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doi:10.1016/j.jocn.2008.06.024

Acute inflammatory encephalomyelitis following *Campylobacter* enteritis associated with high titre antiganglioside GM1 IgG antibodies

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ARTICLE INFO

Article history:
Received 17 November 2007
Accepted 4 May 2008

Keywords:
Acute disseminated encephalomyelitis
Bickerstaff's brainstem encephalitis
Campylobacter jejuni
Fisher syndrome
GM1 ganglioside
Guillain-Barré syndrome

ABSTRACT

Campylobacter enteritis is commonly associated with various forms of the Guillain-Barré syndrome but not central nervous system (CNS) inflammation. We present a case of *Campylobacter* enteritis associated with acute inflammatory encephalomyelitis and high titre antiganglioside GM1 IgG antibodies. The finding of antiganglioside antibodies in inflammatory demyelination of the CNS may identify avenues for research into pathogenesis. The relationship between antiganglioside antibodies and CNS inflammation is discussed.

1. Introduction

Acute disseminated encephalomyelitis (ADEM) and Bickerstaff's brainstem encephalitis (BBE) are both monophasic, acute inflammatory encephalitides, commonly following antecedent infection. ADEM is characterised by demyelination of the central nervous system (CNS) with perivascular inflammation and oedema. Symptoms include focal neurological deficits related to demyelination, lethargy and urinary retention. MRI demonstrates increased T2 signal in the CNS white matter, which may enhance with gadolinium. Cerebrospinal fluid (CSF) examination demonstrates a mononuclear pleocytosis without oligoclonal bands.[1] BBE is clinically characterised by drowsiness, symmetric ophthalmoplegia and ataxia.[2] MRI demonstrates increased T2 signal in the brainstem, thalamus, cerebellum or CNS white matter, and CSF examination demonstrates albuminocytologic dissociation.[3]

2. Case report

A previously healthy 20-year-old woman developed fever, bloody diarrhoea and vomiting. Eight days into the illness she was admitted to hospital with dehydration and persistent diarrhoea. Stool culture prior to admission grew *Campylobacter* species. On admission she was alert, orientated, apyrexial and clinically dehydrated, with generalised abdominal tenderness without peritonism. There were no focal neurological signs. Sodium concentration was 140 mmol/L and remained normal throughout the illness. The remainder of her electrolytes, full blood count, and abdominal and chest X-rays were normal. On day 4 she developed profound lethargy with a reduced level of consciousness, progressive generalised weakness and urinary retention. Neurological examination demonstrated a Glasgow Coma Scale (GCS) score of 13 with intermittent response to commands, generalised decreased tone, global weakness including facial and bulbar muscles, and a complex ophthalmoparesis. Coordination was not obviously impaired. Tendon reflexes were exaggerated, but plantar responses remained flexor. Cranial and spinal MRIs were performed without gadolinium enhancement. The T2-weighted MRIs demonstrated extensive, confluent high signal in the dorsal aspect of the pons extending into the base of the left middle cerebellar peduncle, and in the cervical and thoracic cord (Fig. 1A, B). Examination of the CSF revealed 71 white cells/μL, 97% lymphocytes, protein 540 mg/L and glucose 3.4 mmol/L. Oligoclonal bands were not detected by simple electrophoresis. She was treated with 1 g/day of intravenous methylprednisolone. Forty-eight hours later she was increasingly drowsy and unable to clear secretions. Her GCS score was 9, and there was profound face and limb weakness with complete ophthalmoplegia. The reflexes were brisk and the plantars unresponsive. She was admitted to intensive care, intubated and mechanically ventilated. The first of five cycles of plasmapheresis was commenced, and methylprednisolone was continued daily for a further three days. She slowly improved and on day 34 was

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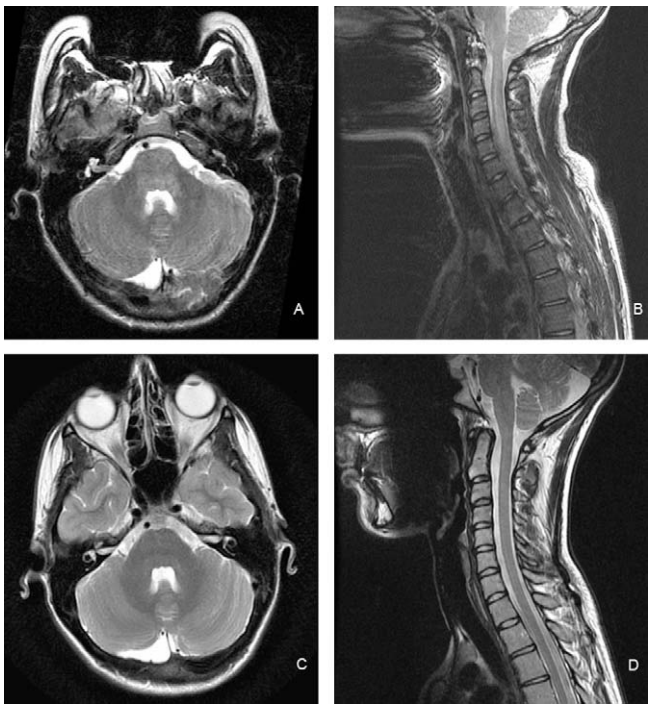

Fig. 1. A T2-weighted MRI of the axial brain (A, C) and sagittal cervical spine (B, D). (A, B) High signal is seen in the pons extending into the left middle cerebellar peduncle and cervical cord. (C, D) A follow-up MRI six months later showing resolution of T2 signal changes.

extubated. On day 46 she was discharged home with urinary urgency as her only symptom. Follow-up cranial MRI at six months showed complete resolution of the T2 signal changes (Fig. 1C, D).

Serum antiganglioside antibody titres (determined using enzyme-linked immunosorbent assay, ELISA) performed before plasmapheresis demonstrated elevated IgG GM1 antibody, titre > 12,500 (reference range <500), and IgM GM1 = 700 (reference range < 500). Anti-GQ1b, anti-GD1a, anti-GD1b and anti-GT1b antibodies were negative. Serum protein electrophoresis and thyroid function tests were normal. Cytomegalovirus and herpes simplex virus (HSV) type 1 and 2 serology, CSF for enterovirus RNA, varicella and HSV DNA were negative. Nerve conduction studies were not performed, but there was no evidence of a peripheral neuropathy during the illness. Our patient met clinical, radiological and CSF criteria for the diagnosis of ADEM, and has had no recurrence of disease over two years.

3. Discussion

Campylobacter jejuni is a frequent antecedent of axonal and, less frequently, demyelinating forms of the Guillain-Barré syndrome (GBS).[4] Antibodies against a range of glycolipids in the peripheral nervous system have been identified.[5] Specific antibodies reported in GBS variants include anti-GM1 antibodies in the predominant motor variant acute motor axonal neuropathy (AMAN), and anti-GQ1b antibodies in Fisher syndrome (FS).[6,7] The lipopolysaccharide layer of *C. jejuni* is thought to molecularly mimic these glycolipids and initiate an immune response through poorly understood mechanisms. Although the glycolipids expressed on gangliosides are present throughout the nervous system, the resulting immune responses rarely involve the CNS.[5] The mechanisms through which antiglycolipid antibodies do involve the CNS are also poorly understood.

One clue may be the striking resemblance of FS to BBE. FS is characterised by ophthalmoplegia, ataxia and areflexia, and is associated with antecedent illness and albuminocytologic dissociation.[8] Furthermore, BBE is also associated with anti-GQ1b antibodies, suggesting a common pathogenesis for the two diseases.[9] BBE is also associated with GM1 IgG antibodies.[3]

While our patient's acute inflammatory encephalomyelitis fits clinical criteria for BBE, the radiologic changes of extensive demyelination within the brainstem and spinal cord, CSF pleocytosis, the absence of albuminocytologic dissociation and the relative paucity of ataxia are more consistent with a diagnosis of ADEM. The description of this patient and two other instances of ADEM with high titre IgG GM1 antibodies after *Campylobacter* infection demonstrates that GM1 IgG antibodies may be associated with the development of inflammatory demyelination of the CNS.[10,11] Whether BBE and ADEM develop from the same immunopathological mechanism or represent different manifestations of the same condition is unclear. However, the finding of high titre IgG GM1 antibodies in our patient is of interest and may provide an avenue for further investigation of the immunological trigger for ADEM-like illnesses. To our knowledge there have been no systematic studies of GM1 antibodies in acute inflammatory encephalomyelitis, and further analysis may be useful.

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doi:10.1016/j.jocn.2008.05.028