SLE.^{7, 18–20} These patients develop acquired hypocomplementaemia due to immune complex activation of the classical pathway leading to consumption of C3 and C4, resulting in defective opsonisation and chemotaxis,²¹ or the terminal membrane attack complex formation²² and increased risk of infection. The persistent consumption of C3 may also affect the ability to activate the alternative pathway; the very low C2 and C4 levels prevent the complement activation via the MBL pathway.

Our patient's C4 level has not returned to normal, raising the question of abnormal C4 alleles. C4B deficiency has been linked to meningococcal disease, but as for MBL deficiency, this typically presents in childhood.²³

Our patient had acquired classical complement pathway deficiency as seen in active SLE; simultaneously she had MBL deficiency, which acted as a contributing factor to her increased susceptibility to meningococcal infection.

Management of complement deficiency consists primarily of preventive measures including immunisation with polysaccharide and available conjugated meningococcal, pneumococcal and *Haemophilus influenzae* b vaccines. In addition, the patient should be educated to early recognise signs and symptoms of meningitis.

Conclusion

A high index of suspicion for an underlying complement deficiency should arise when a patient presents with recurrent meningococcal disease or a disease caused by uncommon serogroups, particularly Y, W135, and X.

Although urticaria is a common condition, atypical features should alert the doctor to the possibility of urticarial vasculitis and an underlying autoimmune systemic disease.

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Bickerstaff's brainstem encephalitis related to *Campylobacter jejuni* gastroenteritis

Campylobacter species are microaerophilic spiral-shaped Gram-negative bacilli which cause diarrhoeal and systemic illness in humans and animals. They are the most commonly identified cause of bacterial intestinal disease in the UK and elsewhere in the developed world. The bacterial cell wall of the organism contains an endotoxin which, when released, can result in acute enteritis and complications such as reactive arthritis, erythema nodosum, peripheral neuropathy, haemolytic uraemic syndrome and Bickerstaff's brain stem encephalitis (BBE). Here we report a case of BBE following a gastrointestinal infection with *Campylobacter*

jejuni. The patient presented with acute onset of confusion and ophthalmoplegia. The cerebrospinal fluid (CSF) showed lymphocytic pleocytosis and raised protein. This acute presentation was preceded by an episode of *Campylobacter*-related diarrhoea as confirmed by high titres of *Campylobacter*-specific IgM antibodies.

Over 50 000 laboratory confirmed cases of *Campylobacter* intestinal disease are reported annually in England and Wales.¹ *Campylobacter jejuni* is the most common species of the genus *Campylobacter* identified in clinical samples.¹ Transmission occurs throughout the year but rises in late spring and early summer, and requires only small inoculums.² Clinical features of *C. jejuni* infection range from an absence of symptoms to fulminant sepsis and death. In rare cases a potentially life threatening form of post-infectious encephalitis affecting the brainstem can arise.³ Initial colonisation occurs in the jejunum and ileum, which spreads distally to involve the colon and rectum. After a prodromal illness, the patient may develop abdominal pain and bloodstained diarrhoea. Other common complications include septic polyarthritides and peripheral polyneuropathy.

In 1957 Bickerstaff described eight patients with brainstem encephalitis presenting with ophthalmoplegia, ataxia and a reduced level of consciousness. Our extensive literature search has revealed only a few documented cases of BBE secondary to intestinal infection with *Campylobacter*.⁴

Case report

A 54-year-old man presented with a 1-week history of fever, anorexia and vomiting. On arrival at hospital he was febrile, confused and slightly dysarthric but there were no signs of meningism. Neurological examination showed a generalised weakness of all four limbs. He had absent lower limb reflexes and diminished reflexes in the upper limbs. The right plantar response was extensor while the left was equivocal. Owing to his confusion, adequate sensory testing could not be performed.

Initial investigations were unremarkable. In view of a working diagnosis of encephalitis, a lumbar puncture was performed following a

Table 1 Serological markers of *Campylobacter jejuni* infection

	Day 1	Day 6	Day 98
IgM	<80	1280	160
IgG	80	5120	320
IgA	<80	320	80

Table 2 Diagnostic criteria of Bickerstaff's brainstem encephalitis

Progressive symmetrical ophthalmoplegia
Ataxia
Decreased level of consciousness
Pyramidal signs
Bilateral limb weakness
Characteristic MRI findings
Absent or disappearing F-waves on electromyographic studies

normal CT brain scan. Laboratory examination of the CSF showed 270 white blood cells/mm³ (66% lymphocytes, 34% neutrophils) with a protein level of 0.79 g/l. In view of the clinical presentation and CSF findings, treatment was aimed at a presumptive diagnosis of meningoencephalitis with a combination of ceftriaxone and aciclovir. Serum and CSF samples were sent for herpes simplex virus (HSV) and Epstein-Barr virus (EBV) titres and PCR, which were later reported as negative.

On transfer to the intensive care unit he was electively intubated and ventilated. Treatment with intravenous piperacillin-tazobactam and ionotropes was commenced. Elective surgical tracheostomy was performed on day 8 and sedation ceased to allow for regular neurological examination. By day 11 there had been no neurological improvement, with no response to deep pain stimuli and hypotonia. The Glasgow Coma Score was estimated to be 7/15 at this point. An MRI scan of the brain revealed an ill-defined T₂ hyperintense area in the brainstem which was reported as an area of infarction secondary to cerebrovascular ischaemia. An MRI scan of the spine also showed mild degenerative changes. An EEG was performed which excluded non-convulsive status epilepticus.

On day 13 he was noted to be more responsive to stimuli but remained quadriplegic. By day 15 he was alert, obeyed commands, and had begun to recover some upper limb control. By day 18 his upper limbs continued to improve although his lower limbs remained paralysed. Electromyography on day 22 revealed mild subacute axonal loss, no evidence of demyelination and absent F-waves. On day 30 he was weaned off positive pressure ventilation.

The laboratory reported a high titre of *C jejuni* IgM on day 37. Because detection of the IgM antibody response to *C jejuni* could be unreliable,⁵ we confirmed the diagnosis of *C jejuni* infection by demonstrating a significant rise and subsequent fall in the titres of IgM, IgG and IgA antibodies (table 1). After careful consideration, a 5-day course of immunoglobulin was commenced to treat possible BBE. Before starting this treatment, serum for anti GQ1b antibodies was sent to the laboratory which was later found to be negative. Although many features of this case fit into the classical description of BBE, there were a number of atypical findings such as a CSF pleocytosis and a negative anti GQ1b. Other conditions mimicking the presentation of BBE such as multiple sclerosis, acute disseminated encephalomyelitis, brainstem tumour, myasthenia gravis, botulism, Wernicke's encephalopathy and vasculitis were excluded. On day 52 the patient was transferred to the local brain injury unit where he continued to display neurological recovery with intensive rehabilitation. The patient has now regained most of his neurological function.

Discussion

BBE is a rare complication of *Campylobacter* food poisoning⁷ resulting in an ascending polyneuropathy.⁸ It may be related to certain genetic polymorphisms in the host which can be correlated with the severity of the disease. A high incidence of autoantibodies against glycoconjugates such as GM, GD1a and GD1b is found among these patients.⁹ Similar epitopes have been shown to occur in the lipopolysaccharide antigens of *C jejuni* which

Take-home messages

- Bickerstaff's brainstem encephalitis is a rare but potentially life threatening complication of *Campylobacter jejuni* gastroenteritis.
- A high index of clinical suspicion and a close liaison with laboratory staff can facilitate an early diagnosis.
- For confirmation of the diagnosis it is essential to test sequential serum samples to demonstrate a significant rise and subsequent decline of IgM, IgG and IgA antibodies to *C jejuni*.

may represent the immunogenic stimulus. In addition, there is cross-reactivity between antigens from *C jejuni* and the P2 protein of the myelin sheath which may explain the pathogenetic connection between *C jejuni* infection and brainstem encephalitis.⁸

The lymphocytic pleocytosis and raised protein level in the CSF led us to start empirical treatment for both bacterial and viral meningitis. However, the acute onset of ophthalmoplegia, generalised limb weakness and reduced level of consciousness suggested BBE (table 2). *Campylobacter* was considered as an aetiological agent after a detailed history revealed that the patient had suffered an episode of diarrhoea a week before becoming acutely unwell. Subsequent serological examination confirmed the diagnosis of *C jejuni* infection. Although *C jejuni* infection can lead to a wide spectrum of neurological complications, this case did not display features consistent with a classical presentation of Miller Fisher syndrome or Guillain-Barré syndrome.

Further investigations of these patients include neuroimaging and electrophysiological studies. High-intensity areas on T₂-weighted images of the brainstem, thalamus, cerebellum and cerebrum on MRI are present in approximately one-third of patients, and these lesions can be erroneously reported as infarcts.⁷ EEG studies may show slow wave activity in the θ to δ range. Electromyography may reveal decreased motor nerve conduction studies, prolonged distal latency, reduced compound muscle action potential and absent or prolonged F-waves. As in this case, these findings are highly suggestive of axonal loss. Patients may have raised levels of anti-GQ1b IgG antibody, which is strongly associated with ophthalmoplegia.

Most patients can be managed by immunotherapy, using plasmapheresis or intravenous immunoglobulin either singly or in combination. Those patients who fulfil the diagnostic criteria of BBE usually have a good prognosis. Optimal effective treatment has not been established. Intravenous immunoglobulin has proved as effective as plasma exchange, while combined treatment with methylprednisolone and intravenous immunoglobulin is controversial.^{10 11}

BBE is a rare but important complication of *C jejuni* gastroenteritis. A high index of suspicion together with a detailed history and examination are essential in making an accurate diagnosis.

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Dermatofibrosarcoma protuberans in a patient with X-linked agammaglobulinaemia

This is the first case report of dermatofibrosarcoma protuberans (DFSP) arising in a patient with X-linked agammaglobulinaemia