Long-term follow-up of lupus-related subacute myelopathy treated by plasmapheresis and pulse cyclophosphamide

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Central nervous system involvement has been reported in up to 60% of patients with systemic lupus erythematosus (SLE), however myelopathy is a rare and severe complication (1-2% of cases) (1). Subacute presentation is rarer than acute transverse myelitis (2). No standard therapy has been established, however intravenous (i.v.) pulse corticosteroids and cyclophosphamide (Cyc) are more frequently used (2, 4, 5). Plasmapheresis has been recently advocated in the treatment of serious SLE complications (6, 7). We describe the long-term follow-up of a patient with SLE-related subacute myelopathy treated by plasmapheresis and subsequent i.v. Cyc.

In April 1999, a 50-year-old woman with SLE was admitted to another institution with a one-month history of superior limbs and trunk hypoesthesia. Cervicothoracic spinal cord lesion worsened at MRI (Fig. 1 A-D). Oral 6-methylprednisolone (16 mg/day) and monthly pulse therapy including i.v. 6-methylprednisolone (1000 mg/day) for three days, and i.v. Cyc (1 g) for one day were administered. After two months of relatively good health, the patient’s symptoms worsened. Neurological examination showed severe left brachiocephalic hemiparesis with hyperreflexia, positive Babinski sign and deep sensory deficit. MRI was unchanged. She was then treated with a monthly therapy including one filtration plasmapheresis followed by i.v. Cyc (1 g) for one day. Oral 6-methylprednisolone was maintained at 16 mg/day. Within a few days, neurological symptoms regressed to almost complete recovery, with only slight residual left brachiocephalic hemiparesis. In May 2000, due to a stable clinical picture, the interval of therapy was prolonged to two months, i.v. Cyc dose was reduced to 750 mg, and oral 6-methylprednisolone was decreased to 8 mg/day. In September 2002, she suffered a car accident and stopped therapy. In January 2003, she worsened and monthly therapy including plasmapheresis and i.v. Cyc (1 g) was re-instated, resulting in clinical improvement. In September 2003, neurological examination showed left brachiocephalic hypotonia, more evident in upper limbs, and brisk deep tendon reflexes mostly on the left side. MRI did not show signs of disease relapse (Fig. 1 E-H). Therapy interval was then prolonged to 2 months. In September 2004, she was in good health, plasmapheresis and i.v. Cyc were discontinued and maintenance therapy with i.v. immunoglobulin was initiated (8).

Plasmapheresis is an accepted therapeutic procedure in many diseases mediated by pathogenic autoantibodies (9). The effect of plasmapheresis, apart from rapid removal of immune complexes and autoantibodies, results from different immune modulator effects, including an increase in proliferating B cells which are then more vulnerable and sensitive to cytostatics such as Cyc (6). Furthermore, it has been demonstrated that plasmapheresis positively modulates Th1/Th2 type cytokine-secreting cell imbalance in patients with SLE, this leading to a decrease in concentration of anti-ds-DNA antibodies (6). The role of plasmapheresis alone or with i.v. Cyc has recently been advocated in the treatment of severe neuropsychiatric SLE (7).

In our patient, myelopathy relapsed despite initial satisfactory response to i.v. steroid and Cyc. A therapy including plasmapheresis and pulse Cyc resulted in clearcut clinical improvement. Trauma and/or temporary treatment interruption resulted in clinical worsening, while re-initiation of therapy led to progressive stable improvement. In conclusion, although SLE is not included in the absolute indications for plasmapheresis, and no controlled studies for SLE myelopathy have been performed using plasmapheresis, we would advocate consideration of this therapeutic option to prevent serious neurological sequelae.

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References

Fig. 1. MRI of the cervicothoracic spinal cord performed in September 1999 (A-D) showed its diffuse swelling, increased signal intensity (asterisks) from C1-C2 to D1-D2 levels on T2-weighted sagittal (A) and axial (C) images, and contrast-enhancement (black arrows) from C1-C2 to C5 levels on gadolinium-enhanced T1-weighted sagittal (B) and axial (D) images: these findings were consistent with subacute myelopathy including edema and inflammation. MRI performed in September 2003 (E-H) showed shrinkage and abnormal signal intensity of the cervicothoracic spinal cord predominantly in the left side (white arrows) as chronic evolution of the first clinicoradiological manifestation, and a signal alteration (asterisk) in the thoracic spinal cord from T4 to T6 levels on T2-weighted sagittal image (E) consistent with the chronic stage of the last clinical relapse in January 2003.