Case report

A 22-year-old driver complained of six days' malaise, left-sided pleuritic chest pain, and sweating. Three days later he developed a headache, slurred speech, an unsteady gait, and his tongue felt too large for his mouth. Lobar pneumonia was diagnosed and treatment with oral penicillin begun. After an epistaxis three days later his condition deteriorated and he was admitted to hospital. On admission he was dyspnoeic and ill, pulse 112/min, and temperature 39°C. He had the classical signs of a left upper lobe pneumonia. He also had widespread bronchospasm. He was dysarthric and hypotonic with mild neck stiffness. His white cell count was $8.7 \times 10^9/l$ ($8700/mm^3$) but the neutrophils showed toxic granulations and a left shift. The haemoglobin was 15.8 g/dl and the platelet count $40 \times 10^9/l$ ($40\,000/mm^3$). Bone marrow aspirate was histologically normal and, apart from a slight rise in the fibrin degradation product concentration to 40-80 mg/l, there was no other evidence of disseminated intravascular coagulation. Normal commensals were grown from the sputum and cultures from the blood and cerebrospinal fluid were sterile.

Treatment with erythromycin and flucloxacillin was started with a presumptive diagnosis of staphylococcal pneumonia or LD. He had a further epistaxis, but the clinical and radiological signs of infection improved. The cerebellar dysarthria worsened with the evolution of hypotonia, intention tremor, and dysidiadochokinesia in the left arm, which resolved over the next five days. Direct laryngoscopy was normal together with a normal computerised axial tomogram of the brain and normal CSF on lumbar puncture. The diagnosis of LD was based on a serum antibody titre five weeks after discharge of over 1020. No other significant antibody titres were found and a screen for infectious mononucleosis was negative. No other cause was found for the thrombocytopenia. Notably there was no evidence of disseminated intravascular coagulation and the aspirated bone marrow was normal. The platelet count gradually rose to $180 \times 10^9/l$ ($180\,000/mm^3$) five days after admission. Since then it has been normal and his subsequent progress has been uneventful apart from a deep vein thrombosis of the right calf.

Comment

Although neurological manifestations of this disease and associated gastrointestinal bleeding have been described,¹ we believe this is the first description of thrombocytopenia associated with LD.

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¹ Vella, E E, *Journal of the Royal Society of Medicine*, 1978, **71**, 361.

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Functional independence in post-anoxic myoclonus: contribution of L-5-HTP sodium valproate and clonazepam

Action myoclonus is a well-recognised complication of cerebral hypoxia which may result in long-term disability and make heavy demands on nursing and related health care resources. Successful treatment with L-5-hydroxytryptophan (L-5-HTP) has suggested a selective deficiency of the neurotransmitter 5-hydroxytryptamine (5-HT); renewed interest in the pharmacological management of this incapacitating condition¹⁻³; and reduced patient dependency. Although a form of myoclonus responsive to L-5-HTP has been characterised by electrophysiological studies,³ not all cases respond satisfactorily to the 5-HT precursor, which is not surprising in view of the diffuse and variable nature of the cerebral insult in patients with post-anoxic myoclonus (PAM).

We describe a patient with severe PAM with minimal intellectual

impairment who regained functional independence only with the combination of L-5-HTP, a decarboxylase inhibitor (carbidopa), sodium valproate, and clonazepam.

Case report

A 30-year-old woman with steroid-dependent asthma sustained a respiratory arrest, the length of which was not documented. She was comatose and without focal neurological signs on admission to the intensive care unit. Assisted ventilation was continued for the 18 days she was unconscious. The day after admission spontaneous and induced myoclonus started and a single major seizure occurred. Parenteral phenobarbitone, diazepam, and oral phenytoin had no effect on the jerking.

On regaining consciousness and rational communication she was incapacitated by myoclonus, which was readily induced by any auditory or visual stimuli and voluntary or passive movements and which often became generalised. Nitrazepam, methylphenobarbitone, and carbamazepine were also unhelpful but clonazepam produced improvement. Three months later she remained completely dependent, unable to feed herself, or walk without help. In addition to spontaneous and induced focal distal, proximal, and generalised myoclonus there was a mild spastic tetraparesis and truncal ataxia. An electroencephalogram (EEG) showed central intermittent single and short-duration multiple spike and slow-wave complexes against background 6-7 Hz theta activity. One in three such discharges was associated with spontaneous myoclonus.

After cinematographic records and baseline values had been recorded, including cerebrospinal fluid 5-hydroxyindoleacetic acid (5-HIAA) and 24-hour urinary 5-HIAA concentrations, L-5-HTP and carbidopa were started with the patient's informed consent. L-5-HTP 1200 mg/day and carbidopa 300 mg/day produced a dramatic improvement, so that the patient could feed and dress herself and walk unaided. 5-HIAA concentrations were increased (in the cerebrospinal fluid from $0.26 \mu\text{mol/l}$ (49 ng/ml) before treatment with L-5-HTP to $2.2 \mu\text{mol/l}$ (422 ng/ml) after; in urine from $19 \mu\text{mol/l}$ (3.6 mg/l) to $488 \mu\text{mol/l}$ (93 mg/l)); the EEG showed more alpha-activity and less spike activity without associated jerking. The methylphenobarbitone and carbamazepine were withdrawn without effect and the clonazepam was continued. Although the generalised jerking was suppressed, the degree of overall control fluctuated considerably from day to day, and stimulus-responsive distal jerks continued.

The L-5-HTP became temporarily unavailable after nine weeks and a placebo was given with the carbidopa, resulting in increased myoclonus and reduced 5-HIAA concentrations. The addition of sodium valproate 1800 mg/day effected a significant though less dramatic improvement. With the reintroduction of L-5-HTP to the regimen of valproate, clonazepam, carbidopa, and phenytoin the patient was better than at any earlier stage. She negotiated stairs independently and there was less variability in day-to-day control and less distal jerking. Pulmonary function did not change during L-5-HTP administration.

Comment

Although most cases of PAM respond satisfactorily to L-5-HTP and clonazepam, perhaps by different mechanisms,³ some cases do not.¹⁻³ The clinical features of the myoclonus and the response to L-5-HTP in our patient suggested so-called reticular reflex myoclonus.³ The residual, stimulus-sensitive, distal jerking resembled cortical loop reflex myoclonus³ and was controlled by valproate. This may have resulted from an effect on gamma-aminobutyric acid (GABA), as experimental depletion of striatal GABA in combination with cortical damage produces focal myoclonus,⁴ and valproate has been shown to increase GABA levels.⁵ The addition of valproate in the present case also improved the day-to-day control and led to functional independence.

We suggest that valproate should be tried in patients with PAM whose response to L-5-HTP and clonazepam is suboptimal, particularly if more than one type of myoclonus is present.

¹ Lhermitte, F, *et al*, *Revue Neurologique*, 1971, **124**, 21.

² Van Woert, M H, *et al*, *New England Journal of Medicine*, 1977, **296**, 70.

³ Chadwick, D, *et al*, *Brain*, 1977, **100**, 455.

⁴ Tarsy, D, *et al*, *Brain*, 1978, **101**, 143.

⁵ Godin, J, *et al*, *Journal of Neurochemistry*, 1969, **16**, 869.

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