Case Report

Toxic megacolon complicating a Clostridium difficile infection in a pregnant woman

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Clostridium difficile infection (CDI) in non-hospitalized patients has been reported with increased frequency, whereas an association between CDI and pregnancy has not been highlighted. We report a case of toxic megacolon complicating a severe CDI during the second trimester of pregnancy in a patient without traditional risk factors, such as antibiotic use, immunodeficiency, and prolonged and recent hospitalization.

Introduction

Clostridium difficile is a spore-forming, Gram-positive anaerobic bacillus that is the most common cause of infectious diarrhoea in hospitalized patients (Poutanen & Simor, 2004). The pathogenesis of C. difficile infection (CDI) involves exogenous infection by spores that often are acquired from the environment, along with disruption of the patient’s normal flora, which is usually caused by the use of broad-spectrum antibiotics that allow the overgrowth of C. difficile (Barbut & Petit, 2001). CDI can range from asymptomatic carriage to fulminant colitis, sepsis and death. When indicated, metronidazole or oral vancomycin, the latter preferred during pregnancy, are used.

The incidence of CDI is increasing worldwide because of the increased use of broad-spectrum antibiotics, patient comorbidities and an ongoing epidemic caused by a clonal strain that is associated with increased mortality rates (McDonald et al., 2005). This epidemic strain produces increased amounts of toxins A and B, and is considered a hypervirulent strain (McDonald et al., 2005), and causes fluid secretion, inflammation and mucosal damage.

Reports of CDI in non-hospitalized patients have also occurred with increased frequency (CDC, 2005). In 2005, 33 cases of CDI from a population that was thought to be at low risk for CDI were reported and included 10 peripartum women. During pregnancy increased susceptibility to CDI has not been considered historically, but four cases of peripartum CDI have recently been reported (Garey et al., 2008).

Case report

A 39-year-old woman (gravida 2/para 0) at 29 weeks and 4 days of gestation was admitted to our hospital because she had been suffering from a large volume of watery diarrhoea (>14 bowel movements per day) for 2 weeks, which was accompanied by a 2 kg weight loss and dehydration. The diarrhoea was associated with red blood and mucus. The patient suffered from non-complicated haemorrhoids. She complained of acute periumbilical pain, but she did not suffer from nausea and emesis. She had received at home therapy with loperamide for 7 days without symptom resolution.

Vital signs on admission included a temperature of 36.4 °C, blood pressure of 115/60 mmHg and a pulse rate of 94 beats per minute; she had leukocytosis (1.444 × 10⁶ white blood cells mm⁻³). Coproculture was immediately performed.

Ultrasound examination of the fetus showed biometric parameters corresponding to gestational age; the amniotic fluid index appeared normal. Monitoring of the fetal heart rate showed it to be regular.

The patient’s serology did not show a defect of immunoglobulins (1230 mg IgG dl⁻¹, 247 mg IgA dl⁻¹, 145 mg IgM dl⁻¹), she did not have a prior history of hospitalization in the last 2 years and she did not use antibiotics until 3 months prior to the development of the symptomatology. The patient was immediately treated with 500 mg metronidazole intravenously three times daily and 40 mg deltacortene (prednisone) daily for 2 weeks ex adjuvantibus (i.e. before having the faecal culture results).

A faecal culture, cytotoxicity assay and Triage C. difficile panel assay were all performed within 48 h of the arrival of the samples, which were kept at 4 °C. The Triage immunosassay (Bioite Diagnostics) for detecting both a specific antigen of C. difficile (glutamate dehydrogenase)
and toxin A gave a positive result. Treatment with 125 mg vancomycin, orally, four times daily was immediately started. The diagnosis of *C. difficile*-associated disease was confirmed by the presence of the pseudomembranes observed during colonoscopy (Fig. 1). The abdomen ultrasound showed the presence of pelvic fluid and the magnetic resonance imaging evidenced a pancolitis with dilated and thickened loops (4–6 cm) and pneumatosis, suggesting the development of toxic megacolon complicating a severe infection of *C. difficile*.

After 3 weeks the patient had a significant decrease in diarrhoea, but was febrile (＞38 °C); blood cultures showed a *Candida albicans* septicaemia, probably due to the antibiotic therapy and prolonged hospitalization. Therefore, in the 32nd week of gestation, a female infant in cephalic presentation was delivered by Caesarean section, with a birth weight of 2175 g and Apgar scores of 8 at 1 min and 9 at 5 min. She was taken to the Neonatal Intensive Care Unit, while the mother was transferred to the Intensive Care Unit because of respiratory insufficiency. Computed tomography scans evidenced bilateral pleural effusion, which was immediately treated with thoracentesis.

After a few days, the patient was transferred to the Department of Infective Disease (Ospedale cà Foncello) and discharged 3 weeks later without the need for gastrointestinal surgery. Further cultures for *C. difficile* gave negative results. The patient was free of symptoms at a follow-up evaluation 6 months later; the baby was growing well.

**Discussion**

*C. difficile* is the most common cause of infectious diarrhoea in hospitalized patients. Mutations that confer antibiotic resistance, increase toxin production or facilitate sporulation have substantially worsened the prevalence and virulence of this opportunistic pathogen (McDonald *et al.*, 2005). Historically, both peripartum *C. difficile*-associated disease and the disease during pregnancy has been considered an unusual occurrence, and, when present, has generally been a mild disease. However, in 2005, a report (CDC, 2005) raised concern about a possible increase in both the frequency and severity of CDI in pregnant women, including severe complications such as those resulting in Intensive Care Unit admission, toxic megacolon, colectomy, death and fetal loss.

Although it hasn’t been determined whether peripartum disease is increasing in frequency, or is definitively associated with higher morbidity and mortality, there is recent evidence that *C. difficile*-associated disease severity and frequency may be increasing not only in high-risk populations (hospitalized, immunocompromised or elderly patients) but also among younger and healthier patients from the community (CDC, 2005).

The pathophysiology of the infection in pregnancy remains poorly understood (Rouphael *et al.*, 2008). Although antibody production is generally increased during pregnancy, this production may not be specific or protective in severe CDI cases.

The recent changes in the epidemiology of CDI may indicate a need for a change in treatment approach. Oral vancomycin is the only USA Food and Drug Administration-approved medication for the treatment of CDI and can be used in pregnancy; however, its high cost and the emergence of vancomycin resistance in other organisms, particularly enterococci, have made metronidazole the first line drug for treating the disease (HICPAC, 1995), even if there is a low level of resistance to this therapy in *C. difficile* (Baines *et al.*, 2008).

New therapeutic modalities are now available, including new antimicrobials, toxin-binding products, and active and passive immunization (Aslam *et al.*, 2005). For example, intravenous immunoglobulin has been used to treat patients with severe, refractory infections who did not show a response to standard therapy. Their role in severe *C. difficile*-associated disease and their safety in pregnancy are still unclear.

**Fig. 1.** Colonoscopy images showing the presence of pseudomembranes.
Most importantly, the optimal management of the infection in pregnant women must include a low threshold for testing, early recognition, and close monitoring for signs and symptoms of deterioration, such as an increase in abdominal tenderness and distension, elevation of leukocyte counts over 20 000 or a rising creatinine level (Pépin et al., 2004). Furthermore, it is essential to involve consultants such as infectious disease specialists, gastroenterologists and general surgeons. A subtotal colectomy can be life-saving in severe cases; indications for gastrointestinal surgery include dilated (>10 cm) intestinal loops, peritonitis, perforation and persistent sepsis with a leukocytosis of more than $2.0 \times 10^4$ white blood cells mm$^{-3}$ (Gourevitch & Hawkey, 2009).

Ultimately, it is likely that a broadly based approach of responsible antibiotic use, infection control measures and the application of new non-antibiotic agents targeting obstetric patients will be needed to turn the tide against this antibiotic-induced endemic disease.

References


