Transverse myelitis is a rare but serious neurological complication of systemic lupus erythematosus (SLE). A longitudinal involvement of the spinal cord with lupus related transverse myelitis is even more unusual. We report the case of a 27-year-old woman who had a catastrophic onset of paraplegia within two days of diagnosis of SLE. Magnetic resonance imaging of the spine established the diagnosis of longitudinal myelitis extending from C6-L1 level. Despite early aggressive treatment with combination of methylprednisolone and cyclophosphamide pulse therapies, her condition did not improve till 4 months of follow-up. Her case is peculiar because longitudinal myelitis involving almost the entire spinal cord is exceedingly rare.

**Keyword**: Systemic lupus erythematosus, Longitudinal myelitis, Magnetic resonance imaging.

**Introduction**: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease predominantly affecting women. The most common targets of SLE are the joints, skin, kidneys and blood vessels. Central nervous system (CNS) involvement is reported in 24-51% of cases and often carries a poor prognosis. Common neurolupus manifestations include seizures, psychosis, depression, cognitive dysfunction, headache, cerebrovascular accidents and aseptic lymphocytic meningitis. Myelitis is a rare but well established complication of SLE. It occurs in 1-3% of SLE patients and is usually implicated with the presence of antiphospholipid (aPL) antibodies reactivity. It presents as a rapidly progressive motor, sensory and autonomic dysfunction with uncertain pathophysiology. The common presenting symptoms are weakness of lower extremities, numbness, paraesthesia, paraparesis, quadriparesis, urinary retention, and fecal incontinence. Preferred diagnostic tool is magnetic resonance imaging (MRI), which typically shows increased signal intensity in T2-weighed images and a diffuse edema of the spinal cord. Prognosis is generally poor, despite early aggressive immunosuppressive therapy with methylprednisolone and cyclophosphamide. In SLE-related myelopathy, the most common pattern described is transverse myelitis (TM) whereas longitudinal myelitis pattern is seldom reported. Longitudinal myelitis (LM) is a rare variant of SLE-related myelopathy which is defined by the continuous involvement of more than four spinal cord segments. It is characterized by an acute catastrophic onset, a closer association with antiphospholipid antibody (aPL) syndrome and an unfavorable prognosis. Herein we report an uncommon case of longitudinal myelitis involving almost the entire spinal cord as an early manifestation in an SLE patient.

**Case-report**: A 27 year old woman was admitted with high grade fever, cough, headache, myalgia and joint pains for 3 days. She had experienced similar episodes over the past 3 months. She also complained of easy fatigability, oral ulcers, alopecia, and loss of weight. There was no history of rash, photosensitivity or psychiatric illness. On admission, her temperature was 38.3°C, blood pressure was 100/80 mm Hg, and pulse rate was 90 beats/min. Examination of the lungs, heart and abdomen were unremarkable. Initial neurologic examination revealed no focal neurological deficits. Complete blood count showed white blood cells of 6,400 cells/mm², hemoglobin of 11.4 g/dl and a platelet count of 1,73,000/mm³. The erythrocyte sedimentation rate (ESR) was 61 mm/hr. Urine analysis, chest x-ray, serum electrolytes, serum creatinine, Liver function tests, Thyroid function tests, Prothrombin time, activated partial thromboplastin time (APTT) were all normal. Blood and urine cultures were sterile. HIV serology was negative. On the fourth day of the admission, the patient had features suggestive of acute psychosis. She was treated with antipsychotics and there were no further psychiatric symptoms. In accordance with the pertinent history, connective tissue disorder work-up was done. It revealed positive antinuclear antibodies (ANA by immunofluorescence assay) in a titer of 1/640 with nucleolar pattern, positive anti-double stranded DNA antibodies (anti-dsDNA), positive cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA), positive anti-Sm and anti-nRNP antibodies. Anticardiolipin antibody was positive. Lupus anticoagulant was negative. A decisive diagnosis of SLE was made based on American College of Rheumatology (ACR) criteria. On the sixth day of the admission, she developed sudden onset of flaccid paraplegia with bladder and bowel involvement. She had a power of 0/5, absent deep tendon reflexes in lower extremities and bilateral extensor plantar response. The sensory deficit was consistent with below T10 level. Cranial nerves were normal. An emergent spinal cord MRI was done. The T2-weighted MRI (Figure 1) revealed diffusely increased signal intensity extending from C6-L1 level with mild cord expansion. Suggestive of longitudinal myelitis. MRI of the brain was normal.
Peripheral white matter degeneration by vascular changes such as vasculitis or thrombosis; large SLE-related myelitis includes softening of spinal cord accompanied either been normal or shown pleocytosis, elevated protein and is compatible with our case. CSF analysis in previous reports, had been normal (10U/L) Gram stain and acid fast stain for mycobacterium were negative. Microbiological cultures (for bacteria, acid fast bacilli, virus, and fungi) were sterile. The oligoclonal IgG band was negative. With a diagnosis of SLE-related catastrophic-onset longitudinal myelitis, aggressive immunosuppressive treatment was started immediately. The patient received intravenous (i.v.) pulse methylprednisolone (1.0 g/day for 5 days) and two i.v. monthly pulse cyclophosphamide (0.75g). After i.v. methylprednisolone, she was maintained on oral prednisone 60mg daily. Despite early aggressive treatment with steroids and cyclophosphamide, she showed no improvement in neurological status throughout the hospital stay for 2 months. Subsequently she received cyclophosphamide 0.75 g per month for 4 months and prednisone was slowly tapered to a maintenance dose of 20mg daily. After four month of follow-up, she did not have any remission in neurological deficits.

Discussion:

Myelitis is a rare neurological complication of SLE, first described by Dr Suchett-kaye at St. Charles Hospital in London in 1948[14]. It can be the initial manifestation of SLE or can develop within five years of diagnosis and generally carries a poor prognosis[4,14-16]. Transverse myelitis is far more common in SLE patients than longitudinal myelitis. Thus only 12 cases of SLE-related longitudinal myelitis have been reported[17,18]. Reports about LM as an initial manifestation of SLE is even rarer, with only 3 reported cases[19]. Extensive involvement of the entire spinal cord has been reported only in 2 earlier reports[19,20]. In our patient, Catastrophic longitudinal myelitis involving almost the entire spinal cord occurred within 2 days of diagnosis of SLE. Ropper et al found three types of the disease onset: a smoothly progressive onset with ascending neurological symptoms; a sub acute gradually developing type; and a hyperacute, catastrophic-onset type. Of these the acute catastrophic onset type is rarer than acute or sub acute onset and has the worst prognosis[18]. Our patient’s neurological symptoms showed an abrupt catastrophic onset and represent the most severe form of the disease. MRI is the diagnostic method of choice[18] and the findings reported in earlier studies were spinal cord edema and high intensity signal on T2 weighted images[9-11], which is compatible with our case. CSF analysis in previous reports, had either been normal or shown pleocytosis, elevated protein and hypoglycorrhachia[19]. There are also reports on detection of SLE autoantibodies in CSF[21]. The pathological findings described in SLE-related myelitis includes softening of spinal cord accompanied by vascular changes such as vasculitis or thrombosis; large subdural hematoma in the spinal cord without vasculopathy and peripheral white matter degeneration[18].

An Initiative of The Tamil Nadu Dr. M.G.R. Medical University University Journal of Medicine and Medical Specialities

The pathogenic mechanisms triggering these changes remain unclear, however it is postulated that immune-complex mediated vasculitis, antineuronal antibodies, white matter degeneration and hypercoagulability from aP4 may play a role[2,22]. Heinlein et al studies showed marked inflammatory response contributing to the disease manifestation[19]. A stronger association between SLE-related myelitis and antiphospholipid syndrome has been reported[9]. Deodhar et al suggested that longitudinal myelitis has a much closer association with aP4 syndrome when compared to TM[17]. Thus, longitudinal myelitis seems to be related to a vascular occlusive phenomenon of the spinal cord mediated by aP4 or as a direct interaction between aP4 and spinal cord phospholipids. Being a rare entity, lupus related myelitis lacks treatment guided by controlled trials. Current recommended therapy includes early use of i.v. pulses methylprednisolone and cyclophosphamide[15,23]. The therapy has been successful in TM. However, Tellez-Zenteno et al indicated that the therapy had an unfavorable outcome in most cases of longitudinal myelitis[11]. Ropper too emphasized that a catastrophic-onset type of longitudinal myelitis results in a poor outcome[9]. Our patient with a catastrophic onset of LM did not show any improvement despite early aggressive immunosuppressive therapy with methylprednisolone and cyclophosphamide, as observed in earlier reports.

In SLE myelitis patients with an antiphospholipid antibody, the use of antithrombotic therapy remains controversial[11,17,24]. Plasmapheresis or intravenous immunoglobulin has been used with controversial results[20]. Mok et al suggested the use of combined corticosteroid and mycophenolate mofetil, especially if refractory to cyclophosphamide[25]. Lehnhardt et al found autologous stem cell transplantation to be successful in patients with severe SLE related longitudinal myelitis who had failed glucocorticoid and cyclophosphamide therapy[27]. Newer treatment strategies such as intrathecal methotrexate, dexamethasone[28], and rituximab[29] are under evaluation. To conclude, we have presented a rare case of longitudinal myelitis with extensive spinal cord involvement in a recently diagnosed SLE patient. All patients presenting with longitudinal myelitis should be tested for SLE and antiphospholipid antibody syndrome (APAS). As permanent neurological disability is significant even in treated cases, multicenter trials to establish guidelines for optimal treatment are essential.

References: