Pseudomembranous colitis associated with changes in an ileal conduit

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SUMMARY A case of antibiotic associated pseudomembranous colitis following total cystectomy is reported, in which there was involvement of the ileal conduit. The small bowel remaining in situ was uninvolved. Bacteriological studies revealed Clostridium difficile and the toxin in both colon and ileal conduit. Relevant publications concerning pathogenesis are discussed, in relation to the unusual site described in this case. Epidemiological evidence is reviewed which suggests that isolation of patients with pseudomembranous colitis is a logical course of action.

Pseudomembranous colitis is now firmly associated with Clostridium difficile and toxin production. Reported cases often complicate antibiotic therapy particularly ampicillin, and involvement of the colon is the predominant effect, with uncommon and atypical changes in the ileum. We describe a case in which pseudomembranous colitis occurred in a patient following total cystectomy for carcinoma of the bladder. The typical colonic lesions are described along with identical lesions within the isolated ileal loop. The ileum in situ proximal to the ileocaecal valve was uninvolved.

Case report

A 70-year-old man underwent a total cystectomy in November 1982 for a transitional cell carcinoma of the bladder. He also had ischaemic heart disease and chronic obstructive airways disease. Prior to this the tumour which had been diagnosed in 1979 had been irradiated in 1980. Initially the lesion appeared to have been controlled but by early 1982 recurrence was detected. Recurrent infections, pain on micturition and intractable bleeding necessitated a cystectomy. During the months prior to cystectomy several courses of antibiotics including cephradine metronidazole and ampicillin, were given for repeated urinary tract infections. Five days after the cystectomy in addition to postoperative metronidazole and neomycin, a course of ampicillin (500 mg six-hourly for 11 days) was given because of patchy consolidation of the right middle lobe. Twenty-one days after the cystectomy he complained of nausea and abdominal pain together with vomiting. On examination his abdomen was distended and tense with hyperactive bowel sounds.

Intravenous feeding was instituted until bowel movements which were loose commenced seven days later. He was allowed home but had to be admitted after eight days because of recurrent diarrhoea, abdominal pain and weight loss. His wife commented that the ileal loop had been offensive for a few days prior to his readmission. He was treated symptomatically for five days with no improvement. Sigmoidoscopy at this stage revealed the classical plaques of pseudomembranous colitis. Despite treatment by vancomycin the patient died the next day, 44 days after his cystectomy and 16 days after the onset of his diarrhoea.

Necropsy

The body was that of an elderly man with evidence of considerable recent weight loss. There was severe chronic bronchitis and emphysema. The large bowel revealed the irregular raised yellowish-white plaques set against a hyperaemic mucosa characteristic of pseudomembranous colitis throughout its length (Fig. 1). This change terminated abruptly at the ileocaecal valve. Identical macroscopic features were present on the mucosa of the ileal conduit (Figs. 2 and 3). The ureters were intact and drained into the conduit. Postmortem samples from the rectum, colon and ileal conduit were taken immediately to the bacteriology laboratory. Isolation of Cl. difficile was by both a selective medium (Oxoid Cl. difficile agar base plus 7% defibrinated horse blood and Oxoid antibiotic supplement) and the use of alcohol, at a final concentration of 50%, to select
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The colonic mucosa shows aggregates of yellowish-white plaques set against a hyperaemic mucosa throughout its length.

Discussion

The weight of evidence both from experimental and clinical sources indicates that antibiotic-associated pseudomembranous colitis is of an infective aetiology reviewed by Ashley Price. Cl difficile is the organism identified in a number of these cases and the production of a toxin is important in producing experimental lesions. However, Cl difficile is a pathogen only rarely found in the intestine of healthy adults. Evidence is emerging that in order for the organism to produce pseudomembranous colitis the bowel must be in a susceptible state. Fekety et al found that cultures of Cl difficile which had been washed free of toxin had no effect on the intestine of normal hamsters; in contrast to the development of caecitis when instilled into animals which had previously been given antibiotics. Pierce et al found a predilection to develop pseudomembranous colitis in patients who had been subjected to diagnostic or therapeutic gastrointestinal procedures, and related this to possible bowel stasis. Thus it appears that in order to contract pseudomembranous colitis a patient must have a susceptible intestine and come into contact with the organism. Credence is given to this concept since animals survive when kept in sterile or non-contaminated conditions after vancomycin treatment or clindamycin administration, but contract pseudomembranous colitis if a contaminated animal is introduced. Environmental factors are relevant clinically. Miller and Jick pointed out clustering of cases and this has been subsequently substantiated all adding to the concept of an infective lesion. Burdon et al report the introduction of the disease into a ward with the transfer of a patient with pseudomembranous colitis. Recently Malamou-Ladas et al examined the en-
Fig. 3 Mucosal plaques against a hyperaemic background in the ileal conduit.

Fig. 4 A fibrin cap infiltrated by polymorphs overlying dilated colonic mucosal glands characteristic of pseudomembranous colitis. The adjacent mucosa is autolysed but mildly inflamed. Haematoxylin and eosin × 35.

Fig. 5 Changes identical with pseudomembranous colitis are seen in the small intestinal mucosa of the ileal conduit. Haematoxylin and eosin × 35.

vironment of hospital wards and isolated the organism in significant numbers from items subject to faecal contamination. Their work substantiates the work of Kim et al. who were able to culture the organism not only from inanimate objects but from the hands and stools of asymptomatic hospital per-
sonnel. Household pets may act as a reservoir, and this may be increased by antibiotic therapy.\textsuperscript{13}

Whilst ampicillin was the antibiotic used in our case Bartlett\textsuperscript{14} reports pseudomembranous colitis associated with a wide range of antimicrobial agents and points out that nearly any antibiotic may be responsible. Cases of pseudomembranous colitis associated with antibiotics usually affect the large bowel only and stop abruptly at the ileocecal valve. This was the situation in the case reported, the terminal ileum showed no evidence of plaques. The only part of the small intestine involved in our case was the segment isolated as the ileal conduit draining the ureters. The pattern of involvement was identical to that seen in the colon and contrasted with the less discrete circumferential pattern seen when pseudomembranous colitis traverses the ileocecal valve. The local conditions in the ileal loop must have rendered the mucosa more susceptible than that in the remainder of the small intestine. The cause of the increased susceptibility remains something of an enigma. An endogenous bowel metabolite such as bile acids\textsuperscript{15} would appear untenable in this case since the loop had been totally isolated from the bowel for some six weeks. The physicochemical milieu of the intestinal mucosa is considerably modified in a loop. This may play an important role in increasing adherence and penetration of organisms as suggested by Smith\textsuperscript{16} thus allowing the clostridium to colonise the conduit in contrast to the in situ small intestine.

The presence of microthrombi in the lesions suggests the possibility of a local Swartzman reaction. This has been investigated by Behan and Mills\textsuperscript{17} who demonstrated reduced serum complement concentrations in patients with pseudomembranous colitis and make the analogy to endotoxic shock. The numbers of cases are small and the complement profiles are not strictly comparable. The concentrations quoted could equally be interpreted as a consequence of pseudomembranous colitis rather than the cause. The evidence for a local Swartzman reaction in pseudomembranous colitis remains equivocal.

The indications are that pseudomembranous colitis is an infective disease. Potential sources of infection include not only inanimate objects subject to faecal contamination, but the hands of hospital personnel in contact with affected patients and objects contaminated by them. Organisms can survive on a floor for up to five months\textsuperscript{12} and isolation of such patients would appear to be logical.

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References


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