PSEUDOMEMBRANOUS ENTEROCOLITIS — A COMPLICATION OF MULTIPLE ANTIBIOTIC THERAPY

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SYNOPSIS

A 29 year old woman developed fatal aplastic anaemia and pseudomembranous enterocolitis following multiple antibiotic therapy for an elective ovariectomy for a benign ovarian cyst.

INTRODUCTION

Pseudomembranous enterocolitis (PME) is an uncommon condition, but is becoming increasingly recognised since its association with the use of clindamycin and lincomycin was described in the early 1970s. It occurs at any age but most frequently afflicts middle-aged and elderly patients. It may arise after major surgery or during chronic debilitating illness. Besides clindamycin and lincomycin, an association has been noted with other antibiotics such as ampicillin, tetracyclin, penicillin and co-trimoxazole. It is especially common with multiple antibiotic therapy after abdominal surgery.

The clinical spectrum of the disease varies from a mild diarrhoeal illness to a fulminant enterocolitis with fever, dehydration and shock. Symptoms usually develop after a few days to a few weeks of treatment but may even appear a week or more after the antibiotics have been stopped. Diarrhoea is usually prominent; stools are watery and may be accompanied by mucus and blood. Occasionally this enterocolitis may present as an acute abdomen with or without signs of a pelvic abscess or free fluid in the abdomen. There is often leucocytosis. Diagnosis is difficult and often it is made only at necropsy. However, the possibility of PME should be considered in patients developing diarrhoea after being given antibiotics or following surgery. Repeated sigmoidoscopic examinations may have to be performed in order to detect the characteristic pseudomembrane which should be biopsied. The histological appearances are diagnostic. With increasing awareness of this condition more cases are diagnosed during life; the apparent incidence will, of course, depend on the degree of awareness on the part of clinicians and pathologists. However, there may be other factors determining the precise incidence in a given locality.

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As the condition has not been reported in this country we wish to describe this case, and briefly review the condition.

CASE REPORT

A 29 year old Chinese housewife had an elective left ovariectomy for a benign ovarian cyst. Penicillin and streptomycin were given after the operation but since she developed a skin rash after 3 days, doxycycline was used, followed by a course of co-trimoxazole for another week. One week after the operation a haematoma in the left rectus sheath was noted. Haemoglobin level was then 6.4 gm/100 ml and total white cell count 6,300/ul. Blood transfusion was given and sutures were removed, (No pre-operative blood count was available). Eleven days later the haemoglobin level was 7.4 gm/100 ml and total white cell count 3,400/ul. Haematinics were given.

Five weeks after the operation she had epistaxis, haemoptysis, vaginal bleeding and haematuria. This was followed by fresh blood admixed with mucus, alternating with melaena, per rectum. She was given more antibiotics and, as she did not improve, she was transferred to the University Hospital.

On admission she was pale. She had widespread bruises and petechiae on the palate and the legs. The blood pressure was 120/80 mmHg. There was no bone tenderness or lymphadenopathy. The abdomen was soft, bowel sounds were normal and there was no hepatosplenomegaly. There was, however, shifting dullness, suggesting free fluid in the abdomen. Rectal examination confirmed the malaenic stools, and vaginal examination revealed bleeding through the os. Other systems were normal.

Blood counts repeatedly showed depression of all cell elements, but no primitive cells were seen. Reticulocyte count was 0.2%. Bleeding and clotting times were prolonged but there was no evidence of intravascular coagulation. Marrow showed hypoplasia of all elements. Despite repeated blood and platelet transfusion, generalised bleeding continued. Her condition deteriorated and she died 8 days after admission, 56 days after the abdominal surgery.

AUTOPSY FINDINGS

Permission for autopsy was limited to the chest and abdomen. The left and right pleural cavities contained some blood-stained fluid. There was no evidence of infection in the lungs. The heart was normal, but there was 150 ml of straw-coloured fluid in the pericardial sac.

Almost 2000 ml of blood-stained fluid was present in the peritoneal cavity. Extensive fibrinous adhesions were present, especially between adjacent loops of large bowel and the abdominal wall, and in relation to the spleen, posterior and lateral to which there were 200 ml of clotted blood.

The kidneys were congested, and there were clots in the renal pelves. Microscopically the submucosa of the pelves showed marked haemorrhage and the parenchyma was congested and contained mild haemorrhages. The right ovary and tube and the uterus were normal. The site of removal of the left ovary was identified.

Approximately 150 ml of 'coffee grounds' material was present in the stomach, the mucosa of which showed acute haemorrhagic erosions. There was no fresh or altered blood in the duodenum or jejunum, but from approximately the level of the ileum, through the entire length of the large bowel, there was brown-to-black altered blood (malaena). The outer surface of the wall of the large intestine was intensely congested, and the inner surface showed focally haemorrhagic pseudomembranous enterocolitis, with yellow pseudomembranes (up to 5 mm diameter). The congested areas were of similar dimensions and often raised from the surface, i.e. projecting into the lumen, many with pseudomembranes on their surfaces (Fig. 1).

Histologic examination showed established pseudomembranous enterocolitis, with all three characteristic lesions, ranging from early 'summit' lesions, through groups of disrupted and necrotic glands, to complete, though focal, mucosal necrosis (Fig. 2). In addition, there was extensive intramural haemorrhage; especially within the submucosa, with no thrombosis, a reflection of the pancytopenia.

The small intestine was essentially normal.

The bone marrow was hypoplastic, with a diminution in mature forms of all three elements, and a relative increase in inmature cells and plasma cells.

No other significant abnormalities were found during the autopsy. A heavy growth of E. coli was obtained from a swab of a colonic pseudomembrane, but no other organism was isolated.

DISCUSSION

While the exact pathogenesis is not clear, recently Clostridium difficile has been isolated from patients with PME. We were, however, unable to isolate this organism from our patient.

In this patient, although there was no diarrhoea, the presence of mucus in the stool and bleeding per rectum, as well as free fluid in the abdomen, could have prompted the diagnosis. The aplastic anaemia, however, precluded a leucocytosis.

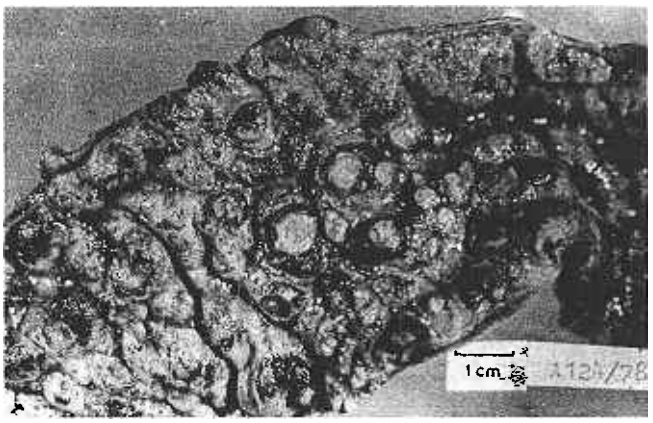

Figure 1
Mucosal surface of large intestine
This shows pseudomembranous enterocolitis, with pseudomembranes and related intense congestion and haemorrhage.

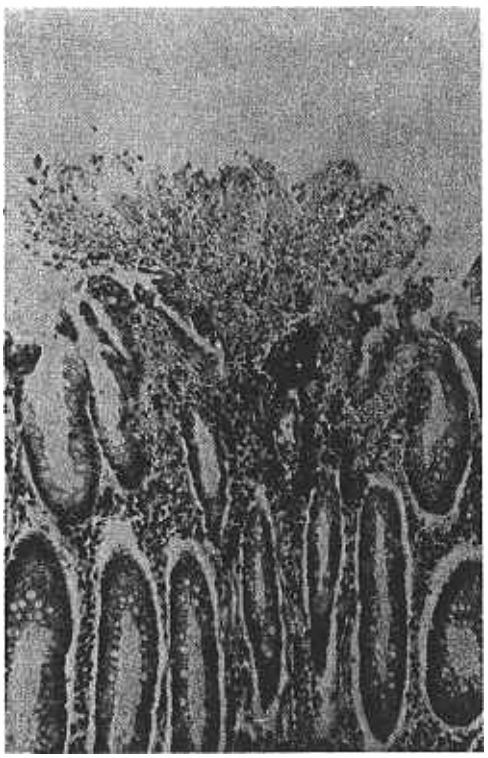

Figure 2
Photomicrograph of large intestine.
(Haematoxylin and eosin, X 300)
This shows a characteristic established lesion of pesudomembranous enterocolitis, with a group of disrupted and necrotic glands surrounded by normal mucosa.

Although the aplastic anaemia was immediately responsible for her death, it must be noted that PME itself is associated with a mortality rate of up to 20-45%.

The PME in this patient is likely to have developed post-operatively as a result of multiple antibiotic therapy. The aplastic anaemia is also likely to have developed after the operation, for the surgeon would surely have recognised the anaemia and bleeding tendency pre-operatively. This case illustrates why antibiotics should not be exhibited unnecessarily, and that elective operations do not normally need prophylactic antibiotics, unless contaminated by gut contents or septic material.

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