Severe vasculitic neuropathy in systemic lupus erythematosus and response to cyclophosphamide

Neuropathy may be caused by illnesses producing systemic vasculitis including polyarteritis nodosa, rheumatoid arthritis, Wegener's granulomatosis, various forms of granulomatous and other more benign non-systemic vasculitic disorders: severe vasculitic neuropathy due to systemic lupus erythematosus (SLE) appears to be very rare. We report a case in which the neuropathy occurred as a clinical feature of a relapse of SLE and which responded to pulses of cyclophosphamide.

Over a period of four weeks, a 24 year old woman, of mixed Philippino and West Indian race, developed night sweats, fever, numbness ascending to the knees and elbows and worsening limb weakness distally and then proximally. SLE had been diagnosed at the age of eight when she developed a rash, fever, haemolytic anaemia, thrombocytopenia and seizures. Subsequently she had episodes of arthralgia and weight loss, splenomegaly and fever, psychological symptoms (general biopsies consistent with SLE but without vasculitis), and lastly pancreatitis four years previously.

She looked unwell and had a persistent fever of up to 38.5°C. She was alert and orientated. Her cranial nerves were normal except for a nuchal patch corresponding to the left nasociliary distribution. Her limbs were flaccid, areflexic and grossly weak (MRC grading: shoulders 2, hips 2, knees 1 but zero elsewhere). All modalities of sensation were absent to mid-thigh and mid-humeral levels. No other signs appeared during admission except for some livedo reticularis in the hands.

Blood and urine chemistry (including porphyrins) were normal except for a low albumin and raised liver enzymes (bilirubin normal). Haemoglobin was 9.6 g/l (negative direct Coomb's test, 'chronic disease' pattern iron studies), white cell count 18.1 x 109/l (16.4 neutrophils, 1.45 lymphocytes), platelets 547 x 109/l. Bone marrow was normal (including microscopy and culture for acid fast bacilli, fungi and leishmania, but C-reactive protein (CRP) was grossly elevated at 110 mg/l (normal <10). Microbiological assessment was normal, including blood cultures and CSF, VDRL, HIV and other viruses. Complement levels were normal. DNA binding was 56 μmol (normal <25) and ANA titres were >1 in 320 as IgG but only one in 10 as IgM, both with diffuse patterns. CSF pressure, constituents and electrophoreses were all normal.

Nerve conduction studies revealed that compound motor action potentials and sensory action potentials were absent or greatly diminished in some sites tested, but with normal conduction velocities. A sural nerve biopsy showed acute Wallerian degeneration of axons. One small epineural vessel had fibrinoid material within its wall, and was also infiltrated by chronic inflammatory cells, as were almost all epineural vessels.

After 13 days of 40 mg/d prednisolone without any effect, five daily intravenous infusions of 500 mg methylprednisolone were given but this had no effect on her clinical condition, fever, CRP or platelet count, though her white cell count and alanine transaminase did return to normal. Prednisolone was continued at 60 mg per day. Eight days after the methylprednisolone, cyclophosphamide (9 mg/kg) was given intravenously at weekly intervals for four weeks (each with Mesna cover), without any serious complications, except by azathioprine (1.5 mg/kg) orally. Her fever settled within 36 hours of the first cyclophosphamide dose, as did her CRP and platelet counts over the next few days. Her power began to improve within the first 24 hours of the first dose, closely followed by a proximal to distal return of sensation. She could walk with the aid of one assistant after six weeks, and independently after six months with foot drop. Arm strength also improved. She continued on azathioprine and a reducing dose of prednisolone. On review one year later, she had marked wasting and weakness in the muscles of her hands, feet, and anterior tibial compartment. More proximal power was normal. There was residual loss of proprioception and cutaneous sensation in her fingers and left foot. On repeat electro-physiology, compound motor action potentials and sensory action potentials were again absent or greatly diminished. Conduction velocities were normal or mildly reduced. Electromyography showed signs of denervation in all muscles tested, with evidence of reinnervation in all except distal muscles.

Neuropathies in SLE may present as a multiple mononeuropathy, sometimes with a vasculitic pathology, or as a vasculitic polyneuropathy,1 as in this case. The pathogenesis of this latter distribution may or may not be vasculitic. In our case the vasculitic nature was suggested by the nuchal patch in the left nasociliary distribution and confirmed by sural nerve biopsy.

Severe acute peripheral neuropathy in SLE is quite rare and almost always accompanied by evidence of active disease in other systems including the organs of the autonomic system,2 though exceptionally it may be the presenting feature. Coincidental axonal Guillain-Barre syndrome3 was excluded by the systemic features, normal CSF protein four weeks into the illness and biopsy findings. The patient appeared unwell and had fever: the laboratory indices of neutrophilia, normal complement levels, normal ESR and raised CRP were consistent with a severe illness with little elevation of DNA binding and IgM ANA titres. Her fever, tachycardia and laboratory indices failed to respond to acute doses of steroids alone. Reports2,4 suggested a coincidental infection rather than a flare of SLE, and led to initial caution in the use of immunosuppression.

While a delayed effect of the steroid therapy cannot be discounted, her improvement seemed temporally related to starting cyclophosphamide. The neuropathy showed a delay of about three weeks before improvement was evident, but the other features of her illness settled within a few days. Cyclophosphamide is the preferred treatment of severe vasculitic neuropathy,5 whose prognosis is otherwise dismal. This patient's impressive response suggests that it may be similarly useful in this rare complication of SLE.

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