

LETTERS TO THE EDITOR

Treatment of persistent hiccups

Persistent hiccups are difficult to treat and apart from various manoeuvres, drug treatment has included chlorpromazine, haloperidol, nifedipine, and various anticonvulsants. Two patients have been described who responded to baclofen,^{1,2} one of whom had familial hiccups. This letter describes a further patient, whose hiccups followed surgery, who responded dramatically to this treatment.

A man aged 76 years had surgery for left-hip replacement in January 1988. He was troubled with hiccups immediately after recovering from the anaesthetic and the hiccups settled into "ten days on, ten days off" cycles. There was no evidence of neurological deficit when he was examined at that time. He obtained temporary relief by stimulating the back of his throat to the point of vomiting. He was treated with chlorpromazine and then by a variety of anticonvulsants to no effect. Baclofen was then introduced after the cyclic attacks had been continuing for 20 months. At that time he was very distressed and said that he "could not go on". The patient had an immediate response to Baclofen, 5 mg three times daily, but improvement was of short duration and the dose was increased to 10 mg three times daily. The hiccups stopped on the first day of this higher dosage and he was clear for 12 days, when hiccups reoccurred and the dose was increased to 20 mg for three doses. The hiccups then resolved; the dose was reduced to 10 mg four times daily and reoccurred again five days later and lasted for five hours. They occurred six days later and lasted 10 hours and 12 days later when they lasted for 12 hours. The dose of his baclofen was gradually reduced over the following month during which the problem reoccurred for two periods of three hours each. A month later he had hiccups for 30 minutes only. He gradually reduced his tablets to 5 mg and stopped two weeks later, since when no medication has been necessary and no further attacks of hiccups have occurred. The total duration of treatment was three months.

There was an immediate change in the pattern of hiccups on the introduction of baclofen; instead of the bouts lasting about 10 days they continued for only a few hours. Even with these very short periods, they occurred in the same cyclic fashion over the next two months. The attacks have now stopped.

Treatment of persistent hiccups is generally so unsatisfactory that the possible advantage of a trial of baclofen should be added to other possible treatments.

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- Burke AM, White AB. Baclofen for intractable hiccups. *N Engl J Med* 1988;319:1354.
- Lance JW, Basil GT. Familial intractable hiccup relieved by baclofen. *Lancet* 1989; ii:276-7.

Severe vasculitic neuropathy in systemic lupus erythematosus and response to cyclophosphamide

Neuropathy may be caused by illnesses producing systemic vasculitis^{1,2} including polyarteritis nodosa, rheumatoid arthritis, Wegener's granulomatosis, various forms of granulomatosis and also a more benign non-systemic vasculitic disorder: severe vasculitic neuropathy due to systemic lupus erythematosus (SLE) appears to be very rare.^{2,4} We report a case in which the neuropathy occurred as the predominant 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, psychosis, proteinuria (renal biopsy 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. Cranial nerves were normal except for a numb 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 $18.1 \times 10^9/l$ (16.4 neutrophils, 1.45 lymphocytes), platelets 547×10^9 . Bone marrow was normal (including microscopy and culture for acid fast bacilli). ESR was 15 mm/hr, but C-reactive protein (CRP) was grossly elevated at 110 mg/l (normal <10). Microbiological assessment was normal, including blood cultures and serology for Borrelia, Mycoplasma, HIV and other viruses. Complement levels were normal. DNA binding was 56 µl (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 electrophoresis were all normal.

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

After 13 days of 40 mg/d prednisolone without any effect, five daily 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 then 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, followed 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 three weeks 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 electrophysiology, 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 signs of reinnervation in all except distal muscles.

Neuropathies in SLE may present as a multiple mononeuropathy, sometimes with a proven vasculitic pathology,⁴ or as a peripheral polyneuropathy,² as in this case. The pathogenesis of this latter distribution may or may not be vasculitic.² In our case the vasculitic nature was suggested by the numb 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 organs, including the central nervous system,² though exceptionally it may be the presenting feature.⁴ Coincidental axonal Guillain-Barré syndrome⁵ 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 contrary to those expected, with little elevation of DNA binding and IgM ANA titres. Her fever, tachycardia and laboratory indices failed to respond to adequate doses of steroids. These features suggested a coincidental infection rather than a flare of SLE, and led to initial caution in the use of immunosuppression.

Whilst 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,¹ 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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