Antiphospholipid antibody syndrome presenting as transverse myelitis

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The antiphospholipid syndrome (APS) is characterized by arterial and/or venous thrombosis and pregnancy morbidity in the presence of anticardiolipin antibodies and/or lupus anticoagulant. APS can occur either as a primary disorder or secondary to a connective tissue disease, most frequently systemic lupus erythematosus. Central nervous system involvement is one of the most prominent clinical manifestations of APS, and includes arterial and venous thrombotic events, psychiatric features, and a variety of other nonthrombotic neurological syndromes. Although the mechanism of neurological involvement in patients with APS is thought to be thrombotic in origin and endothelial dysfunction associated with antiphospholipid antibodies. APS presenting as acute transverse myelitis is very rarely seen with a prevalence rate of 1%. We are describing a foreigner female presenting as acute transverse myelitis which on evaluation proved to be APS induced. So far, very few cases have been reported in literature with APS as etiology.

Keywords:
antinuclear antibody, antiphospholipid antibody, antiphospholipid antibody syndrome, acute transverse myelitis, cytomegalovirus, herpes simplex virus, low molecular weight heparin

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Introduction

Transverse myelitis is characterized by acute inflammation affecting a local area of the white matter of the spinal cord usually involving thoracic cord [1]. Patients age at the time of disease onset vary widely, ranging from childhood through the 80s [2]. The clinical presentation is characterized by the development of motor neurologic dysfunction, which is associated with sensory abnormalities (sensory level) and abnormalities of the autonomic nerves (sphincter disturbances).

Etiologically, acute transverse myelitis (ATM) has diverse causes. The five groups of disorders that present as acute myelopathy are demyelination, infections, other inflammatory disorders, vascular, and neoplastic and paraneoplastic. The first three are considered inflammatory disorders. Among these, demyelinating disorders are the most common. Demyelinating disorders include multiple sclerosis, neuromyelitis optica, acute demyelinating encephalomyelitis, and idiopathic myelitis. Infections include viral, bacterial, fungal, and parasitic. Common infectious causes are herpes simplex virus (HSV), herpes zoster virus, cytomegalovirus (CMV), and Epstein–Barr virus [3].

Connective tissue disorders and granulomatous disorders presenting as acute or subacute myelitis are systemic lupus erythematosus (SLE), Sjogren's syndrome, scleroderma, mixed connective tissue disorder, Behcet's disease, and sarcoidosis [4–6]. Paraneoplastic disorders also cause acute/subacute myelitis [7].

Involvement of the neuropsychiatric system in antiphospholipid syndrome (APS) causes high morbidity and mortality, with stroke and transient ischemic attack as the most common manifestations [8]. ATM is mainly associated with SLE and Sjogren's syndrome [9]. It is a rare neurologic complication of APS with a prevalence estimated at less than 1% of APS patients [10,11]. We are describing a very rare case of APS presenting as ATM.

Case report

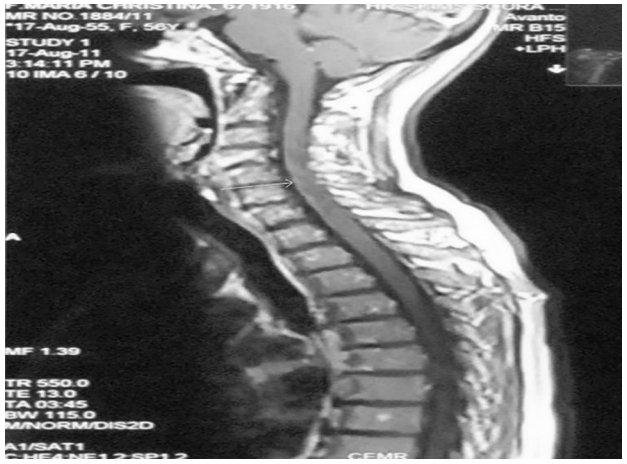
A 56-year-old female foreigner from Italy was on tour to Kashmir when she started with progressive asymmetric weakness of both lower limbs with loss of sensations, more on the right lower limb than the left. This weakness was progressive over a period of 1 week with subsequent inability to get up and walk. This was associated with incontinence of urine. She denies recent infections, vaccinations or recent trauma. She never had an event like this before and considers herself to be

'very healthy'. There was significant past history of her recurrent pregnancy loss around 23 years back. She was evaluated that time in her home town, which proved to be due to APS, with positive antinuclear antibody and antiphospholipid antibody (APLA). Finally patient conceived and was on aspirin and low molecular weight heparin during pregnancy. At present she has two children 20 and 18 years old. On examination, her vitals, higher mental functions, and bulk were normal. Her lower limbs were hypotonic, power of grade I in right lower limb and grade II in left lower limb, with brisk reflexes and extensor planter response. Sensations were absent in both lower limbs with a level on trunk at T4–T5. Rest of clinical and systemic examination was normal. An impression of transverse myelitis was made in this patient.

On evaluation her hemogram, liver function test, kidney function test, electrolytes and blood gases, chest radiography, and ultrasonography of abdomen were found normal. Her coagulogram was deranged with activated partial thromboplastin time of 44 s (control 24 s), antinuclear antibody positive, and APLA positive. Viral serologies for HIV, Epstein–Barr virus, CMV, and hepatitis A, B, C, E, and HSV were negative. Computed tomographic brain was normal and MRI whole spine revealed a lower cervical and upper thoracic cord lesion that enhanced after gadolinium administration, a finding that is consistent with transverse myelitis (Figs. 1 and 2).

Finally an impression of APLA induced transverse myelitis was made and patient was put on intravenous steroids and low molecular weight heparin combination. Power and sensations improved within a period of 1 week and she was able to walk. Patient was discharged on oral steroids.

Figure 1



Contrast MRI of cervicothoracic region of cord showing contrast enhancement.

Discussion

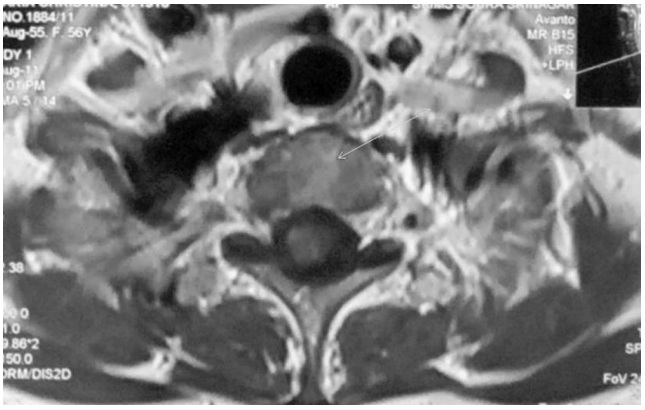
ATM has an estimated incidence of 1.34 to 4.6 per million [12,13], but has been reported to be as high as 3.1 per 100 000 patient-years [14]. There does not seem to be a familial or ethnic predisposition for ATM and there is no evidence of geographic variation in its incidence [15]. As such, myelitis has been reported with increased incidence among women, but multiple sclerosis may partially explain this finding [15].

Acute transverse myelitis can be presented as pyramidal (motor), sensory, and/or autonomic dysfunction to varying degrees. Symptoms typically develop over hours to days and worsen over days to weeks. Sensory symptoms usually present as paresthesia/hypoesthesia ascending from the feet with a demarcation at or near the level of the myelitis. Motor symptoms often include weakness that preferentially affects the flexors of the legs and the extensors of the arms (pyramidal distribution of weakness) and can include sphincter dysfunction [16]. Autonomic involvement is also common and can frequently cause bowel and bladder dysfunction, temperature dysregulation, or even bouts of hypertension which can be quite severe [15].

When an acute myelopathy is suspected, a thorough neurological evaluation helps to determine the region of the spinal cord affected and then the next diagnostic step is to evaluate for a compressive or structural etiology. MRI with gadolinium contrast is the preferred imaging modality.

Once myelitis has been detected through MRI studies of the cord and cerebrospinal fluid evaluation showing signs of inflammation, the underlying etiology of the myelitis must be considered. While the most commonly identified cause of myelitis is demyelinating disease, infection in one study caused

Figure 2



Contrast MRI coronal section at upper thoracic region showing contrast enhancement.

up to 12% of myelitis cases [17], and must be the first diagnosis considered as it is important to identify treatable infections in the acute setting such as syphilis, herpes viruses, HIV, and tuberculosis [18]. Infectious or para infectious myelitis can be viral, bacterial, fungal, and/or even parasitic in etiology. The most common viral causes of myelitis are varicella zoster, enteroviruses, HSV-2, and CMV [19].

APS is one of the rare etiologies of ATM. The APS is characterized by arterial and/or venous thrombosis and pregnancy morbidity in the presence of anticardiolipin antibodies and/or lupus anticoagulant [20]. Harris *et al.* [21] described the case of a 45-year-old woman who developed transverse myelitis in the context of a lupus-like illness. Although the mechanism of neurological involvement in patients with APS is thought to be thrombotic in origin. There is evidence that APLA may interfere with endothelial cell function and promote the procoagulant activity of endothelial cells [22]. Diagnosis is usually confirmed with contrast MRI and positive antibody test.

In light of the severe clinical presentation of ATM and its high rates of morbidity and mortality, early diagnosis and aggressive treatment are vital for therapeutic success. Sherer *et al.* [1] reported four cases of transverse myelitis associated with APLAs, and they suggest that early aggressive treatment (usually with pulses of methylprednisolone and cyclophosphamide) might improve the prognosis of these patients. Similarly, Chan and Boey [23] reviewed nine SLE patients with transverse myelitis who were treated with pulses of methylprednisolone and/or cyclophosphamide, and whose functional outcomes were considered good. Longitudinal case series of acute transverse myelitis reveal that approximately one-third of the patients recover with little to no disability; one-third are left with a moderate degree of permanent disability, and one-third have severe disabilities [12,24,25].

Our patient was aggressively treated with high-dose steroids and her recovery was fast within a period of 1 week.

Conclusion

In light of the severe clinical presentation of ATM with APS and its morbidity and mortality, early diagnosis and aggressive treatment are vital for therapeutic success.

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Conflicts of interest

There are no conflicts of interest.

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