopathy which is characterised by sensory loss in the extremities. In our patient, this may have also contributed to neuropathy.

A subset of SLE, SSc, and polymyositis clinical characteristics are incorporated into MCTD. A high level of anti-U1 RNP, a particular autoantibody, distinguishes it. Since a high titer of anti-U1 RNP is frequently associated with the sequential occurrence of the distinctive overlapping features of SLE, SSc, and inflammatory myopathy, the diagnosis frequently becomes challenging[8]. Anti-U1 RNP titers in our patient were extremely high, but there were no features like puffy fingers, Raynaud's phenomenon, myalgia, or synovitis. The patient even fulfilled the SLICC classification criteria 2012. Thus, the patient was eventually diagnosed with SLE with neuropathy as a result of the same disease process.

In a patient presenting with neuropathy, one should suspect a connective tissue disease when the patient presents with progressive sensory symptoms and weakness in the extremities, sometimes associated with burning pain and paraesthesiae. Such patients can also

present with multiple mononeuropathies or their presentation can also mimic GBS or chronic inflammatory demyelinating polyneuropathy CIDP. These are often associated with fever, polyarthralgia or other constitutional symptoms.

Peripheral neuropathy usually develops in the advanced stages of SLE and very rarely from the outset. Previous studies revealed that patients with SLE-related PN had an essentially higher Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-2K, which is a marker of disease activity and chronic inflammation[9-11]. In contrast to these studies, our patient presented with peripheral neuropathy early in the course of the disease, even before the development of other manifestations of active disease such as fever, mucocutaneous involvement, arthritis, or myositis. The disease activity, according to SLEDAI, was also low in our patient. However, our patient had unusually aggressive peripheral neuropathy in the form of bilateral distal sensory loss, bilateral distal muscle weakness along with muscle atrophy and ulnar claw hand deformity.

Since neuropsychiatric SLE can manifest as organ-threatening peripheral neuropathy, she was prescribed high-dose pulse methylprednisolone, i.v., for 3 days with cyclophosphamide 500 mg, i.v., monthly for 6 months for induction therapy. After being discharged on oral prednisolone, she was subsequently prescribed hydroxychloroquine. In the follow-up, the patient had significant improvement in the neuropathic pain; weakness improved from power 1/5 to 3/5.

Conclusion

Patients of SLE any have neurological symptoms. Although peripheral neuropathy does not pose a threat to life, it is linked to significant morbidity and has a substantial impact on the quality-of-life, particularly in younger individuals. The diagnosis of vasculitic neuropathy can be made without invasive procedures like nerve biopsies on the basis of serological profile alone. SLE should be considered as one of the differential diagnoses in all patients with polyneuropathy to aid in timely diagnosis and prompt initiation of treatment.

Declaration of patient consent

The author certifies that all appropriate patient consent forms have been obtained. In the form, the patient consented to her images and other clinical information being reported in the journal. The patient understands that her name and initials will not be published, and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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