PostScript

LETTERS

Transient neonatal Lambert-Eaton syndrome

The Lambert-Eaton myasthenic syndrome (LEMS) is caused by serum IgG anti-voltage-gated calcium channel (anti-VGCC) antibodies.¹ Although transient neonatal myasthenia gravis, caused by passive placental transfer of maternal anti-acetylcholine receptor (anti-AChR), is well recognised,² as far as I am aware, this phenomenon has not previously been reported in LEMS.

A diagnosis of LEMS was made in a woman at the age of 25 years. She had noted difficulty in keeping up with other children since she was 13. Two years later, she became aware of ptosis. In her late teens, she developed weakness in the limb and had difficulty in speech, chewing and swallowing. She was noted to have bilateral ptosis, facial weakness, poor palatal movements and weakness of neck flexion and extension. The limbs were hypotonic with global weakness, worse proximally, and tendon reflexes were absent.

Anti-VGCC antibodies were positive on three occasions (titres 105–282 pmol/l: positive >50 pmol/l) and anti-AChR antibodies were negative. Neurophysiological studies strongly supported the diagnosis of LEMS with up to a 15-fold increase in compound muscle action potentials after maximum voluntary contraction (MVC). Treatment with plasma exchanges and prednisolone and azathioprine showed marked improvement, although marked residual disability was noted.

She was first seen by BRFL in 1999 when she was 30 years old. At this time, she had fluctuating facial, neck and limb weakness and also a dry mouth. She could walk slowly, for about 200 m. At this stage, she was taking azathioprine 100 mg/day and prednisolone 7.5 mg/day.

The tendon reflexes were depressed with marked post-MVC potentiation. The compound muscle action potential of abductor digiti minimi increased 178% after MVC. After treatment with 3:4 diaminopyridine 10 mg four times daily, increasing to six times daily, she showed marked improvement and the prednisolone was tapered off. The improvement in her disability was maintained.

A positive pregnancy test was noted in April 2004, and she had an uneventful pregnancy. Treatment with azathioprine and 3:4 diaminopyridine was continued. The baby was born by normal delivery at full term and birth weight was 3050 g, with an Apgar score of 10 at 5 min. Mild persistent hypotonia was seen with preserved tendon reflexes, but there was no problem with feeding. Anti-VGCC antibodies were not measured. At 3 weeks, the hypotonia had fully resolved and the infant has remained well.

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Informed consent was obtained from the patient for publication of her and her infant's details in this report.

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References

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Fulminant Devic disease successfully treated by lymphocytapheresis

Devic disease is a demyelinating disease characterised by acute optic neuritis and transverse myelitis. Although there are differences in the pathogenesis of Devic disease and multiple sclerosis, the treatment for Devic disease is the same as that for multiple sclerosis. We report a patient with Devic disease who was resistant to high-dose intravenous methylprednisolone and intravenous immunoglobulin (Ig) treatments, but was effectively treated with lymphocytapheresis (LCP). The profiles of cytokines during the clinical course are discussed.

Case report

In August 2001, a 27-year-old woman developed acute loss of vision and sensory disturbance in both lower extremities after coughing. The next morning (day 2), she was totally blind and was admitted to our hospital. Neurological examination showed total blindness, papilloedema, moderate muscle weakness of the hip and thigh muscles, positive pathological reflexes of the limbs, hyper-reflexia and sensory loss below the T4–5 level. Loss of vesicorectal function and perspiration below the chest were also observed.

Laboratory examination disclosed a normal C-reactive protein level, positive antinuclear (titre 1/160) and antithyroglobulin antibodies (0.8 U/ml (normal range <0.3)) in serum, normal CD4:CD8 ratio (0.90 (normal range 0.69–1.74)) and an increased percentage of CD8 T cells (45% of total T cells (normal range 12–30%)). Anti-neutrophil cytoplasmic antibodies, anti-phospholipid antibodies and rheumatoid factor were negative. No significant increase of antibodies in the serum or CSF was seen against the following microorganisms: herpes simplex virus, varicella zoster virus, cytomegalovirus, Epstein-Barr virus, enterovirus, hepatitis B virus, mumps, measles, rubella, coxsackie virus, *Borrelia burgdorferi*, syphilis, chlamydia, legionella and *Mycoplasma pneumoniae*.

Neuromyelitis optica (NMO)-IgG¹ was negative. CSF analysis was normal except for an increased concentration of myelin basic protein (660 pg/ml (normal limit <102 pg/ml)) on day 2, but pleocytosis (112/mm³) and increased protein concentration (152 mg/dl) were observed on day 12. MRI of the brain showed enlarged optic nerves without enhancement. T2-weighted MRI of the spinal cord showed high signal intensity in the cervical cord (C6–7) on day 3, and diffuse swelling in the whole spinal cord with T2 hyperintensity on day 15.

Two courses of methylprednisolone treatment (1 g/day for 3 days) were given from day 3, and, in addition, intravenous Ig (0.4 g/kg/day for 5 days) was given from day 16. The patient, however, showed no response to these treatments. Thereafter, she fell into complete tetraplegia, with sensory loss below the neck and frequent sharp pains from the shoulder to neck, which were considered to be painful tonic spasms. Then, on day 23, we performed LCP with a centrifuge, "COBE Spectra" (GAMBRO, Tokyo, Japan), that processed 7–8 l of blood and removed about 3–4 × 10⁹ lymphocytes per procedure. On the day of treatment the sharp pain disappeared immediately after the first LCP, and the following day her vision showed improvement, going from total blindness to the level of finger counting. Thereafter, LCP was performed once or twice weekly for a total of 11 LCP treatments. Her vision was almost normalised, with improvement of the sensory deficit and recovery of weakness of the upper extremities to grade 4 or 5 on the manual muscle test.

The T-helper (Th)1:Th2 balance represented by the ratio of intracellular interferon γ to interleukin (IL) 4 in the CD4 T cells increased markedly both before the first LCP (22.2 (normal limit <10)) and after the last LCP (17.5). CSF IL-6 and serum IL-12 levels were markedly reduced after the first LCP, even when compared with those on the same day before treatment (table 1). No relapse has occurred in 4 years.

Comment

Devic disease presents with a poor prognosis, including death, and frequent sequelae, including visual disturbance or paralysis.² Marked improvement was achieved by 2–5 treatments a week over about 6 weeks in only one other reported case of Devic disease that was treated by lymphocytapheresis, including the removal of both lymphocytes and plasma.³ In our patient, who was resistant to methylprednisolone and intravenous Ig treatments, remarkable improvement of the symptoms, especially visual loss, was immediately obtained by LCP, which removed only lymphocytes but not plasma. LCP might reduce clonally expanding pathogenic T lymphocytes in the peripheral blood, and has been used as an adjunct to standard immunosuppressive treatment for acute transplant rejection. The removal of lymphocytes may therefore augment immunosuppression.³ LCP may have induced the improvement in our patient through these mechanisms.