Cerebral infarction complicating intravenous immunoglobulin therapy in a patient with Miller Fisher syndrome

Benjamin Turner, Adrian J Wills

Abstract
Intravenous immunoglobulin (IVIg) therapy is being increasingly used in a wide range of neurological conditions. However, treatment is expensive and side effects may be severe. A patient with Miller Fisher syndrome who developed cortical blindness as a consequence of occipital infarction precipitated by IVIg is reported on.

Keywords: Miller Fisher syndrome; intravenous immunoglobulin; cerebral infarction

Case report
A 60 year old woman presented with a 5 day history of left sided ptosis, diplopia, paraesthesia of the hands and feet, and impaired manual dexterity. One week previously she had had a diarrhoeal illness lasting 24 hours.

On examination she was apyrexial and mildly tachycardic. Her forced vital lung capacity was 1.45 l. Examination of the cranial nerves showed a left sided ptosis with a total external ophthalmoplegia of the left eye and impaired abduction of the right eye. The pupillary reflexes were normal to light and accommodation. She had a bulbar palsy causing dysarthria and mild dysphagia with bilateral facial weakness. Examination of the peripheral nervous system showed mild (4/5 MRC scale) weakness in the arms and legs associated with loss of deep tendon reflexes. There was severe loss of proprioception and diminished vibration sense in the hands and feet with associated limb ataxia yet pain and temperature sensation was relatively preserved. She was unable to walk.

It was considered that she had the Miller Fisher variant of Guillain-Barré syndrome complicating a campylobacter jejuni infection 1 week earlier. Subsequent investigations disclosed raised IgG antiganglioside antibodies to GQ1b glycolipids (titre of 1/3000) and high IgM (+1280) and IgA (+320) titres against campylobacter jejuni. There was neurophysiological evidence of an axonal sensory neuropathy (sensory conduction in the left sural and radial nerves was absent; left median motor compound muscle action potential was 7.2 mV with a conduction velocity of 43.4 m/s). Electrolytes and brain CT performed at the referring hospital were normal. A lumbar puncture was performed on day 5 of the illness and demonstrated normal CSF constituents with a protein concentration of 0.1g/l. Intravenous immunoglobulin (IVIg) was given for 5 days at a dose of 0.4 g/kg/day starting 6 days after the onset of neurological symptoms.

On the second day of IVIg treatment it was noted that the plasma sodium had fallen to 128 mmol/l, with a urinary sodium of 205 mmol/l, random cortisol of 510 nmol/l, and normal renal function, fulfilling the criteria for the syndrome of inappropriate antidiuretic hormone (SIADH). Five days later the plasma sodium reached 124 mmol/l and a 1.5 l/day fluid restriction was instigated. Her neurological status began to improve but after 3 days she became acutely confused. Within a few hours her confusion had settled but she complained of visual loss. Examination showed that she had perception of light only in both eyes with normal pupillary responses. Magnetic resonance imaging showed bilateral occipital lobe infarcts (figure).

Magnetic resonance image showing bilateral occipital infarction (arrows).
Cerebral infarction, immunoglobulin treatment, and Miller Fisher syndrome

791

Fisher syndrome there are high titres of gangliosides.3 In 90% of patients with Miller
Campylobacter jejuni arise due to molecular mimicry between of 10%.1 In 1956 Fisher described three
generalised muscle weakness and has an joint position sense had normalised. Romberg’s test was negative and
had normal power in her limbs but remained areflexic. By the time of discharge the patients’ vision
had improved to 6/9 bilaterally. Her left eye remained moderately paretic and her right eye
was normal. The left sided ptosis and facial weakness had improved and bulbar function
was normal. She was able to walk unaided and had normal power in her limbs but remained areflexic. Romberg’s test was negative and joint position sense had normalized.

Discussion
Guillain-Barré syndrome is an acute monophasic peripheral neuropathy characterised by generalised muscle weakness and has an incidence of 1–2/100 000/year and a mortality of 10%.1 In 1956 Fisher described three patients with a syndrome consisting of ophthalmoplegia, ataxia, and areflexia. This is considered a variant of Guillain-Barré syndrome. About 6% of patients with Guillain-Barré syndrome start as Miller Fisher syndrome, half of which go on to develop marked weakness and half remain pure Miller Fisher syndrome. In Miller Fisher syndrome the external ophthalmoplegia usually begins symmetrically with abduction affected initially. Ptosis, bilateral but asymmetric, is present in over half the patients and facial and bulbar palsy does occur.1 The ataxia may involve the limbs or gait equally often with clumsiness of fine finger movements; however, loss of joint position sense is not invariable. Most patients have a preceding illness and this is often Campylobacter jejuni enteritis.1 It is thought that these postinfectious syndromes are caused by the production of antibodies to gangliosides, which are substantial components of neuronal membranes and have regulatory roles.4 These antibodies may arise due to molecular mimicry between Campylobacter jejuni lipopolysaccharides and gangliosides.5 In 90% of patients with Miller Fisher syndrome there are high titres of antibodies to the GQ1b ganglioside.5

In clinical practice the aetiology of SIADH is often unclear but it is recognised in association with Guillain-Barré syndrome. The diagnosis of SIADH requires hyponatraemia with low plasma osmolality, increased urinary sodium excretion, absence of volume depletion, and normal renal, adrenal, and hepatic function. Symptoms of hyponatraemia range from a mild confusion, clouding of consciousness to coma, and seizures.6 In our patient the acute onset of loss of vision and short lived confusion are more consistent with acute ischaemia of the occipital lobe than “hyponatraemic encephalopathy”.

Intravenous immunoglobulin is being used to treat an increasing number of neurological illnesses including Guillain-Barré syndrome, multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, dermatomyositis, and multifocal motor neuropathy with conduction block. Immunoglobulin treatment has been quoted as having a minor complication rate of 59% and 4.5% of patients have serious complications including neutropenia, congestive heart failure, and renal failure.7 There have been three previously reported cases of cerebral infarction after IVIg, and cerebral vasospasm, cerebral vasculitis, and serum hyperviscosity have been implicated in the pathogenesis.8 In our patient cerebral infarction may have arisen as a consequence of IVIg related hyperviscosity exacerbated by fluid restriction. All patients receiving IVIg must have careful fluid balance management and if SIADH occurs fluid restriction should only be instigated when hyponatraemic symptoms are severe.6 In view of the risk of serious adverse events in those patients receiving IVIg, the treatment must be clearly justified.

3 Yuki N, Tahi T, Takahashi M, et al. Molecular mimicry between GQ1b ganglioside and liposaccharides of Campy-