Clin Rheumatol (2007) 26: 445–447
DOI 10.1007/s10067-005-0158-1

CASE REPORT

Sumeet Bhinder · Kevin Harbour · Vikas Majithia

Transverse myelitis, a rare neurological manifestation of mixed connective tissue disease—a case report and a review of literature

Received: 29 September 2005 / Accepted: 16 October 2005 / Published online: 4 January 2006

Abstract Although neurological involvement occurs in about 10% of patients with mixed connective tissue disease (MCTD), acute transverse myelitis (TM) has only been described in seven cases of MCTD. We hereby report a case of 70-year-old white female with transverse myelitis complicating her underlying MCTD. Our patient presented with lower extremity weakness, loss of sensation and incontinence one year after her diagnosis of MCTD. Her work-up revealed an abnormal MRI, with findings consistent with TM. She had an excellent response to initial therapy with six cycles of monthly intravenous immunoglobulins and steroids, with subsequent maintenance on azathioprine. She had a good neurological recovery with mild residual sequelae only. On basis of this case report and review of literature, we recommend ongoing surveillance and reporting of this rare neurological presentation in MCTD.

Keywords Mixed connective tissue disease · Transverse myelitis

Introduction

Involvement of nervous system occurs infrequently in mixed connective tissue disease (MCTD). Although exact numbers are not known, neurological involvement complicates MCTD course in about 10% of patients [1]. Both central and peripheral nervous systems may be affected, but the neurological manifestations are usually mild, most common being trigeminal neuralgia [1]. Serious affliction such as acute transverse myelitis is rarely described in MCTD, although it is well recognized as a complication of systemic lupus erythematosus (SLE) [1]. We report a case of 70-year-old female with transverse myelitis complicating her underlying MCTD.

S. Bhinder (✉) · K. Harbour · V. Majithia
University of Mississippi Medical Center,
2500 N State St/ L-525,
Jackson, MS 39216, USA
e-mail: skbhinder@medicine.umsmed.edu
Tel.: +1-601-9845545
Fax: +1-601-9845535

Case report

The patient is a 70-year-old white female with history of MCTD diagnosed in 2003. Her primary manifestations were arthritis, Raynaud's phenomenon, sicca symptoms, and photosensitivity. She had a positive test for antinuclear antibodies (ANA) and anti-ribonucleic protein (RNP) in high titer but anti-ds DNA, and the rest of antibody specificities including anti-Sjögren's syndrome antigen (SSA/SSB) were negative. Panel for antiphospholipid antibodies (APLS) was negative as well. She presented in November 2004 with neck, shoulder, and bilateral upper extremity pain and bilateral lower extremity weakness, along with a sensory loss, constipation, urinary retention with overflow incontinence and abdominal pain. Upon physical examination, she had stable vital signs. Pertinent positives on her neurological exam were loss of sensation affecting her left lower extremity, anterior chest and abdomen with a sensory level at T4 dermatome, decreased strength of both lower extremities with strength on the right quantified as 4/5 diffusely and left being 3/5 proximally and 1/5 distally. Reflex testing demonstrated hyper-reflexia of the left lower extremity. The cerebral and cerebellar signs were negative. She had evidence of episodic Raynaud's phenomenon without digital ulcerations. The abdomen was soft with decreased bowel sounds. The rest of the physical examination was unremarkable. Complete blood count, chemistry, and liver function tests on admission were all unremarkable. Sedimentation rate was elevated at 53 mm/h. Magnetic resonance imaging (MRI) of the spine revealed contrast enhancement of the cord from the level of T2 to T9 without epidural mass or mass effect.

Based on clinical findings and MRI results, she was diagnosed as transverse myelitis. Treatment was initiated with IVIG at a dosage of 0.4 g/kg per day for 5 days and

pulse dose therapy with IV methylprednisolone 1 g/day for 3 days. Steroids were subsequently changed to oral prednisone at 60 mg daily. Azathioprine at a dose of 1 mg/kg per day was also initiated and later on increased to 2 mg/kg per day. She demonstrated remarkable response to therapy with significant improvement in lower extremity weakness and resolution of bowel and bladder incontinence. Upon discharge, the strength was normal in the right leg and 3/5 in the left leg.

Monthly IVIG was continued for a period of 6 months, and the prednisone dosage was slowly tapered to 10 mg per day over the same time. She is still being treated with azathioprine. A repeat MRI at 6 months showed stable myelomalacia of the cord from T3 to T6, but no active disease was observed.

She has continued to do well during the follow-up period of 9 months without any relapse of her spinal disease. She has normal muscle strength throughout except left proximal lower extremity, which is slightly weak. She continues to have good bowel or bladder control. Her course was complicated by major depression, which has required intensive treatment with ECT and medications but was well controlled upon last follow-up. Throughout the course of her treatment, she received intensive physical therapy and, at this time, ambulates well with occasional assistance from a walker.

Discussion

A variety of neurological symptoms may occur in conjunction with the MCTD [1–4]. As mentioned earlier, neurological disease in MCTD can involve central or peripheral nervous system. The most frequently reported presentations are peripheral neuropathy, trigeminal neuralgia, aseptic meningitis, cerebellar dysfunction, psychosis, and convulsions [1–4].

Transverse myelitis occurring in conjunction with MCTD is considered an extremely rare neurological manifestation [1]. There are only eight reported cases of transverse myelitis with MCTD, according to our review of published literature [1–4]. Postulated mechanisms of transverse myelitis in MCTD include vasculitis of small arachnoid arteries of the cord and arterial thrombosis, leading to microinfarction of the spinal cord because of necrotizing vasculitis or the presence of a circulating antiphospholipid antibody such as the anticardiolipin antibody and the lupus anticoagulant [2].

Transverse myelitis has been noted to occur relatively early in the evolution of MCTD, although in no patient it has been reported as a presenting feature [2]. By contrast, retrospective studies of patients with SLE and transverse myelopathy found that transverse myelopathy was a presenting feature in 50% [5, 6]. All the reported cases of MCTD-related transverse myelopathy involved the thoracic spinal cord with one also having concomitant cervical cord involvement [2]. By contrast, in SLE, cervical cord was found to be the most commonly affected site (50%) in a retrospective analysis [6]. The onset was reported as progressive in all cases with MCTD, although the duration of symptom onset was not precisely identified in every report [2]. By contrast, 50% of cases of SLE-related transverse myelopathy evolved over less than a day [2].

MRI has become an important diagnostic investigation for acute transverse myelitis and other spinal cord diseases. It can exclude compressive lesions, is noninvasive, and more sensitive than myelography in showing up cord swelling and signal changes within the spinal cord substance during the acute stage of transverse myelitis [4].

In SLE-related transverse myelitis, immunosuppression with high-dose steroid, cyclophosphamide and sometimes plasmapheresis are required [5]. The optimal therapeutic strategy of acute transverse myelitis in MCTD is, however, less well defined because of its rarity. An aggressive approach with prompt treatment with high-dose steroid (prednisone 1 mg/kg per day) and immunosuppressives is recommended in order to minimize permanent neurological damage to the cord [2].

Neurological improvement or resolution with only mild sequelae followed treatment with high-dose prednisone and azathioprine in five of the seven cases of transverse myelopathy related to MCTD [2]. The clinical course of transverse myelopathy related to SLE is variable, although historically prognosis is relatively poor [2]. In one series of SLE and transverse myelopathy, 70% of patients received steroid treatment, 50% died in less than 6 weeks, 35% had permanent neurological deficits, and 15% had a near normal recovery [7]. In another study describing seven patients with a similar involvement, four died and one remained wheelchair-bound [5]. In SLE, early aggressive therapy with high-dose steroids and cytotoxic agents has been associated with a satisfactory outcome [2, 5, 6].

Our patient shows a number of similarities to the reported cases. She developed transverse myelitis early after a diagnosis of MCTD was established in her. She also showed considerable improvement with high-dose steroids, IVIG, and azathioprine and has done well over 9 months of follow-up. This case and the previously reported ones highlight that serious neurological manifestations such as transverse myelitis may rarely complicate the course of MCTD but seem to intrinsically have a better prognosis than a similar presentation in SLE. We recommend ongoing surveillance and reporting of these rare presentations in MCTD so that we can better define possible mechanisms of these associations.

References

1. Weiss TD, Nelson JS, Woolsey RM et al (1978) Transverse myelitis in mixed connective tissue disease. Arthritis Rheum 21 (8):982–986
2. Weatherby SJM, Davies MB, Hawkins CP (2000) Transverse myelopathy, a rare complication of mixed connective tissue disease: comparison with SLE related transverse myelopathy. J Neurol Neurosurg Psychiatry 68:532–541
3. Pedersen C, Bonen H, Boesen F (1987) Transverse myelitis in mixed connective tissue disease. Case report. Clin Rheumatol 6:290–292

4. Mok CC, Lau CS (1995) Transverse myelopathy complicating mixed connective tissue disease. Case report. Clin Neurol Neurosurg 97:259–260
5. Harisdangkul V, Doorenbos D, Subramony SH (1995) Lupus transverse myelopathy: better outcome with early recognition and aggressive high-dose intravenous corticosteroid pulse treatment. J Neurol 242:326–331
6. Mok CC, Lau CS, Chan EY et al (1998) Acute transverse myelopathy in SLE: clinical presentation, treatment and outcome. J Rheumatol 25:467–473
7. Andrianakos AA, Duffy J, Suzuki M et al (1975) Transverse myelopathy in systemic lupus erythematosus: a report of three cases and a review of the literature. Ann Intern Med 83:616–624