Rare disease

A microbiological hazard of rural living: *Clostridium septicum* brain abscess in a child with *E coli* 0157 associated haemolytic uraemic syndrome

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Summary

Clostridium septicum infection in humans is rare and this is the second case report of focal *C septicum* brain abscesses associated with *Escherichia coli* 0157 haemolytic uraemic syndrome (HUS). The case presented in a child who lived on a rural farm. The abscesses initially progressed despite 7 months of appropriate antibiotic therapy and repeated image-guided aspiration. After definitive resection and prolonged antibiotic therapy, there was no recurrence. This case reminds us of this rare but important neurological complication of HUS and supports consideration of early definitive neurosurgical intervention in similar unusual cases.

BACKGROUND

This is the second paediatric case report of focal *Clostridium septicum* brain abscesses associated with *Escherichia coli* 0157 HUS in a boy who lived on a dairy farm. This case report reminds us of this very rare but important complication of HUS and documents the progression of this focal infection despite appropriate antibiotic therapy and repeated aspiration.

CASE PRESENTATION

A previously fit 2 1/2-year-old boy presented with haemolytic uraemic syndrome (HUS) associated with *E coli* 0157 sepsis. He lived on a dairy farm in the rural northwest of England. He presented with 4 days of bloody diarrhoea and then became progressively lethargic, pale and oliguric. *E coli* 0157 was isolated from his stool. As his condition worsened he was found to have evidence of mild anaemia, thrombocytopenia, renal dysfunction and slightly raised bilirubin (Hb 12 g/dl, platelets 62×10^9 /litre, urea 14.0 mmol/l, creatinine 94 μ mol/l and bilirubin 40 μ mol/l). He was transferred to a tertiary hospital for ongoing care. He remained oliguric with deteriorating renal function and associated haemolysis and received renal support with peritoneal dialysis and haemodialysis, and underwent plasma exchange. Six days (day +6) into his renal management, he became irritable, drowsy and hypertonic. He was transferred to the local paediatric intensive care unit and started on antibiotics (initially ceftriaxone, metronidazole and teicoplanin intravenously). An MRI showed large bilateral haemorrhagic/ischaemic lesions in the temporo-parietal areas which was felt to be consistent with neuro-vascular and coagulopathic complications found in HUS. Two weeks later (day +21), and 2 days after his antibiotics were stopped, the patient developed febrile status epilepticus. An urgent MRI showed that the

bilateral temporo-parietal lesions had enlarged with extensive parenchymal oedema.

INVESTIGATIONS

His inflammatory markers were mildly raised (white cell count 16×10^9 /litre (neutrophils 12.9×10^9 /litre) and C reactive protein 22). He was started on meropenem (20 mg/kg three times a day, intravenous) and metronidazole (7.5 mg/kg three times a day, intravenous) to cover for intracranial sepsis, and a biopsy of the right-sided lesion identified *C septicum* on enrichment culture, with histological findings of a subacute abscess.

TREATMENT

He initially improved clinically on antimicrobial therapy. An MRI 2 weeks (day +39) later showed progression of the bilateral lesions to discrete walled abscesses with surrounding oedema (figure 1A). At this stage both lesions had burr hole ultrasound-guided aspirations and 50 ml of pus was removed from each side, which again identified *C septicum* on culture. Complicating the management the boy also developed a florid urticarial rash at this stage which was thought to be drug allergy and he was switched to a combination of amoxicillin (50 mg/kg three times a day), clindamycin (40 mg/kg three times a day) and metronidazole intravenously. Home intravenous therapy was arranged and he continued on these antibiotics at home. Clinical and radiological improvement was confirmed on MRI on day +115. One month later (day +145) he was reviewed with fever, headaches and lethargy. An urgent CT showed that the left parietal abscess was unchanged in size but the associated oedema had significantly increased. His antibiotics were switched to meropenem, metronidazole and linezolid (10 mg/kg three times a day, intravenous) and further ultrasound-guided

Figure 1 (A) Day +21: Post-contrast MRI demonstrating ring-enhancing lesions bilaterally, suggestive of intracerebral abscesses. (B) Day +188: Post-contrast MRI following treatment demonstrates multiple bilateral residual lesions.

aspiration of the right abscess identified pus, which was sterile on culture.

Over the next 2 months, three further ultrasound-guided aspirations were performed. *C septicum* was again identified from these samples and linezolid was stopped, while continuing meropenem, metronidazole and restarting clindamycin. Repeated MRI scans showed the formation of small but unambiguously new ring-enhancing lesions adjacent to the existing abscesses (figure 1B).

On day +226 he had a craniotomy and image-guided (MR) resection of the left abscess. Brain swelling was considerable and the deeper part of the enhancing tissue was not resected. On day +233 he had a craniotomy and resection of the right abscess. Operating conditions were more favourable and the entire enhancing area was removed and intralesional vancomycin instilled. The left side was also re-explored and again with favourable conditions all remaining enhancing tissue was removed. *C septicum* was again isolated from both sides. These operations were well tolerated and the patient made good recovery with no neurological deficit. He completed six further months of meropenem, clindamycin and metronidazole with regular surveillance MRIs after resection.

OUTCOME AND FOLLOW-UP

After resection and further prolonged antibiotics, the outcome for this boy was good. His latest MRI at day +462 shows good recovery and no residual abscesses. His development remains normal to date. He has been investigated for underlying risk factors that may predispose him to cranial abscesses.

DISCUSSION

C septicum is an anaerobic, spore-forming gram-positive bacillus first described by Louis Pasteur in 1877. Its reservoir is the gastrointestinal system of herbivore animals. Clostridial spores are thought to be passed to humans via contaminated soil or faeces introduced to the gastrointestinal tract or directly to traumatised tissues. Its virulence is promoted by the exotoxin that it produces called alpha-toxin, which is a pore-forming cytolysin that causes intravascular haemolysis and necrosis of host tissues.¹

C septicum was first described as causing gas gangrene in the First and Second World Wars. Disease in humans is

now rare and the incidence in the UK is reported as 0.4–1.0 cases per million of the population.² Myonecrosis from direct inoculation is rare and the presumed portal for entry for spontaneous infections is the gastrointestinal tract, by local invasion or translocation in immunocompromised individuals, in the majority of cases. A recent review of all reported children with *C septicum* infections documented that the primary risk factors for this were haematological malignancies and congenital/cyclical neutropaenias causing disruption of mucosal integrity.³

HUS is a syndrome characterised by renal failure, haemolysis and thrombocytopenia and is most commonly associated with gastroenteritis caused by a Shiga toxin-producing organism *E coli* 0157. This gastroenteritis from HUS compromises the integrity of gastrointestinal mucosa and therefore predisposes to the translocation of colonising gastrointestinal flora to the blood stream. As both *E coli* 0157 and *C septicum* are zoonotic and found in similar rural environments, it is not surprising that these infections co-exist and just over 10% (5/47) of children described with *C septicum* infection have HUS as their underlying risk factor.³

Neurological complications occur in about a third of children with HUS, presenting (similar to our child's initial presentation) with seizures, cerebral oedema and neuro-vascular lesions.⁴ These devitalised and anaerobic areas of brain tissue are ideal environments for *C septicum* to settle and hence allow CNS infection. Four of the six published cases of HUS and *C septicum* infection have a neurological focus; however, unlike our case, the majority are described as meningitis or cerebritis^{5–7} with only one previous case described as having focal brain abscess.⁸ The other cases were myonecrosis⁹ and septicaemia.²

The management of *C septicum* infections consists of supportive care, antibiotics and surgery/debridement of focal infections. Recommended antibiotics include high-dose penicillin, clindamycin, meropenem and metronidazole¹⁰ but there is no evidence-based treatment regime. Not surprisingly, antibiotic treatment in adults and children with *C septicum* infections has been shown to reduce mortality.³ Surgical intervention is felt to be crucial in clostridial infections, and paediatric reviews of *C septicum* infection suggest a considerable survival advantage in children who received therapeutic surgery compared to those who did not (84% compared to 12%).³ The two surgical treatment strategies for brain abscesses are repeated aspiration leaving the abscess wall in place, and complete excision of the wall. The latter approach has the highest chance of cure but a higher morbidity and specifically a high morbidity when an abscess is large. The hybrid approach now widely used is repeated aspiration initially and excision of any residuum that is not controlled. That strategy was adopted here. Repeated aspiration was associated with reducing size of the abscesses and clinical stability. It was the development of new abscess cavities despite this strategy that prompted resection. The standard surgical strategy for abscess management was successful in this case but from our experience earlier complete resection could be considered on the grounds of stable disease and the presence of *C septicum*.

Learning points

- *Clostridium septicum* should be considered in neurological infectious complications of haemolytic uraemic syndrome in children
- In this case the *C septicum* brain abscesses progressed despite appropriate antibiotic therapy and repeated aspirations. A good outcome was seen with complete excision

Competing interests None.

Patient consent Obtained.

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