Encephalopathy associated with intravenous immunoglobulin treatment for Guillain-Barré syndrome

The use of intravenous infusions of immunoglobulin in the treatment of Guillain-Barré syndrome has become widespread. However, this treatment is not without morbidity. We describe an acute encephalopathy occurring in a patient receiving intravenous immunoglobulin infusions for Guillain-Barré syndrome.

A 55 year old woman was admitted with a four week history of malaise and occasional rigors and a one day history of pleuritic chest pain. She had a raised white cell count of 12.5 x 10^9/l, a lymphocyte count of 7.20 x 10^9/l, and a monocyte count of 1.32 x 10^10/l. Many atypical lymphocytes were seen on the blood film. Liver enzymes (IU/l) were slightly raised (aspartate transaminase 81, normal 10–34; alanine transaminase 135, normal 7–33; γ-glututaryl transpeptidase 90; normal 3–20). A chest radiograph and abdominal ultrasound were normal. Five days after admission the patient complained of low back pain and three days later she developed progressive weakness of her limbs and trunk. There was a slight right sided facial weakness, moderate limb weakness, and a slight reduction in proprioception in the feet but no other sensory loss. Deep tendon reflexes were absent and plantar responses were extensor. A cerebrospinal fluid contained 2 white cells/mm^3 and had a protein content of 1.2 g/l. A diagnosis of Guillain-Barré syndrome was made. Electroencephalogram findings were normal and a somatosensory neuropathy with slowing of motor and sensory conduction.

Weakness progressed over the next 24 hours and she became unable to stand. A five day course of intravenous immunoglobulin (Venologulin, Alpha Therapeutic UK Ltd) was given at a dose of 22 g/day.

At the end of the first day of immunoglobulin infusion the patient complained of the development of visual loss over 30 minutes. She reported that she could see only shadows. On examination she was unable to count fingers but could perceive movement. Neurological examination was otherwise unchanged, in particular fundoscopy and pupil reactions were normal. Pulse, blood pressure, arterial blood gases, urea, electrolytes, and blood glucose were also normal. Serum total protein concentration was 83 g/l with an albumin content of 41 g/l and globulin content of 42 g/l. The erythrocyte sedimentation rate was 52 mm in the first hour. Haemoglobin was normal but lymphocytosis persisted (total white cell count 8.5 x 10^9/l, 55% lymphocytes) and the platelet count was slightly increased (568 x 10^9/l). No visual evoked potentials could be obtained, with either pattern reversal or flash stimuli. The next day immunoglobulin infusion was continued. In the evening the patient became confused and disoriented. She was able to see only a small field in the left visual field. A few hours later she had two generalised tonic clonic seizures a few minutes apart. She was cyanosed during these attacks, but recovered rapidly and subsequently maintained normal arterial blood gases on air. Brain CT was normal. Infusion of immunoglobulin was stopped and an intravenous loading dose of phenytoin (750 mg) and dexamethasone (4 mg six hourly) was given. An EEG recorded several hours after the convulsions showed widespread, symmetric slow wave activity.

The next day the patient was alert and oriented and the following day her vision had returned to normal. Brain MRI performed two days after the immunoglobulin infusions were discontinued showed only a small area of increased signal in the white matter of the left occipital lobe on T2 weighted images. Recovery began a few days later. A second EEG recorded 18 days after the first was essentially normal.

The cause of the encephalopathy in this case is unknown. Hypotension was recorded nor any period of respiratory failure. No metabolic cause was identified. It is difficult to be certain whether the unidentified infection assumed to have caused the Guillain-Barré syndrome also caused the encephalopathy or whether the intravenous immunoglobulin was responsible. A postinfectious encephalitis could have developed in addition to Guillain-Barré syndrome, and postinfectious encephalitis may respond rapidly to steroids, particularly in children. However, recovery began almost immediately after the immunoglobulin infusion was discontinued and MRI two days later showed little change.

If the intravenous immunoglobulin was the cause of the encephalopathy, one possible mechanism is a transient hyperviscosity syndrome. A second possible mechanism is an intravenous infusion of large doses of immunoglobulin.

Referred neurological manifestations in patients with a hyperviscosity syndrome secondary to Waldenström's macroglobulinaemia include encephalopathy, convulsions, and vasospasm. Vasospasm is another explanation, suggested in a recent report of a patient who developed a similar reversible encephalopathy during intravenous immunoglobulin treatment for Guillain-Barré syndrome. Transcranial ultrasound showed increased flow rates in the middle cerebral and basilar arteries, which returned to normal as the patient recovered. There were two published cases of cerebral vasospasm associated with immunoglobulin infusion, but frank infarction did not occur in the patient reported here. The manufacturers of the preparation received by our patient are not aware of any reports of encephalopathy developing in a patient given this preparation. The committee on safety of medicines, however, has received three reports of convulsions and one of an encephalopathy associated with immunoglobulin usage (Committee on Safety of Medicines, personal communication).

We suggest that a reversible encephalopathy may be a rare side effect of intravenous immunoglobulin treatment.
Encephalopathy associated with intravenous immunoglobulin treatment for Guillain-Barré syndrome.

K Harkness, S J Howell and G A Davies-Jones

*J Neurol Neurosurg Psychiatry* 1996 60: 586
doi: 10.1136/jnnp.60.5.586

Updated information and services can be found at:
http://jnnp.bmj.com/content/60/5/586.1.citation

**These include:**

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/