CASE REPORT

Emphysematous cystitis due to recurrent *Clostridium difficile* infectionMichel E van Genderen,¹ Jeroen G J Jonkman,² Michiel van Rijn,³ Adriaan Dees¹¹Department of Internal Medicine, Ikazia Hospital, Rotterdam, The Netherlands²Department of Radiology, Ikazia Hospital, Rotterdam, The Netherlands³Department of Microbiology, Ikazia Hospital, Rotterdam, The Netherlands

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SUMMARY

A 78-year-old woman with long-standing obstipation presented herself to the hospital with diarrhoea and progressive abdominal cramping since 2 days. Acute abdomen developed and an emergency exploratory laparotomy was indicated, which showed no signs of bowel ischaemia. After admission to the internal ward, stool *Clostridium difficile* PCR was tested positive. Hence the diagnosis of pseudomembranous colitis became apparent. Abdominal imaging demonstrated multiple gas foci in the wall of the bladder and extensive pseudomembranous colitis. The patient was initially treated with oral vancomycin and secondarily with metronidazole for recurrent *C. difficile* infection. Resolution of diarrhoea and abdominal cramping was noted on 6-week follow-up visit.

BACKGROUND

Emphysematous cystitis (EC), characterised by air within the bladder wall, is a rare diagnosis. The underlying disease is usually caused by anaerobic bacteria. Prompt diagnosis and treatment are warranted to prevent the potential mortality of this infectious condition. Owing to increased use of radiological imaging, emphysematous conditions are more often diagnosed. Previous reports have described the association of *Clostridium difficile* infection to pneumatosis intestinalis. We present a patient with recurrent *C. difficile* infection that provoked pseudomembranous colitis-associated EC.

CASE PRESENTATION

A 78-year-old woman was transferred from her nursing home to the outpatient clinic. She was admitted because of progressive abdominal cramping and diarrhoea for past 2 days. She had a history of long-standing obstipation and non-insulin-dependent diabetes. An open cholecystectomy had been performed in the past. She was recovering from a stroke, 2 months before. Owing to the vascular incident, she had difficulty comprehending our questions and explaining her illness.

Vital signs on admission showed a blood pressure of 137/92 mm Hg, a heart rate of 120 bpm and an afebrile temperature. Physical examination revealed a diffuse abdominal tenderness throughout the left side and a mild flank pain. Laboratory findings showed marginal increased inflammatory markers with a C reactive protein of 28 mg/L, erythrocyte sedimentation rate of 12 mm/h, and a white cell count of $22.1 \times 10^9/L$. There were no signs of liver or kidney failure. Direct examination of urine was negative for urinary tract infection.

At the internal ward she deteriorated and bowel sounds, which had been normal on the day of admission became absent. An 'acute abdomen' developed and intestinal ischaemia was suspected. An emergency laparotomy showed no signs of ischaemia. Postoperatively, she was admitted to the intensive care unit (ICU). The following days, abundant diarrhoea persisted. An abdominal CT scan and a total colonoscopy were performed.

INVESTIGATIONS

The abdominal CT scan demonstrated extensive wall thickening of the transverse colon suspected for colitis; there was also the presence of gas in the peritoneum and multiple gas-filled cysts within the wall of the bladder (figure 1). A colonoscopy revealed multiple irregular ulcerations covered with pathognomonic fibrinous pseudomembranes and mucosal oedema in the descending colon, sigmoid and rectum (figure 2). The colonic biopsy revealed signs of non-specific mild inflammation on which ischaemia could not be ruled out. By then, the results of the initial stool cultures had become available. The cultures did not show bacterial pathogens like *Salmonella* or *Yersinia* spp. However, the initial stool PCR tested positive for *C. difficile*.

TREATMENT

Treatment with oral vancomycin at 125 mg four times daily was started. Thereafter, her respiratory and haemodynamic parameters rapidly improved and the patient could be transferred back to the ward after a 2-day ICU stay. The following week she further recovered with a reduced frequency of

Figure 1 Abdominal CT scan showing emphysematous cystitis.

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Figure 2 Endoscopy showing pseudomembranous colitis.

defaecation and a marked improvement in the abdominal comfort. Shortly after completing her vancomycin course, diarrhoea recurred up to 6–10 times daily. Oral metronidazole 500 mg three times daily for a total of 6 weeks was prescribed, with a quick resolution of diarrhoea. Three subsequent *C. difficile* toxin stool PCR tests yielded negative results.

OUTCOME AND FOLLOW-UP

The patient improved slowly and could be discharged in a stable condition, 8 weeks after admission. She was seen for follow-up 6 weeks after discharge in the outpatient clinic. She further recovered during her stay in her nursing home with adequate intake of food and fluids and without recurrence of diarrhoea. We did not perform any follow-up abdominal imaging as she remained asymptomatic.

DISCUSSION

In recent years, *C. difficile* has emerged as a leading cause of gastroenteritis hospitalisations and death. An American study between 1999 and 2007 has shown that 70% of all-cause gastroenteritis deaths are associated with *C. difficile* infection.^{1 2} A 2.5-fold increase in 30-day mortality, which is even higher for patients of 65 years and older, has been reported.³ The clinical spectrum of *C. difficile*-associated disease ranges from watery diarrhoea to a more severe presentation with pseudomembranous colitis, multiorgan failure and even death.⁴

Previous reports have described *C. difficile*-related pneumatosis intestinalis, for example, the finding of gas cysts within the intestine wall. To the best of our knowledge *C. difficile*-associated EC, as demonstrated here, is only sparsely reported in literature.

Several gas-forming infections will be able to manifest as cystitis, pyelitis or pyelonephritis. Bladder pneumatosis or EC is a rare complication.⁵ It was first reported at the end of the 19th century and was further defined by Bailey in 1961.⁶ Because the diagnosis of EC is diagnosed radiologically, the incidence of reported cases has been increasing since the past years due to the increased use of plain abdominopelvic imaging.^{7 8}

Although the exact mechanism of gas formation in emphysematous conditions is still poorly understood, several theories have been proposed for the pathogenesis of EC. One of the most accepted hypotheses is that mixed acid fermentation of glucose by Enterobacteriaceae is the major pathway of gas formation. The majority of reported cases of EC are in patients with diabetes.⁵ The fermentation of high glucose concentration in the urine and tissues will probably act as a favourable substrate for organisms to produce gas (CO₂ and H₂). The most prevalent

pathogens are *Escherichia coli* and *Klebsiella pneumonia*, which account for approximately 80% of cases. As to *C. difficile* infection in particular, butyric acid fermentation might be the underlying process of gas formation.^{8 9} In patients without diabetes it has been hypothesised that urinary albumin might act as the substrate for gas production.¹⁰ This theory resembles explanations made with respect to the pathophysiology of pneumatosis intestinalis.^{11 12} In our patient, pseudomembranous colitis could have led to EC by disruption of the mucosal barrier with pseudomembranes and local ischaemia. In this way, pneumatosis intestinalis as well as EC should be regarded as a complication of an underlying disease detected on radiographic imaging, rather than being a disease per se.^{5 12}

In accordance with the pathophysiological considerations, diabetes mellitus and urinary tract infections are among the most predisposing risk factors to develop EC. Patients with diabetes in particular, might present themselves with a wide spectrum of infectious disease, ranging from asymptomatic urinary tract infections, to a scenario of rapidly developing peritonitis and septic shock.⁸ With respect to *C. difficile*, 'silent' infections can present with abdominal pain and distension, in the absence of appreciable diarrhoea.¹³ In retrospect, our patient presented herself with similar atypical 'silent' symptoms. In these cases, diagnosis often will be difficult. The time for culturing *C. difficile* requires 48–72 h to complete and stool evaluation sensitivities ranges from 67% to 92%. Because our patient developed signs of peritonitis, we instantly performed a laparotomy to rule out bowel ischaemia.¹⁴ It has been shown that emergency surgery may reduce mortality in patients with fulminant colitis in case of inflammatory bowel disease or ischaemia, only when a colectomy is performed.^{15 16} In such high-risk patients, early identification and early surgical intervention, the sooner the better, is warranted.^{17 18}

As for the treatment of *C. difficile* infection, metronidazole and vancomycin are widely used. The risk factors for the development of recurrent *C. difficile* infection include persistent disruption of the colonic flora, advanced age, long hospitalisations and administration of non-*C. difficile* antimicrobial therapy. The risk of recurrence after a single episode is high, with 8–50% of patients having at least a recurrent episode after treatment. Paradoxically, these antibiotics may themselves interfere with the re-establishment of the normal colonic flora, contributing to higher odds to develop a recurrent episode.^{13 19}

In conclusion, *C. difficile* infection might be associated with the occurrence of EC. Suspicion should be maintained in patients with diabetes and in those who are at risk for urinary tract infections, in particular. The underlying illness should be recognised and treated early to prevent complications and unnecessary treatment based on the radiographic finding of EC.

Learning points

- ▶ Emphysematous cystitis or bladder pneumatosis can be associated with recurrent *Clostridium difficile* infection.
- ▶ Presence of emphysematous cystitis is a sign, not a disease per se. It should be interpreted in relation to the patient's overall clinical condition rather than a sign.
- ▶ Treatment of emphysematous cystitis is best directed at the underlying disease process, in this case appropriate antibiotic treatment of *C. difficile*, respectively, metronidazole or vancomycin therapy.

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Competing interests None.

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