Fatal intestinal amoebiasis

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Summary

The clinical presentations of amoebic colitis are diverse. Amoebiasis is comparatively rare in the U.K. and, unless the clinician is aware of the condition, wrong diagnosis often leads to delay in appropriate treatment resulting in high mortality. Diagnosis rests on clinical suspicion, stool examination, sigmoidoscopy with rectal biopsy and serological tests. Amoebiasis is readily treatable and death from it should be very rare.

Introduction

Although amoebiasis is more common in tropical and subtropical climates, it is a universal disease and has been reported from places as remote as Alaska. About 3 deaths from amoebiasis and probably about 200 new cases of clinical amoebiasis occur annually in England and Wales (Stamm, 1975).

Amoebiasis is an infestation of human tissues by the pathogenic unicellular *Entamoeba histolytica* which exists in 2 forms—the cystic (sporozoite) and vegetative (trophozoite). Man is the main reservoir of infection. Infection is acquired by swallowing the cysts (passed in the stools of patients or of asymptomatic carriers) in food, contaminated by faecally soiled fingers or by the use of human faeces as fertilizer on soil.

The amoebae, in vegetative forms, normally thrive only in the large bowel. They may be harmless and ingest bacteria and other particles of faecal matter. As they travel along the colon, and as the faeces become more and more solid, the amoebae encyst and are excreted as the mature infective cyst. Although often amoebae in the colonic lumen are harmless, owing to some ill-understood factors they may invade the gut wall. Immune-suppression due to any cause, and other bowel infections favour this invasion. Amoebae invade the tissues by secreting lytic enzymes. This lytic activity of the amoeba is the cause of its penetration and necrotizing activity in the tissues. From the colonic wall, it sometimes invades other tissues, such as the liver, by the flow of blood.

When amoebae invade mucosal and submucosal tissues of the colon, they form typical flask-shaped ulcers. In rare instances, they invade muscle layers and further outward invasion of tissues results in

perforation of the gut. This invasion of tissues depends on the virulence of the amoeba and the host-resistance. Various precipitating causes for perforation have been mentioned, e.g. parturition, external trauma, surgery, etc. (DeSa, 1974).

Material

This article presents 3 cases of fulminating amoebic colitis which were treated in the Dartford group of hospitals. Patient no. 1 was treated in 1977 and patients nos 2 and 3, which were treated in 1970, were collected from the medical records.

Case histories

Patient no. 1

A 50-year-old white male patient, who had recently returned from Nigeria after a business trip of 2-3 months, was admitted with abdominal pain of 2 weeks' duration. He had had pyrexia for the past 10 days, which he had attributed to influenza. The pain had become severe over the past 2 days and was mainly located in the right hypochondrium. During those 2 weeks he had developed anorexia and had lost 9.5 kg in weight. He also gave a history of constipation followed by watery diarrhoea with a large amount of slime, but no blood, for 3 days (10-12 bowel actions/day). He did not suffer from indigestion or fat intolerance and he consumed 2-3 pints of beer every day.

Examination revealed: a heavily built, slightly obese man in severe pain. He was hot and flushed and toxic; temperature 38.5°C; pulse 120/min, regular; BP 100/50 mmHg; abdomen distended with tenderness and rigidity in the right upper quadrant of the abdomen; bowel sounds present; per rectal—tenderness present.

A provisional diagnosis of acute cholecystitis was made. Investigations revealed: Hb 13 g/dl, WBC $17 \times 10^9/l$, serum electrolytes—sodium 124 mmol/l, chlorides 88 mmol/l, potassium 4.5 mmol/l, bicarbonate 23 mmol/l, urea 10 mmol/l, amylase 60 Somogyi units.

Chest X-ray—consolidation of right lower lobe, raised right dome of diaphragm. X-ray of abdomen—no gas under diaphragm, fluid levels present.

He was kept under observation with nil by mouth;

nasogastric aspirations; intravenous fluids; analgesics (60 mg/4–6 hr i.m. pentazocine) and antibiotics (i.m. ampicillin with cloxacillin 500 mg/6 hr).

On day 2, his condition remained the same, but he was sweating profusely and was cold and clammy. Temperature 37°C; pulse 100/min; BP 140/99 mmHg; abdomen was slightly distended; blood film for malarial parasites was negative; a blood sample was sent for amoebic CFT. As he still had offensive diarrhoea, stools were sent for examination. They were reported later as negative for pathogens.

On day 3, he still had profuse intermittent sweating, although he was afebrile. Of interest was an area of skin over the right upper quadrant of the abdomen, which was cold compared to the rest of the abdomen; the cold area disappeared in 2 hr. He continued to have offensive diarrhoea. Repeat blood examination gave similar findings as on the 1st day, indicating leucocytosis. In the night his condition deteriorated and he became delirious. He had hiccoughs, tachycardia (pulse 120/min) and was sweating profusely. The abdomen was distended, but bowel sounds were present. A large paracolic abscess was suspected and gentamicin 80 mg thrice/day was added to the ampicillin and cloxacillin injection.

On day 4, he continued to have offensive diarrhoea, was afebrile, and the tongue was clean; pulse 90/min regular; there was good urinary output in the previous 24 hr. He still complained of pain and tenderness in the right side of the abdomen, and there was some guarding in the right iliac fossa (RIF). Repeat X-ray of the abdomen showed a few distended loops of the small gut with a few fluid levels. At 8.00 p.m. about 100 ml of 'coffee-ground' fluid was aspirated via the nasogastric tube; this was positive for blood.

A laparotomy in the night revealed fulminating colitis, with abscesses along the right paracolic gutter and near the splenic flexure and on both sides under the diaphragm. The colon from the caecum to the pelvic colon appeared oedematous, pale, white and friable. A sub-total colectomy with terminal ileostomy was carried out. The colon from the caecum to the upper part of the rectum was removed and the upper end of the rectum was brought out through the lower part of the incision as proctostomy (mucous fistula). The patient had a cardiac arrest and died 45 min after completion of the operation.

The histopathology of the excised colon showed extensive necrosis and perforation of the caecum, most of the caecal wall being converted into a grey slough. There were extensive ulcerations extending throughout the colon. In the splenic flexure, there was an annular slough similar to that in the caecum (Fig. 1). The ulcers showed numerous motile amoebae (trophozoites).

The post-mortem examination revealed a huge amoebic abscess in the right lobe of the liver which had perforated posteriorly under the diaphragm. The fluorescent amoebic antibody test was positive (titre 1:256). Immunofluorescent staining of smears from the colonic ulcer revealed trophozoites of *E. histolytica*.

Patient no. 2

A 63-year-old white male patient, had been diagnosed as a case of ulcerative colitis for the past 9 years and had been treated at various times with prednisolone enemas, prednisolone and salazopyrine tablets with resulting remissions. He was admitted with swelling of the ankles of 2 weeks' duration and diarrhoea, occasionally blood-stained but without mucus, of 4 days' duration. He gave a history of dysentery while in Ceylon in 1944. His general condition was good. Abdominal examination showed slight generalized discomfort, no tenderness.

Investigations revealed: Hb 10.4 g/dl; WBC $9.0 \times 10^9/l$; ESR 34 mm/hr; serum electrolytes—sodium 135 mmol/l; chlorides 106 mmol/l; potassium 3.7 mmol/l; urea 5 mmol/l. Liver function tests—normal. Faeces—no pathogens. Sigmoidoscopy—ulcerations in rectum and lower sigmoid colon. Barium enema—extensive involvement of the colon with obliteration of the normal mucosal pattern.

A procto-colectomy was carried out after a few days, as his symptoms were not improving. His condition deteriorated and he died 2 days after surgery.

The histopathology of the colon showed chronic active ulcerating colitis with a few burrowing ulcers under the submucosa. In some ulcers amoebae were seen. Sections stained by the fluorescent antibody technique were positive for amoebae.

Patient no. 3

A 44-year-old white female with rheumatoid arthritis was admitted with diarrhoea of 5 days' duration, haematemesis for one day, and abdominal pain for 2–3 days.

She had had 'influenza' 4 months before and had subsequently developed nausea, anorexia, and indigestion. Abdominal pain was mainly on the right side; and more severe after food. She had lost 12.7 kg in weight during the past 3 months. Her bowels were basically regular, though loose. Menstruation was regular. She had been taking indomethacin for the past 2 weeks for her arthritic pain. She suffered from fat intolerance. No jaundice in the past. She had never been abroad.

Examination revealed: she was alert and orientated, but dehydrated; pulse 120/min, regular; BP 150/90 mmHg; temperature 38.4°C. Abdominal examination revealed slight fullness and tenderness

FIG. 1. Internal appearance of subtotal colectomy specimen from patient no. 1.

with resonant percussion in the right lower quadrant. No palpable mass. Rectal examination, nothing significant.

Investigations revealed: Hb 12 g/dl; WBC $20.0 \times 10^9/l$; ESR 40 mm in 50 min. Serum electrolytes—sodium 137 mmol/l; chlorides 90 mmol/l; potassium 3.6 mmol/l; bicarbonate 27 mmol/l; urea 15 mmol/l. Faecal occult blood, positive; cholecystogram was normal.

In 2 days her Hb dropped to 10.4 g/dl. She continued to have diarrhoea and lower abdominal distension with tenderness and some guarding in the RIF. Malignancy in the lower abdomen arising either from the colon or the right ovary was suspected and a laparotomy was carried out on the 7th day of admission.

She had a large faecal abscess with a faecal fistula in the RIF which was strongly suspected to be due to carcinoma of the caecum. Stomach, colon and caecum were adherent to each other. The colonic wall was very friable and gangrenous. No attempt was made to explore further. The faecal fistula of the caecum was closed and a colostomy was performed.

Postoperatively her condition gradually deteriorated and she died on the 7th day.

The post-mortem examination showed gangrenous ulceration and perforation of the caecum, ulcerations in ascending and transverse colon. There was no neoplasm. The histology showed numerous amoebae in the colonic wall.

Discussion

The clinical presentation of amoebic colitis is vague and hence the condition is likely to be mistaken for other common abdominal ailments. This is more likely to happen in areas where amoebiasis is rare. If the diagnosis is missed, the condition may lead to high mortality rates. On the other hand, treated in time, it is a curable disease and death from it should be very rare.

These three cases represent a few of the protean clinical manifestations of amoebiasis. They highlight the following features:

1. All 3 patients were diagnosed only after death.
2. Amoebiasis mimics acute cholecystitis, ulcerative colitis, lower intra-abdominal malignancy.

3. An initial influenza-like illness, followed by anorexia and marked loss of weight (patients 1 and 3).
4. Amoebiasis in a patient who has never been abroad (no. 3).
5. Acute amoebic colitis with amoebic liver abscess (no. 1).

In amoebiasis, involvement of the liver usually takes place via the blood stream and by the time it manifests as a clinical entity, amoebic colitis is settled. Few cases of hepatic amoebiasis have concurrent amoebic dysentery. (Sepulveda *et al.*, 1959). Patient no. 1, however, seems to be an exception. Amoebiasis was so fulminating and, probably, the host resistance was so poor, that involvement of the colon and the liver occurred concurrently. The liver abscess found at post-mortem was not detected at the time of operation.

Patients 1 and 3 are examples of acute fulminating necrotizing amoebic colitis which is a rare condition. It is more frequent in adults than in children and is often associated with malnutrition and/or other ailments (Montanez *et al.*, 1967). The clinical picture is vague and hence confusing. Usually it is wrongly diagnosed pre-operatively as fulminating ulcerative colitis or perforated appendix with peritonitis (Chen, Chen and Lin, 1971; Judy, 1974; Kenoyer *et al.*, 1976; Mendonca, Vieta and Korditz, 1977; Solowiejczyk *et al.*, 1973). Unless early anti-amoebic treatment is commenced and appropriate surgery undertaken, the mortality is very high.

Diagnosis of amoebiasis is difficult. Several authors stress the difficulties in differential diagnosis due to similar clinical, sigmoidoscopic and radiological findings (Judy, 1974; Tucker, Webster and Kilpatrick, 1975). Similarity in the clinical features of ulcerative colitis and amoebiasis is remarkable and every case of ulcerative colitis must be serologically tested for amoebiasis before undertaking any surgery or starting steroids in order to avoid the disastrous effects of steroids in amoebiasis.

Diagnosis of amoebic colitis is confirmed by stool examination, sigmoidoscopy and rectal biopsy, and serological tests.

The routine stool examination may or may not reveal cysts and trophozoites, but fresh stool or rectal discharge obtained by sigmoidoscopy may demonstrate trophozoites, which are diagnostic (Pittman, El-Hashimi and Pittman, 1973; Tucker *et al.*, 1975).

Sigmoidoscopy may show typical undermined ulcers in the rectum and lower sigmoid. The mucosa between the ulcers appears normal. A rectal biopsy gives positive results in about 82% cases, even in the absence of ulcerated areas or clinical exacerbations of the disease (Doxiades and Yiotsas, 1965; Juniper, Steele and Chester, 1958; McAllister, 1962).

The serological tests—the indirect haemagglutination test (IHA) is sensitive and specific after the amoebic infection is well established (Knight *et al.*, 1973). An IHA titre of 1 : 128 or more is considered diagnostic but may indicate past rather than present infection and the incidence of false positive results is low (Kagan 1970; Pittman *et al.*, 1973; Tucker *et al.*, 1975). Precipitin reactions such as the gel diffusion test or the cellulose acetate precipitin (CAP) test are rarely positive except in the presence of active disease (Stamm and Phillips, 1977).

Surgical complications develop in 3% of patients who have amoebic dysentery (Stein and Bank, 1970). The incidence of perforation and peritonitis complicating amoebiasis was reported as less than 0.5% by Grigsby (1969) and 6% by Chen *et al.* (1971). Perforation and peritonitis are responsible for 10–30% of deaths attributed to amoebiasis (Barker, 1958; Clark, 1925; Kean, Gilmore and Van Stone, 1956). Although the incidence of perforation and peritonitis is reasonably low, the mortality is high. Barker (1958) reported a 75% mortality rate in adults and 100% mortality rate in children. In the series reported by Chen *et al.* (1971) 7 of the 8 patients died.

Two types of peritonitis occur in amoebic colitis (Wilmot, 1962). In the first type, the patient is ill with severe amoebic dysentery, and generalized peritonitis develops insidiously. The signs of peritonitis are not prominent; therefore, it is difficult to determine the exact time of perforation. In the second type, there are no active symptoms of dysentery at the time of perforation. Acute abdominal pain, tenderness, guarding and rigidity with paralytic ileus develop later.

Fulminating amoebic colitis needs early surgical intervention, in addition to anti-amoebic drugs and intensive supportive treatment. In the past, surgical intervention was shown to be extremely hazardous and this view was widely accepted (Wilmot, 1962; Judy, 1974). However, Chen *et al.* (1971) have demonstrated that surgery lowers the high mortality of 80–100% in this disease. Similarly, Gupta and Sharma (1975) advise simple surgical procedures, in stages, if necessary, for better prognosis. They feel that there is no need for total colectomy and hence only limited resection should be done, as amoebic colitis is a reversible condition and the colon can be used subsequently for restoring bowel continuity.

When a perforative peritonitis due to amoebiasis is diagnosed, immediate anti-amoebic treatment and prompt surgery will give better results. The aim of surgery is to drain the contaminated peritoneal cavity along with the diversion of the faecal stream. It is wiser to treat perforated colonic disease with generalized peritonitis by surgery, supported by

specific medical treatment, but this should be conservative, e.g. exteriorization of a single perforation, local excision of diseased colon with proximal defunctioning colostomy with drainage of the peritoneal cavity. In a few cases, when the diagnosis is either late or not arrived at pre-operatively (as in patient 1) the whole colon is found at laparotomy to be so extensively necrotic that total colectomy seems the only satisfactory procedure. The outcome in such cases, however, is likely to be fatal owing to toxæmia. With the help of early definitive diagnosis by modern serological tests and prompt and effective newer anti-amoebic drugs, it is hoped that the number of cases undergoing total colectomy will be reduced.

Conclusion

Amoebic colitis is a readily treatable, often benign condition. Clinically it presents in various disguises and in every abdominal, hepatic or lower thoracic condition with vague clinical features, it must be excluded by serological and other tests. Wrong diagnosis and delay in the treatment often leads to fulminating disease with a very high mortality. It is increasingly accepted that simple surgical procedures can help to reduce this mortality. With increasing awareness of the condition, along with the early diagnosis by modern serological tests and prompt treatment with effective anti-amoebic drugs, death from amoebic colitis should be very rare.

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