PSEUDOMEMBRANOUS COLITIS: LOCAL EXPERIENCE WITH 3 CASES

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SUMMARY

Three cases of pseudomembranous colitis seen over the past one year in the Medical Unit, University Hospital, Kuala Lumpur, are reported.

The historical background, spectrum of clinical presentation, diagnosis and treatment of the disease are discussed. Early and wider use of sigmoidoscopy in patients with predisposing factors to pseudomembranous colitis have resulted in increased diagnosis of the condition.

INTRODUCTION

Pseudomembranous colitis (PMC) is a severe diarrhoeal disease associated in most instances with the use of antibiotics. It is not surprising that with the greater use of antibiotics, its incidence has increased throughout the world.

However, it has been infrequently reported in local literature.[1]

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We report three cases of pseudomembranous colitis seen in the Medical Unit, University Hospital, Kuala Lumpur, over the past one year (1986). In all three patients, the diagnosis was made by sigmoidoscopy and confirmed by biopsy of the rectal or colonic mucosa.

CASE HISTORY

Case 1

A 79-year-old Chinese female underwent laparotomy for removal of an ovarian tumour. Besides being moribund from the effects of widespread tumour, she was in heart failure.

Pre- and post-operatively, she was not prescribed any antibiotics.

A week following the operation, she developed profuse watery diarrhoea up to 15 times a day; the stools contained mucus but no blood.

She was generally unwell, complained of fairly severe abdominal cramps and had a low grade fever. Physical examination was unremarkable except for diffused, mild tenderness over the abdomen.

A sigmoidoscopic examination was done, which showed multiple discrete white plaques in the rectum and sigmoid colon. Biopsy of the rectal mucosa confirmed the diagnosis of pseudomembranous colitis; it showed surface epithelial ulcera-

tion and a volcano-like eruption composed of mucus, polymorphs, fibrin and sloughed mucosal epithelial cells. Some of the mucosal glands were disrupted and distended with mucus. In the lamina propria there was acute inflammatory cellular infiltration.

Stool cultures for enteric pathogens were negative. Culture for *Clostridium difficile* as well as assay for *C. difficile* toxin were not available.

The patient was treated with oral metronidazole 400 mg t.i.d., with little improvement in her symptoms after two days of treatment.

In view of her terminal illness, the family requested for discharge and she has not been seen subsequently.

Case 2

A 47-year-old Chinese female was admitted because of diarrhoea for two weeks. She had been seen at the onset of her illness in another hospital where a stool culture grew *Salmonella* spp. She was treated with a course of cotrimoxazole with little improvement in her symptoms.

She had been diagnosed to have systemic lupus erythematosus more than eight years ago and has been treated for renal complications of the disease with steroids.

Her diarrhoea, as with the first patient, was profuse with bowel movements up to 10 times a day and consisting mainly of fluid stools and mucus. She complained of mild abdominal cramps.

She was obviously unwell, pale and sallow, and mildly dehydrated. Examination of the abdomen was unremarkable.

Sigmoidoscopy revealed typical pseudomembranes; discrete creamy-white plaques in the rectum. Biopsies of the mucosa showed well defined groups of mucus-distended glands with superficial portions disrupted, associated with overlying superficial ulceration. Clouds of pseudomembrane composed of mucus, polymorphs and necrotic epithelial cells were present (Fig. 1). These lesions were separated by mucosa with near normal glands except for some mucus loss as well as some acute inflammatory cellular infiltration in the lamina propria.

Stool cultures were negative for enteric pathogens. As before, assay for *C. difficile* toxin and culture for *C. difficile* were unavailable.

All antibiotics were stopped and the patient was treated with metronidazole 400 mg t.i.d.; her diarrhoea improved and she made an uneventful recovery.

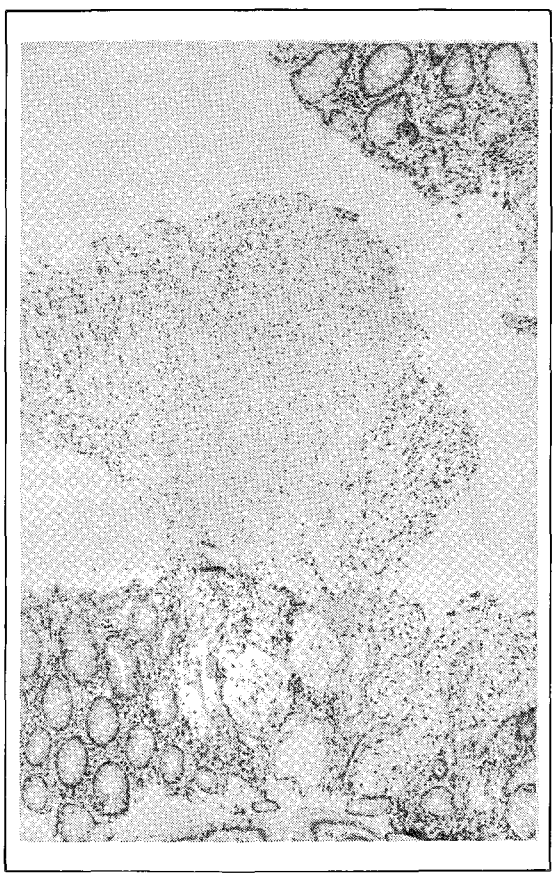

Fig. 1 Superficial ulceration of mucosa with formation of mushroom-like pseudomembrane. The intestinal glands are disrupted and distended with mucus and polymorphs. H & E x 100.

Case 3

A 64-year-old Malay male developed severe diarrhoea while being treated for pneumonia and chronic obstructive lung disease in a private hospital. He had been started on several antibiotics including metronidazole, netilmycin and ceftazidime at the onset of his illness. These drugs were however discontinued a week later when he developed profuse diarrhoea of up to 15 times a day. Stools were noted to be fluid and containing mucus but not blood. He did not complain of any abdominal pain.

On admission to University Hospital, Kuala Lumpur, he appeared ill; he was tachypnoeic, mildly cyanosed and dehydrated. Examination of the chest revealed features of emphysema and a collapsed left lung. Abdominal examination was unremarkable but a flexible sigmoidoscopic examination revealed multiple pseudomembranes in the rectum and sigmoid colon (Fig. 2). Biopsy of the mucosa revealed superficial epithelial ulcerations, distended mucosal glands and infiltration of the lamina propria with polymorphs, plasma cells and macrophages. Fibrinous exudate with desloughed epithelial and inflammatory cells forming a "summit" lesion typical of PMC was also noted. Stool cultures for enteric pathogens were negative.

He was started on oral vancomycin 250 mg q.i.d. with dramatic improvement in the diarrhoea within a day of treatment. However, his general condition deteriorated over the next one week; he developed respiratory failure and septicemia and died shortly after that.

DISCUSSION

Although pseudomembranous colitis (PMC) was first described by Finner[2] in 1893, current interest in the disease probably started in the 1970s when the frequent use of clindamycin and lincomycin led to a dramatic increase in the reported incidence of the disease. The condition has subsequently been described following the use of other antibiotics including the penicillins, sulphonamides, tetracyclines and cephalosporins,[2] either as a single agent or in combination. Nevertheless, cases

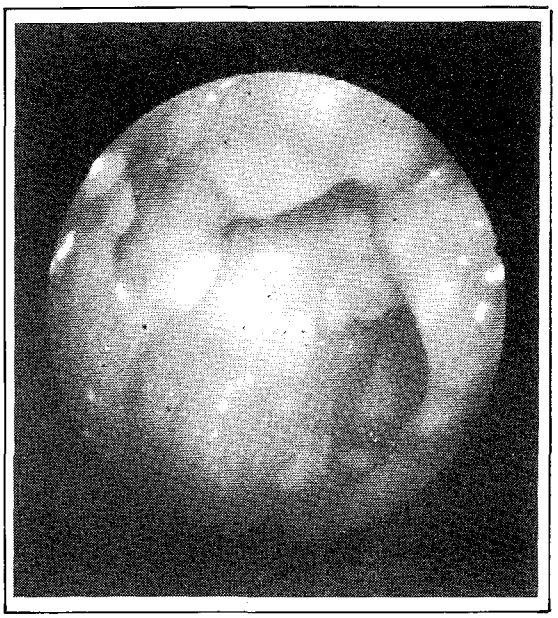

Fig. 2 White mucosal plaques or pseudomembranes as seen during sigmoidoscopy.

occurring without the use of antibiotics have been reported[3] as with our first patient. PMC has also been reported to follow surgery especially abdominal and pelvic surgery, burns and serious medical illness like heart failure or leukaemia.

In 1977, Larson[4] isolated a toxin with unusual cytopathic effect in tissue culture in a patient with PMC. The toxin has subsequently been shown to be produced by *C. difficile* and isolation of the toxin or culture of *C. difficile* from faeces has been found to be virtually present in all cases. With the greater use of assay of *C. difficile* toxin and/or culture of *C. difficile,* a wider spectrum of diseases associated with the use of antibiotics have been identified. This ranges from diarrhoea with normal endoscopic and histological appearance to non-specific colitis and to the full-blown picture of PMC.

Diarrhoea is found in nearly all patients but its severity may vary greatly. In fact, some patients do not detect a change in bowel habits until the implicated drug has been discontinued. The onset of diarrhoea is noted during the course of anti-

biotic treatment in one-half to two-thirds of patients. In the remainder, it may appear as late as four to six weeks following discontinuation of antibiotic treatment.[2] Nothing is distinctive about the diarrhoea which is watery with mucus but seldom bloody. Other signs and symptoms include abdominal pain and tenderness, and a low grade fever. Abdominal pain is usually mild but may occasionally be severe and acute. Serious complications include severe dehydration, electrolyte imbalance, hypotension, hypoalbuminemia with anasarca, toxic megacolon, and colonic perforation. Extraintestinal symptoms are extremely rare.[2]

The diagnosis of PMC can often be made by sigmoidoscopic findings of pseudomembranes. Histopathological examination reveals that the pseudomembrane is composed of fibrin and polymorphs. There are also associated varying degrees of changes in the mucosa, ranging from focal epithelial necrosis with polymorphonuclear leukocytes infiltration, distension and disruption of the intestinal glands to complete structural necrosis of the mucosa. While PMC involves the sigmoid colon in most cases, this segment may be spared while typical changes may be found in the more proximal colon. Small bowel involvement is known but seldom detected.[2] *C. difficile* toxin assay and culture of *C. difficile* have been helpful in further confirming the diagnosis. The former is positive in 95% and the latter in 90% of patients with confirmed PMC.[5]

Management of PMC includes discontinuing the offending antibiotic(s) as well as adequate fluid and electrolyte replacement. Vancomycin has been shown to be an extremely effective antibiotic in the treatment of PMC and is considered as the antibiotic of choice.[6] Oral vancomycin is minimally absorbed and adequate therapeutic faecal levels are readily achieved. It is prescribed at a dose of 125 – 250 mg q.i.d. for five days. Its greatest drawback however is its cost[7] which has led to the use of alternative antibiotics like metronidazole, bacitracin and tetracycline. Metronidazole is much less expensive, easily available in oral form and achieves rapid symptomatic and clinical improvement. However, it is interesting to note that PMC has developed following the use of metronidazole singly or in combination with other antibiotics as with our second patient.[8]

Ion exchange resins like cholestyramine or colestipol have been used in the treatment of PMC but their usefulness has been limited. On the other hand, antidiarrhoeal drugs like loperamide and codeine should be avoided as they may prolong symptoms and predispose to toxic megcolon.

Surgical intervention is rarely required nowadays with the use of effective antibiotic therapy. Severely ill patients with fulminating colitis may need a colectomy or a diverting ileostomy. If ileus is present and precludes the use of oral medication, local instillation therapy may be invaluable.[2]

CONCLUSION

While not all the answers are available, PMC is nowadays accepted as a well-established clinical and pathological entity. With increased awareness of its occurrence and wider use of endoscopic examination, as well as culture of *C. difficule* and identification of its toxin, it is hoped that more cases of PMC will be recognized in this country.

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