Pruritus as Unusual Manifestation of Lupus Myelopathy

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Abstract

Lupus myelopathy is a relatively uncommon manifestation of SLE. Atypical presentation of this rare entity with neuropathic itch has never been reported. We report a young girl who presented with predominant symptom of refractory pruritus which after clinical localization and imaging was detected to have long segment patchy myelitis. Detailed evaluation led to a diagnosis of lupus myelopathy and the patient responded to immunosuppressive therapy with significant clinical and radiological improvement. Maintaining a high level of suspicion for neurological cause in a patient with refractory localized itching resistant to regular antiallergic treatment is important in the right clinical setting.

Introduction

The sensation of itch can only be perceived by a few tissues, specifically the skin and superficial mucous membranes. However, substantial numbers of patients who complain of disabling chronic itch have no apparent cause in the skin. Many of these patients have systemic or medical causes of itch such as drug reactions, metabolic or endocrine disorders, or kidney or liver dysfunction. There is recent interest in neurological disorders as an additional cause of focal or generalized pruritus.[1] Neuropathic itch is still under-recognized by most neurologists despite its localization value. Neuropathic itch is caused by diseased or malfunctioning pruritic neurons firing action potentials without pruritogenic stimuli in contrast to cutaneous or pruritoceptive itch which is caused by pruritogens activating cutaneous nerve endings bearing pruritogenic receptors. Various intramedullary lesions have been shown to cause pruritus in both humans and animals, attesting to the importance of the spinal cord as an itch modulating center.[2] We report a 20 yr old girl who presented initially with severe itching in localized distribution and did not respond to topical and antiallergic therapy and turned out to be lupus myelopathy on detailed work up and finally responded to immunosuppressive drugs. To best of our knowledge this is the first case report of lupus myelopathy presenting as neuropathic itch.

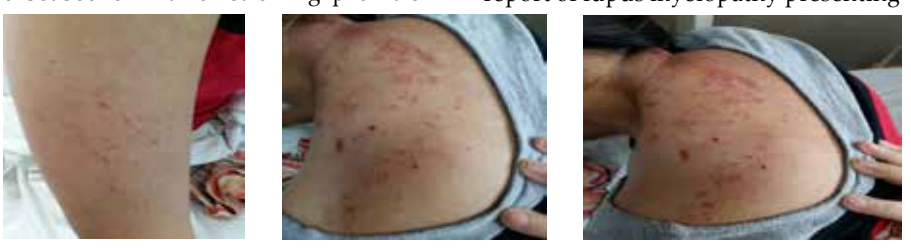

Fig. 1: Itchy areas with dermographism and skin abrasions

Case Report

20 yr old girl MK presented with history of paroxysmal itching in cape like distribution over bilateral upper limbs, neck and upper trunk of 2 months duration which was severe, uncontrollable, associated with forceful scratching and skin abrasion. Itching was associated with parasthesiae with similar distribution and was paroxysmal with variable location and duration and was mostly unpleasant/ painful with burning, tingling and pins and needles sensation. She was treated at skin OPD with various topical and systemic drugs including emollients, antihistaminics, antifungals, antiseptics and steroids with minimal benefit and was associated with periods of severe exacerbations interspersed with mild remissions. Detailed history further revealed symptom of fleeting joint pains, intermittently for last 3 yrs with occasional swelling. There was no history of fever, anorexia, weight loss, skin rash, constitutional symptoms, jaundice, edema, oliguria, nocturia. There was no history suggestive of dysthyroid state. There was no history suggestive of motor weakness, sensory deficits, band like sensation, bowel/ bladder disturbance, cranial nerve deficits, visual disturbances. She denied history of any drug intake prior to the symptoms. On clinical examination she was afebrile, vital parameters were normal and there were

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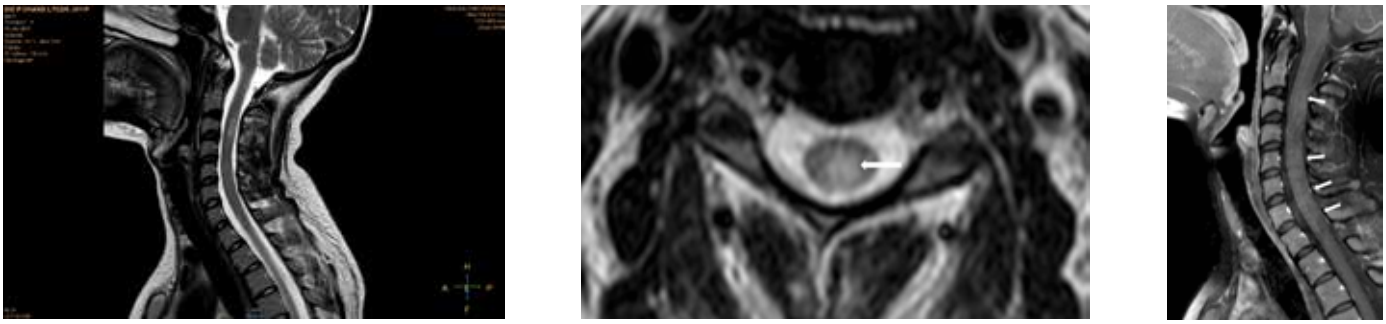

Fig. 2: MRI- TSE T2 sagittal (a) section of the cervical cord shows focal areas of hyperintense signal intensity within the spinal cord. These areas were hyperintense on STIR and isointense on T1WI; (b) Axial section at level of the cranial lesion shows predominant involvement of dorsal and lateral columns (white arrow); (c) Post contrast TSE T1 FS Sag section shows faint patchy enhancement of large segment of the cervical spinal cord (white arrows)

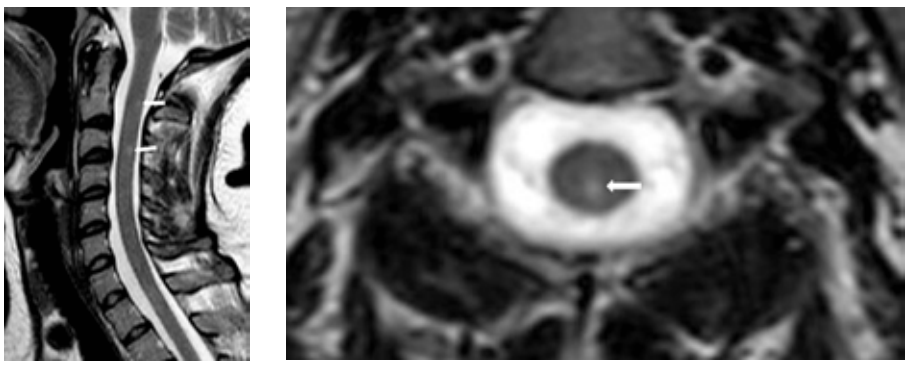

Fig. 3: TSE T2 Sag (a) and axial (b) done three months after initial diagnosis and treatment shows significant reduction in area of involvement (white arrows) as compared to initial study

no features suggestive of connective tissue disorder. Local examination revealed itching areas with erythema and dermographism with multiple excoriations and abrasions (Figure 1).

Neurological examination revealed normal bulk, tone, power in all four limbs with no sensory deficit. Deep tendon jerks were brisk in all four limbs (lower limb> upper limb) with normal plantar reflex. Other systemic examination was normal. After clinical evaluation differential diagnosis of dermatological disorder/ hypersensitivity disorder,functional/ psychogenic disorder, metabolic/ endocrine disorder and Neurological disorder with cervical cord/ peripheral nerve lesions were sought. She was planned for detailed investigations and work up.

Investigations revealed normal complete blood count and liver/ renal function tests. Urine routine/ microscopic examination and 24 hr urinary protein was normal. Serum electrolytes, prothrombin time, lipid profile, thyroid function test, chest X ray, USG abdomen were normal. HIV, HBsAg, Anti HCV was negative. ESR was 17 mm fall at 1 hr and CRP/ Rheumatoid factor was negative. MRI Brain was normal and MRI cervical spine revealed patchy long segment cervical myelitis (Figure 2 a, b, c).

At this stage an etiological diagnosis of Inflammatory CNS demyelinating disorders (MS, Neuromyelitis optica), Connective Tissue Disorders (SLE, Sjogrens Syndrome, Mixed connective tissue disorder)and Para/post infections were kept. To rule out possibility of Multiple sclerosis /Neuromyelitis Optica and other demyelinating disorder cerebrospinal fluid (CSF) study was done which revealed cells – 25/cumm, pred.- polymorphs, protein 85mg/dl,Sugar – 64mg% (random blood sugar – 102 mg%) staining/ culture – neg, CSF Oligoclonal bands – negative, Serum and CSF NMO Ab(Anti AQP4) – negative. Detailed ocular examination revealed normal fundus with visual fields. Visual evoked potential was normal. Collagen profile (Qualitative) revealed positive ANA with antibodies positive for extractable nuclear antigens dsDNA, Nucleosome, PM- Scl. In view of ANA positivity with clinical and neuoimaging features suggestive of myelitis she was planned for quantitative autoimmune markers along with anti phospholipid antibody (APLA) work up which revealed ANA – 166.16 U (<20.00), Anti-ds DNA Ab – 675.46 IU/mL (<30.00),Anti-Cardiolipin Ab – IgG – 26.28 GPL (<15.00),IgM – 11.91 MPL (<12.50) MPL, Anti β2 Glycoprotein1 Ab – elevated with Complement – C3 – 82.5 mg/dL(↓), C4 – 14.5 mg/dl (Normal). With strong positive ANA, Anti dsDNA and antiphospholipid antibody with spinal cord involvement / musculoskeletal and cutaneous involvement, diagnosis of Systemic Lupus Erythematosus with Lupus Myelopathy and Secondary APLA syndrome was made. She was started on IV Methyl Prednisolone pulse – 1 gm IV OD x 5 days followed by oral prednisolone (1mg/kg bw), hydroxychloroquine, antithrombotic drug and other supportive measures. IV cyclophosphamide was not offered as induction agent in view of her age and fertility issues due to its significant gonadal toxicity. She was planned for rituximab as induction agent which was administered 500 mg IV infusion per week x 4 wks. Her itching and parasthesia/dysasthesia gradually subsided. Repeat MRI scan cervical spine 3 months after iv pulse steroid/ iv rituximab showed significant resolution of cervical cord lesions (Figure 3 a, b).

She was being planned for slow steroid taper with continuation of other supportive measures with close watch on recurrence/ relapse of disease and other systemic involvement.

Discussion

Involvement of the nervous system is common in patients with SLE. Depending on the accepted criteria it is estimated that symptoms of nervous system involvement are present in

approximately 25–80% of patients. Myelopathy is one of the less common neuropsychiatric manifestations of SLE (1–3% of patients).[3] The most common form is acute transverse myelitis (ATM). Longitudinal myelitis is less frequently observed.[4] It has been recently recommended that all cases of myelitis – both transverse and longitudinal – in patients with SLE be referred to as lupus myelopathy.[5] In the majority of cases, myelopathy occurs shortly after SLE is diagnosed, usually within the first 5 years from the onset of the disease. In nearly half of patients with lupus myelopathy ATM is the first clinical manifestation of SLE. The disease usually affects young and middle-aged females, although some males might be affected.[6] Recurrence of myelitis within several months after the first episode of myelopathy is relatively frequently observed in patients with ATM in SLE. At least one recurrence of ATM in SLE is noted in 21–55% of patients. Episodes of recurrence were found mainly in untreated patients and in patients receiving long-term therapy with low or medium doses of glucocorticosteroids.[7] Pruritic lesions may occur associated with collagen diseases and the diagnosis of SLE must be excluded in patients with chronic pruritus. In the index case patient had dominant disturbing symptoms of pruritus associated with paresthesia in a distribution pointing to the involvement of dorsal cervical cord. Patchy long segment spinal cord involvement along with other clinical and serological criteria including antiphospholipid antibody led us to definitive diagnosis of lupus myelitis after excluding multiple sclerosis and neuromyelitis optica. In general, the antiphospholipid antibodies may be detected in 30-50 % of patients with systemic lupus erythematosus, while the incidence of antiphospholipid antibodies in systemic lupus erythematosus patients with transverse myelitis has been somewhat higher, to the tune of 55-64 %. Because of low prevalence of myelitis there are no precise and unanimous recommendations for standard therapy of myelopathy in SLE. Currently, use of glucocorticosteroids and cyclophosphamide is a standard therapy of SLE involving the central nervous system, including myelopathy in SLE.[8] In our case treatment with iv cyclosphamide was not offered considering the patient being in reproductive age group and fertility related issues. She was administered iv rituximab as induction therapy. Use of rituximab as induction agent is solely based on case reports/case series from single centre and non-controlled studies. Rituximab rapidly improved refractory neuropsychiatric SLE as evident by improvement of various clinical signs and symptoms and resolution of radiographic findings.[9] At present, there is no treatment strategy for patients with neuropsychiatric SLE who fail to respond to conventional therapies. In such patients some authors postulate repeated cycles of immunosuppression in therapy-resistant cases. However, duration and frequency of the repeated cycles have not been determined. Sole infusions of glucocorticosteroids were effective in some cases of lupus myelopathy.[6] Few studies showed that rituximab is useful as a new treatment for such cases.[9] Preliminary data indicated that rituximab could be beneficial in preventing permanent neurological damage in severe lupus myelopathy.[10] The earlier immunosuppressive therapy is introduced and the more aggressive it is, the better the long-term prognosis is. Patients with inflammatory lesions visible in the MR of the spinal cord that resolve after the first intravenous immunosuppressive therapy have better prognosis. In present case patient has shown marked improvement both clinically and radiologically which indicates good prognosis. There are only few case reports of neuropathic itch secondary to spinal cord involvement but lupus myelopathy presenting as neuropathic itch has never been reported.

Conclusion

Pruritus and the long segment myelitis might be indicators of the lupus disease. Some of the refractory itches, currently attributed to psychiatric illness might be neuropathic instead. Itch can be a presenting symptom of a neurological problem that may require definitive treatment. Although dermatologists are increasingly aware of neuropathic causes of itch, early referral to neurologist could improve the diagnostic possibility in appropriate clinical setting.

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