The role of surgery in pseudomembranous enterocolitis

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Pseudomembranous enterocolitis (PMEC) was first described by Dr Finny in 1893, but it was not until 1978 that Clostridium difficile and its toxins were isolated and identified as the cause. C difficile is a Gram-positive, spore-bearing anaerobic bacillus, which may be present as a part of normal bacterial flora in the gut. The disease spectrum of C difficile infection may range from antibiotic-associated diarrhoea, and antibiotic-associated colitis, to its most severe form, PMEC. The incidence of C difficile infection has increased six-fold in England and Wales in the past five years.

Aetiopathogenesis

C difficile overgrowth due to alteration of bacterial gut flora and subsequent release of exotoxins induces the characteristic inflammatory changes of PMEC. Prior antibiotic exposure is the single important risk factor in the causation of PMEC. All commonly used antibiotics, including ampicillin, amoxicillin, tetracycline and cephalosporins, have been implicated in its pathogenesis. Other predisposing factors are mentioned in box 1. The two important exotoxins released by C difficile are toxin A (enterotoxin) and toxin B (cytotoxin), which induce the inflammatory process by their enteropathogenic and cytopathic effects, respectively.

Pathology

PMEC usually involves the colon in its entire length, although it can involve only a portion. Occasionally it may extend to the small bowel, hence the term enterocolitis. The characteristic macroscopic features are the presence of multiple green to yellowish plaques on the mucosal surface (figure 1). The size of the plaque may vary from a few millimetres to a confluent patch. Each plaque represents a pseudomembrane which, on microscopy, shows the presence of mucous inflammatory cells and fibrin exudate covering an area of necrosis (figure 2). This process of inflammation has been described as fibrinoid necrosis. The underlying crypts may become dilated and disrupted in late stages (figure 2B).

Important complications and differential diagnoses of PMEC are depicted in boxes 2 and 3, respectively.

Clinical features

PMEC commonly presents with moderate to profuse diarrhoea, abdominal pain and tenderness, pyrexia, and tachycardia. Passage of blood in the stools is infrequent, but may occur in fulminant cases. If the disease is
Pseudomembranous enterocolitis

localised to the caecum and the ascending colon, it may present with features of acute appendicitis, leading to an unnecessary laparotomy. Boxes 4, 5 and 6 contain summaries of three pertinent case reports.

### Case report 1

A 72-year-old woman presented with acute onset of abdominal pain with features of peritonitis. She had had a seven-day course of amoxycillin to treat chest infection in the two weeks preceding admission. Investigations revealed a markedly raised white cell count of $69.8 \times 10^9/L$ with severe dilatation of the colon on plain abdominal X-ray. At surgery the colon was dilated and oedematous throughout with multiple areas of impending perforation. She underwent a subtotal colectomy with an ileostomy. Histology revealed extensive pseudomembranous colitis with an incidental Dukes' A adenocarcinoma in the right colon. She made an uneventful recovery.

### Case report 2

A 66-year-old woman underwent an elective open cholecystectomy uneventfully and had 24-h peri-operative antibiotic cover in the form of iv cefuroxime. She developed abdominal pain with distension associated with diarrhoea on the fourth postoperative day. Stool samples were positive for *C difficile* toxin. Proctosigmoidoscopy showed features consistent with PMEC. A trial of conservative treatment including parenteral metronidazole failed and she became toxic with signs of peritonitis. Consecutive plain abdominal X-rays revealed progressive dilatation of the transverse and the descending colon. At emergency laparotomy, she was found to have a severe pancolitis and underwent a subtotal colectomy with an ileostomy. Postoperatively she developed signs of systemic sepsis and required intensive therapy unit admission for 10 days. She made a slow recovery and was subsequently discharged.

### Case report 3

A 67-year-old woman presented with a three-day history of increasing abdominal pain and fever. Abdominal examination showed signs of peritonitis with marked tenderness in the left lower quadrant. At laparotomy, the sigmoid colon was dilated and dusky with multiple black spots on the serosal surface. She underwent sigmoid colectomy with an end colostomy. Histology showed features of ischaemic colitis along with typical pseudomembranous plaques on the mucosal surface. The patient had an uneventful postoperative period and remained well in the follow-up period of six months.

### Diagnosis

The mainstay of diagnosis is the isolation of *C difficile* and detection of exotoxins in the stool sample. Stool examinations have been shown to be culture positive for *C difficile* in 95% and toxin-positive in 97–100% of cases. The detection of toxin B (cytotoxin) in stools has been regarded as the single standard technique in the diagnosis of this condition. Proctosigmoidoscopy will show typical pseudomembranes and may be normal in patients with localised disease. Blood investigations usually reveal marked leucocytosis with neutrophilia. Plain X-ray of the abdomen may show colonic dilatation, with or without loss of hastrations (figure 3). A barium enema should be avoided in emergency cases as it can precipitate toxic megacolon. Computed tomography may show colonic dilation and diffuse thickening of the colonic wall with a doughnut-like appearance. These changes are not specific for PMEC, but can play an important role in recognising this condition.

### Management

The initial management of PMEC primarily consists of isolation of the patient, cessation of the precipitating antibiotics, and correction of fluid and electrolyte imbalance. Nearly 15% of patients respond to this approach. Specific therapy is indicated in the remaining 85% of cases. Vancomycin (oral 125 mg 6
**Figure 3 (A)** Plain abdominal X-ray showing the dilated transverse colon. **(B)** Plain abdominal X-ray in a case of severe PMEC showing dilated small and large bowel.

![Figure 3 (A) Plain abdominal X-ray showing the dilated transverse colon. (B) Plain abdominal X-ray in a case of severe PMEC showing dilated small and large bowel.](image)

**Learning points**
- a careful history with a high index of suspicion, marked leucocytosis, and dilatation of the colon on plain abdominal film will give important clues to the diagnosis of PMEC
- PMEC can present as an acute abdomen
- stool examination and proctosigmoidoscopy should be performed routinely in all patients who develop abdominal pain with diarrhoea in the postoperative period
- subtotal colectomy with an ileostomy is the operation of choice in patients with pancolitis

**Box 7**

hourly or slow intravenous (iv) infusion 500 mg 6 hourly or metronidazole (oral 400 mg 8 hourly or iv 500 mg 8 hourly) are the two specific drugs used in this disorder. The response rate for vancomycin is 88–100% and for metronidazole 77–100%. The relapse rate ranges from 5–24% and is similar in both regimens. In the relapse cases, a pulsed therapy with the same drugs and/or administration of *Lactobacillus GG* have been shown to be effective. In others with defective antibody response to *C difficile* toxins, iv gamma globulin may be useful in producing clinical remission.

The control of spread of infection is equally important, as nosocomial outbreaks may occur. All standard infection control measures must be taken and sometimes this may require closure of wards or even hospitals.

Surgery comes into play in patients with complications and patients who are refractory and/or continue to deteriorate despite the aggressive conservative treatment. A few patients with megacolon may respond to aggressive medical therapy, but in 65–71% surgery is required. The surgical procedure must aim to remove the septic focus and therefore usually involves subtotal colectomy. If the disease is localised, segmental resection may suffice, as documented in one of our cases. A few cases in which PMEC has been successfully treated by diversion procedures, such as ileostomy, caecostomy, and colostomy, have been described in the literature. Preferably, however, such procedures should be avoided as they have been associated with a bad prognosis due to ongoing sepsis. The operative mortality for colectomy is 24% and for diversion procedures 66%. Two of our patients had a subtotal colectomy and the other had a sigmoid colectomy. We speculate that, in the third case, the localised ischaemia of the sigmoid colon predisposed to PMEC, leaving the rest of the colon unaffected. All did well following a resectional surgery.

Medical Anniversary

FRIEDRICH WEGENER, 7 April 1907

Friedrich Wegener (1907–1990) was born in Varel, Oldenburg, Germany. His father was a doctor and his mother a Swedish gymnastic director. With this athletic background and a fine physique, he became, in 1931, German hammer-throwing champion. He graduated MD (1932) in Kiel with a thesis entitled Testicular tumours. He became a pathologist in Kiel, then Breslau, and finally Professor in Lubeck. He described three patients with his syndrome to the German Pathological Society (1936) and during his lifetime saw 12 cases of Wegener’s granulomatosis but never used that eponym. He had seven children and 17 grandchildren when he died on 9 July 1990.

Wegener’s granulomatosis involves nasopharynx, lungs, eyes and kidneys. It was universally fatal until the advent of corticosteroids, cyclophosphamide, and antibiotics. Wegener lived to see two remarkable advances in his disorder. Firstly, the introduction of a most helpful diagnostic blood test; anti-neutrophil cytoplasmic autoantibodies are identified in serum of patients by immunofluorescence microscopy using alcohol-fixed normal human neutrophils. He also derived considerable joy from the second advance, namely treatment. When he first described the condition in 1936 it was associated with 100% mortality. In the succeeding 50 years, he witnessed the introduction of corticosteroids, cyclophosphamide, and antibiotics, all of which have combined to reduce the mortality to 5–10%. He was delighted that earlier diagnosis by a non-invasive procedure led to much earlier treatment and thus a substantial improvement in prognosis. — DG James
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