Bacteraemia and breast abscess: unusual extra-intestinal manifestations of Clostridium difficile infection

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Extra-intestinal manifestations of Clostridium difficile infection are uncommon. Most cases are associated with gastrointestinal disease and often occur as a mixed infection with other gut flora. We report a case of breast abscess following monomicrobial C. difficile bacteraemia in a female with background chronic hepatitis C infection and alcoholic liver disease. No evidence of colitis was found. Our case shows that C. difficile is indeed capable of spreading from the gastrointestinal tract.

Introduction
Clostridium difficile is a known cause of antibiotic-associated pseudomembranous colitis. It is the most common cause of nosocomial diarrhoea. Extra-intestinal manifestations of C. difficile infection have been reported (Feldman et al., 1995; García-Lechuz et al., 2001; Jacobs et al., 2001; Urbán et al., 2010; Wolf et al., 1998). Most cases are usually preceded by gastrointestinal infection. Often, mixed infections with other gut pathogens are found (Libby & Bearman, 2009; Spencer et al., 1984). However, it is difficult to interpret the clinical relevance of such isolates from extra-intestinal sources and in some cases they may only represent contamination with faecal commensals. We report an exceptional case of monomicrobial C. difficile bacteraemia with associated infected breast haematoma in a patient with no evidence of colonic infection.

Case report
A 39-year-old white female, with a past medical history of chronic hepatitis C secondary to intravenous drug use and chronic alcoholic liver disease, presented with menorrhagia and spontaneous bruising. She had no history of diarrhoea or constipation. She stopped drinking alcohol 1 month prior to admission. Her medications included omeprazole, spironolactone, vitamin supplements and lactulose.

On physical examination, she was afebrile, jaundiced with generalized bruising and no features of encephalopathy. She had no history of diarrhoea or constipation. She stopped drinking alcohol 1 month prior to admission. Her medications included omeprazole, spironolactone, vitamin supplements and lactulose.

On physical examination, she was afebrile, jaundiced with generalized bruising and no features of encephalopathy. Hepatosplenomegaly and moderate ascites were also noted. Initial investigations revealed a low platelet count and haemoglobin level, deranged liver function and coagulation profile, and normal C-reactive protein and white cell count. Peripheral blood culture done on admission showed no growth.

The patient was transfused with blood products and commenced on tranexamic acid. Cefotaxime was started empirically to cover for possible intra-abdominal focus of infection. She had repeated abdominal paracentesis for worsening ascites. Examination of the ascitic fluid showed no evidence of spontaneous bacterial peritonitis. A left breast haematoma was noted on the second week of admission. Altered blood was aspirated under ultrasound guidance.

On the third week of hospital admission, the patient developed intermittent fever and fresh rectal bleed with semi-formed stools. No pathogen was isolated in her stools. Her white cell count and C-reactive protein were 16 $\times$ 10$^9$ l$^{-1}$ and 50 mg l$^{-1}$, respectively. Peripheral blood cultures were taken which grew Gram-positive bacilli in the anaerobic bottle after 2 days. A repeat blood culture grew the same organism and she was commenced on metronidazole. Computed tomography of the abdomen and pelvis revealed widespread ascites, irregular liver and upper abdominal varices. No other abnormalities were found. Flexible sigmoidoscopy was normal. Gastroscopy showed varices and gastritis.

The isolates from the blood culture were later identified as C. difficile. The breast haematoma became fluctuant with features suggestive of abscess collection. The abscess was drained under repeat ultrasound guidance (Fig. 1) and C. difficile ribotype 106 was isolated from it. The C. difficile isolates from the blood cultures and breast abscess were sensitive to amoxicillin/clavulanic acid and metronidazole.
The patient had a 2-week course of both antibiotics with significant improvement. The fever and breast abscess resolved. Her white cell count and C-reactive protein returned to normal levels, and she was discharged with follow-up in the outpatient clinic.

Discussion

*C. difficile* is an anaerobic, spore-forming, Gram-positive bacillus that is carried in the gastrointestinal tract in about 3% of the general adult population as part of the normal flora. It causes antibiotic-associated pseudomembranous colitis. Antibiotics eradicate the drug-sensitive members of the normal gut flora, allowing *C. difficile* to multiply and produce exotoxins which have cytopathic effects on enterocytes. The absence of toxin in faeces does not reliably indicate the absence of the organism. The diarrhoea in *C. difficile* colitis is usually non-bloody. Fever, abdominal pain, nausea and anorexia are often seen. Nineteen PCR ribotypes of *C. difficile* have been identified in Wales (NPHS, 2009). Ribotype 027 is the commonest followed by ribotype 106. All strains are susceptible *in vitro* to metronidazole, vancomycin and amoxicillin/clavulanic acid.

Extra-intestinal *C. difficile* infections are uncommon and their clinical relevance is often doubtful. Extra-intestinal infections that have been reported include bacteraemia (Libby & Bearman, 2009), peritonitis (Genta et al., 1984), intra-abdominal abscesses, soft tissue infections (Bhargava et al., 2000), brain abscess (Gravisse et al., 2003), appendicitis (Brown et al., 2007), visceral abscesses (Sakurai et al., 2001; Kumar et al., 1997), reactive arthritis (Ducroix-Roubertou et al., 2005), osteomyelitis and prosthetic joint infections (Pron et al., 1995). These are often related to gastrointestinal disease (García-Lechuz et al., 2001; Wolf et al., 1998). Most of the isolates from these cases are often part of a polymicrobial growth and from sources close to the colon in patients with faecal spillage. Transient *C. difficile* bacteraemia may also play an important role in transmission of infection to extra-intestinal sites (Feldman et al., 1995). García-Lechuz et al. (2001) identified 21 cases of extra-intestinal *C. difficile* over a 10-year period at a tertiary hospital in Spain. Four of these case patients had underlying liver pathology with peritonitis. Polymicrobial infection was found in three cases.

The treatment of the reported cases of extra-intestinal *C. difficile* diseases varied because of the polymicrobial nature of infection. Drug therapy was directed at all pathogens isolated. Intravenous vancomycin and metronidazole were commonly used (Lee et al., 2010; Libby & Bearman, 2009). A crude mortality rate of up to 50% was reported by Libby & Bearman (2009) for *C. difficile* bacteraemia. It is, however, difficult to attribute this solely to the bacteraemia as most of the cases had severe underlying pathology that could have been the cause of death.

Although our patient had a liver pathology, the bacteraemia and breast abscess were monomicrobial, and no evidence of peritonitis or colitis was found. The source of the *C. difficile* bacteraemia in our patient remains unclear. Translocation of bacteria from previously colonized gut may have been responsible for the bacteraemia, which resulted in seeding of the breast collection and resultant abscess (Balzan et al., 2007). Prior antibiotic exposure was recorded in this case.

Conclusions

*C. difficile* is rarely found outside the bowel. Most cases of extra-intestinal manifestations are usually preceded by gastrointestinal diseases and are often polymicrobial. To our knowledge, this is the first reported case of monomicrobial breast abscess due to *C. difficile* bacteraemia. Our case shows that *C. difficile* is indeed capable of dissemination from the gastrointestinal tract and causing serious systemic manifestations in the absence of diarrhoea or colitis.

Fig. 1. Ultrasound scan of the left breast. A 17 mm collection was aspirated under ultrasound guidance. The turbid aspirate was sent for microscopy, culture and antimicrobial sensitivity testing.

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References


