ABSTRACT. Methylprednisolone and cyclophosphamide pulse therapies are the most commonly used for transverse myelopathy in neuropsychiatric lupus. Little is known about the efficacy of other immunosuppressors. We describe the case of a 33-year-old woman with systemic lupus erythematosus, who developed a transverse myelopathy, beginning with a hiccup due to involvement of the medulla oblongata; despite pulses of methylprednisolone plus azathioprine and cyclosporine therapy, she developed paraparesis with involvement of the cervical spine cord. After oral cyclophosphamide, the lesion remained active. Subsequent therapy with mycophenolate mofetil and continuous intravenous infusions of dexamethasone resulted in reduction of the lesion’s size, disappearance of magnetic resonance imaging enhancement, and a complete recovery. (J Rheumatol 2007;34:588–91)

Key Indexing Terms:
TRANSVERSE MYELITIS
DEXAMETHASONE
SYSTEMIC LUPUS ERYTHEMATOSUS
MYCOPHENOLATE MOFETIL

The management of neuropsychiatric manifestations in systemic lupus erythematosus (NP-SLE) is highly controversial because of the absence of controlled studies. Methylprednisolone and cyclophosphamide (CYC) pulse therapies are the most commonly used but resistant cases have been described.

We describe the case of a young woman with SLE and persistently active myelitis, after oral CYC therapy, successfully treated with mycophenolate mofetil (MMF) and courses of intravenous (IV) continuous infusions of dexamethasone as maintenance therapy.

CASE REPORT
The patient was diagnosed with SLE at the age of 22 years with arthritis, malar rash, Raynaud’s phenomenon, lymphopenia, and antinuclear and antidual-stranded DNA antibody positivity. She was initially treated with chloroquine and acetylsalicylic acid.

At the age of 33 years, she suddenly developed nausea and hiccup, then subjective vertigo with diffuse paresthesia. A T2-weighted magnetic resonance image (MRI) showed a hyperintensity localized in the medulla oblongata extending to the junction with the cervical spine cord, with main involvement of the posterior cord. The lesion had a slight enhancement by contrast medium and the main features of an active ischemic lesion. The cerebrospinal fluid was normal and negative for infection. Low titers of antiphospholipid antibodies and no other thrombotic risk factors were detected. She was then treated with a continuous (24 h/day) IV infusion of dexamethasone for 9 days (16 mg/day, 12 mg/day, and 8 mg/day each for 3 days) associated with nadroparin, chloroquine, and acetylsalicylic acid, with disappearance of vertigo, hiccup, and nausea and improvement of the paresthesia. Prednisone was then maintained at the dose of 20 mg/day.

After 3 months she presented with paresthesia at the scalp, arms, and lower limbs, hyperesthesia at the right abdomen, bladder dysfunction, and positive Lhermitte’s sign. The MRI showed the appearance of a new T2-weighted hyperintensity of the cervical spinal cord between C1 and C4 with swelling and enhancement mainly in the posterior portion. She was given IV methylprednisolone pulses (1 g/day for 3 days), followed by oral azathioprine (2 mg/kg), cyclosporine (3 mg/kg), and oral prednisone (25 mg/day tapered), with improvement of neurological symptoms and persistence of mild paresthesia to the arms. She then received 2 other monthly pulses of 6-methylprednisolone (1 g each).

One month after the fifth pulse of methylprednisolone, she developed lower limb weakness and numbness, followed by paraparesis with urinary disturbance and a T10 sensory level; the MRI showed a reduction of the medulla oblongata lesion and an extension of the cervical spine hyperintensity from C1 to C5 level, with cord swelling and diffuse enhancement (Figure 1A, 1B). Treatment with continuous IV infusion of dexamethasone for 9 days (16 mg/day, 12 mg/day, and 8 mg/day each for 3 days) was started, with prompt improvement of the motor and sphincter dysfunctions from the fifth day, followed by oral CYC (2 mg/kg) for 6 months, oral prednisone (20 mg/day tapered to 5 mg/day in 3 mo), nadroparin, and acetylsalicylic acid. After this therapy, a heterogeneous hyperintensity from C2 to C5 level was seen on MRI.
still present on MRI, with pronounced enhancement by contrast medium from C3 to C5 level (Figure 2A, 2B).

Because of the previous failures, MMF (1 g twice a day) was chosen as the next therapy. After 9 months, MRI showed significant reduction of the cord lesion, with enhancement by gadolinium mainly at the C3-C4 level (Figure 3A, 3B). Mild weakness and paresthesia at the right lower limb were still present. Two more courses of continuous IV infusion of dexamethasone (12 mg/day, 8 mg/day, and 6 mg/day, each for 3 days) every 4 months were then administered. Complete disappearance of the enhancement on the MRI after the first infusion was observed, with a complete

Figure 1. A. Spin-echo T2 view: persistent hyperintensity from C1 to C5 level with cord swelling after combination therapy with IV methylprednisolone pulses, cyclosporine, and azathioprine. B. Spin-echo view with contrast medium: cervical cord enhancement after combination therapy with IV methylprednisolone pulses, cyclosporine, and azathioprine.

Figure 2. A. Spin-echo T2 view: persistent heterogenous hyperintensity at C2–C5 after 6 months of therapy with oral CYC. B. Spin-echo T1 view with contrast medium: persistent enhancement in the posterior portion of C3–C5 after 6 months therapy with oral CYC.
The relevant side effect observed was amenorrhea after CYC.

DISCUSSION

Transverse myelopathy (TM) is a rare manifestation of SLE. The low prevalence explains the absence of guidelines for the treatment of this neurologic syndrome. Recently a controlled trial comparing the efficacy of IV CYC versus IV methylprednisolone in severe NP-SLE reported a higher rate of response using IV CYC. In this study, only 4 patients had TM; 2 died before the end of the study and 2 had a good response, one with methylprednisolone and one with CYC. In larger cohorts of SLE patients with TM, the combination of methylprednisolone and CYC appeared to be more effective than methylprednisolone alone. Interestingly, D’Cruz, et al reported 2 cases of TM successfully treated with azathioprine alone, giving evidence of the possible efficacy of other immunosuppressors in this syndrome.

Our patient developed a TM unresponsive to treatment with pulses of methylprednisolone in association with azathioprine and cyclosporine. Confirming evidence from other studies, in the acute phase CYC was effective in controlling the progression of the lesion but not in reducing its extent or deleting the features of an active lesion. MMF was chosen as the next treatment after CYC, based on reports of successful treatment in 5 out of 7 cases of multiple sclerosis and in 2 cases of NP-SLE. During MMF therapy no relapses occurred and a remarkable reduction of the lesion’s extent was observed. There are few reports about the efficacy of MMF in NP-SLE; Grisanti, et al described recovery from brain involvement (psychiatric syndromes, cognitive dysfunctions, and abnormal single-photon emission computerized tomography) in 76.8% of 10 patients treated with MMF. Jose, et al reported a case of lupus psychosis with cognitive decline and choreiform movements, where longterm remission was achieved with MMF. Finally, this drug resulted in success in a case of SLE-related cerebral vasculitis. Our case is the first report on efficacy of MMF in TM. MMF might maintain remission in different types of SLE cerebral involvement, such as psychosis and myelopathy, due to its broad actions on proliferating T and B cells, on the production of autoantibodies, and on the expression of adhesion molecules.

Another point of interest in our case is the use of continuous IV infusion of dexamethasone. The regimen we employed, consisting of about 600 prednisone equivalents, led to response in the acute and chronic phases. This resolved the features of the lesion and allowed a sparing of cumulative steroid dose versus the use of pulse methylprednisolone.

Finally, the neurologic involvement in our patient presented with hiccup, a manifestation reported just once before, in a patient with primary antiphospholipid syndrome. While TM in SLE seems to be more frequent in patients with antiphospholipid antibodies, the low titers observed in our case do not explain its aggressive course. Further, since the character of myelopathies (ischemic or demyelinating) is not easy to define through MRI, antiaggregation or anticoagulation are also warranted in cases of TM.

In conclusion, MMF might be chosen as a maintenance therapy.
therapy for lupus TM. Courses of IV infusion of dexamethasone should be considered as therapy, not only for the acute phase of SLE myelitis but also in chronic active lesions.

REFERENCES