Case Report

Clostridium clostridioforme liver abscess complicated by portal vein thrombosis in childhood

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Pyogenic liver abscesses are rare in children, and show geographical differences in their epidemiology. Mortality rates remain high at 15%. Liver abscesses caused by anaerobic organisms are rare in a paediatric setting, even more so when complicated by portal vein thrombosis (PVT). A 6-year-old girl, previously fit and well, was admitted with fever, lethargy and weight loss of 2 weeks duration. The patient was febrile on examination and a review of the systems revealed no positive findings. An abdominal ultrasound scan showed multiple interconnecting cystic lesions consistent with liver abscesses, which was confirmed by a computed tomography scan. Aspirate of the abscess was cultured, resulting in the isolation of a non-haemolytic anaerobic organism, which was difficult to identify using conventional phenotypic identification tests. 16S rRNA typing identified the organism as Clostridium clostridioforme. The liver abscess in our patient displayed a particularly aggressive clinical course with extension of the abscess to involve the upper pole of the right kidney and the appendix, which was further complicated by PVT. The role of anaerobic organisms in liver abscesses has been underreported in the past. This case, therefore, highlights the importance of incubating biological samples in anaerobic conditions in order to adequately isolate and identify anaerobic bacteria, particularly those associated with abscesses.

Introduction

Pyogenic liver abscesses in paediatric patients are rare in developed countries, underlining geographical differences in the epidemiology of the condition (Israeli et al., 2009). Despite improved diagnostic and treatment modalities, mortality rates still remain high at 15% (Xanthakos & Balistereri, 2007). A review of 96 children with pyogenic liver abscesses showed that anaerobes accounted for 10% of the cases, with Staphylococcus aureus and enteric Gram-negative bacilli accounting for 44 and 25% of the cases, respectively (Pashanker & Schreiber, 2008).

Clostridium clostridioforme is a relatively antimicrobial-resistant anaerobe that has been implicated in a variety of invasive infections but there have been no reports of C. clostridioforme as a cause of liver abscesses in children. The rarity of liver abscesses caused by this organism, along with its potential complications, including portal venous thrombosis (PVT), and the difficulties encountered in the identification of this condition, has prompted us to report this case.

Case report

A 6-year-old girl, previously fit and well, was admitted with fever, lethargy and weight loss of 2 weeks duration. Six months prior to admission, the patient was diagnosed by her family doctor with a non-specific upper airway viral illness but continued to feel lethargic and was off school for a long time. At initial presentation, the patient was febrile, with a temperature of 40°C, and underweight. The abdomen was soft, non-tender without any obvious distension. The rest of the physical examination showed no focal abnormalities. There was no history of recent travel and the family owned no pets. The white cell count was elevated at 23.7 × 10⁹ cells l⁻¹ and the patient exhibited neutrophilia with a neutrophil count of 21.6 × 10⁹ cells l⁻¹. The haemoglobin level was 10.3 g dl⁻¹ and C-reactive protein was at 380 mg l⁻¹. Initial liver function tests were normal. The patient was empirically commenced on cefotaxime for presumed sepsis. She remained unwell and continued to be febrile despite 48 h on cefotaxime. Repeat liver function tests revealed an elevated alkaline phosphatase level with normal levels of transaminases and bilirubin. An abdominal ultrasound scan showed multiple interconnecting cystic lesions consistent with liver abscesses, which was confirmed by a computed tomography (CT) scan. No abnormality of the bowel, pancreas or gall bladder was seen on the scans.

Percutaneous CT-guided drainage of the liver abscess was carried out and the treatment was changed to cefuroxime and metronidazole. Cultures of the aspirate and blood yielded an organism that was initially identified as a Gram-negative...
bacillus under the microscope. The patient continued to be pyrexial with systemic upset even 5 days after the percutaneous drainage and despite being on adequate doses of antibiotics. A repeat CT scan showed a persisting liver abscess that had, by then, spread to the upper pole of the right kidney and the appendix. PVT was also observed on the CT scan. The patient went on to have an open drainage of the abscess and antibiotic treatment was escalated to meropenem, which was continued for 3 weeks. The patient was discharged with a 2-week-supply of oral metronidazole. She made a complete recovery and has remained well based on follow-up clinical evaluation and imaging by ultrasound.

**Microbiology**

Microscopy of the pus sample initially revealed a Gram-staining-negative bacillus. Culturing the aspirate on non-selective anaerobic blood agar at 37 °C yielded grey non-haemolytic colonies with spreading edges, measuring 2–3 mm in diameter after 2 days of incubation. The organism did not grow aerobically. The organism was found to be sensitive to clindamycin and metronidazole but resistant to penicillin. Testing for sensitivity to cephalosporins was, unfortunately, not performed. The results of conventional phenotypic identification tests were inconclusive, initially identifying the organism as a species of the genus *Fusobacterium*. Because the organism could not be conclusively identified by conventional tests and because Gram-staining was later deemed to be variable, the organism was sent for 16S rRNA gene sequencing and was identified as *Clostridium clostridioforme*. In addition, the blood cultures yielded the same isolate, which was obtained by using a BACTEC Plus Anaerobic bottle inoculated with approximately 10 ml of blood. No growth was observed in the aerobic bottle. Both bottles were incubated in a BACTEC 9240 continuous-monitoring automated blood culture system. Positive blood cultures were obtained 84 h after incubation. Subculturing onto a non-selective anaerobic blood agar medium and anaerobic incubation at 35–37 °C yielded the same organism as the aspirate after 48 h of incubation. 16S rRNA gene sequencing also identified the blood culture isolate as *C. clostridioforme*.

**Discussion**

Infections caused by *C. clostridioforme* are poorly described and, to our knowledge, this is the first time a liver abscess caused by this organism has been reported in a paediatric patient. Its association with PVT has also not been previously documented.

This organism belongs to the genus *Clostridium*, members of which are generally anaerobic Gram-positive bacilli; however, *C. clostridioforme* tended to stain Gram-negative. The species *C. clostridioforme* previously comprised several groups of organisms that have now been reclassified into individual species, including *C. hathewayi*, *C. bolteae*, *C. clostridioforme* and, more recently, *C. citronae* and *C. aldenense* (Williams *et al.*, 2010; Finegold *et al.*, 2005; Warren *et al.*, 2006).

The identification of these organisms at species level is useful as *C. clostridioforme* has been known to cause more invasive disease and display a higher degree of antibiotic resistance compared to other species of the genus *Clostridium*, particularly due to β-lactamase production. (Nord *et al.*, 1985; Nord & Olson-Liljequist, 1984; Finegold *et al.*, 2005; Warren *et al.*, 2006). Some strains of *C. clostridioforme* are known to produce β-lactamases and others are resistant to clindamycin and moxifloxacin. The phenotypic variability displayed by this organism (Finegold *et al.*, 2005) can cause problems when trying to accurately identify it using routine biochemical methods, often leading to misidentification of the organism as a species of the genus *Fusobacterium* or *Bacteroides*. The unique colony morphology of *C. clostridioforme* and its appearance as fusiform or boat-shaped rods that may appear as Gram-staining-variable should aid in its identification. In susceptibility tests, the use of 10 μg vancomycin per disc would show that the organism is susceptible to vancomycin and therefore not likely to be Gram-negative; however, 16S rRNA gene sequencing may be required for accurate identification (Woo *et al.*, 2005). Clostridia form part of the colonic microflora and are usually implicated in endogenous infections arising from the bowel; however, extensive investigations failed to reveal the source of the infection in this patient.

The liver abscess in this patient displayed a particularly aggressive clinical course with extension of the abscess to involve the upper pole of the right kidney and the appendix, as well as causing the complication of PVT, which is a rare condition and normally occurs in association with a wide variety of precipitating factors. The overall incidence rate of PVT is 0.05–0.5 % (Okuda *et al.*, 1985), the most common aetiological factor for PVT in children being infection, accounting for 43–52 % of all cases (Thompson & Sherlock, 1964). Infectious precipitants for PVT include appendicitis, biliary sepsis and peritonitis from various sources. It can also occur as a consequence of contiguous spread from an inflammatory process. The specific infectious precipitant for PVT in this patient, however, is unclear. It is not known what percentage of PVT cases arise as a complication of liver abscesses and it is difficult to say at this point if this aggressive pattern of infection is particularly attributable to this organism.

**Conclusion**

The role of anaerobic organisms in liver abscesses has been underreported in the past. This case highlights the importance of anaerobes as significant pathogens, and stresses the need for microbiology laboratories to actively look for and accurately identify anaerobic organisms. The accurate identification of these isolates can be challenging due to their Gram-staining-variability, atypical colonial
morphology and sometimes inaccurate identification by commercial anaerobe kits. Modern molecular techniques, where available, can be used to aid accurate identification of these isolates.

References


