Amoebiasis and giardiasis

Stephen Wright

Amoebiasis

Aetiology

Entamoeba histolytica is a micro-aerophilic protozoan parasite. The motile trophozoite is found in the large intestine in humans. Trophozoites encyst and these cysts, excreted in faeces, are the means of transmission by the faeco-oral route. It was recognized that many individuals appeared to excrete the quadrinucleate, 7.5–15 μm diameter cysts of *E. histolytica* but exhibited no features of tissue invasion, and that many fewer individuals have invasive amoebic disease, dysentery or liver abscess. In 1937, Emile Brumpt suggested that there were two distinct species producing identical cysts – *E. histolytica*, associated with invasion, and *E. dispar*, a harmless commensal. This notion was rejected. In the 1970s, Peter Sargeaunt examined amoebae from asymptomatic cyst-excreters with negative amoebic serology and amoebae from patients with invasive disease, and showed that invasive strains were associated with one group of isoenzyme patterns and non-invasive strains had a consistently different pattern. Other differences were shown.

- Invasive amoebae could be cultured alone *in vitro*, whereas non-invasive strains always required co-cultivation with bacteria.
- Invasive strains were resistant to complement-induced lysis.
- A surface lectin with galactose n-acetyl galactosamine carbohydrate determinants mediated adhesion in invasive amoebae.

Tannich was able to distinguish invasive strains by DNA hybridization, and, later, ribosomal RNA sequence data showed sufficient differences to merit separate species status for *E. histolytica* and *E. dispar*, as Brumpt had suggested.

Epidemiology and transmission

Amoebiasis is mainly a disease of the tropics and subtropics, where sanitation is commonly inadequate, though cases have occurred in individuals who have never been outside the UK. It affects adults more often than children, and males more than females in the case of amoebic liver abscess. True *E. histolytica* cysts are excreted by 2–4% of asymptomatic individuals and are the source of infection in others by contamination of the environment, food and water. Cysts in water are destroyed by boiling and removed by filtration, but are not killed by ordinary levels of chlorination; cysts in food are killed by thorough cooking. It is unknown whether *E. histolytica* is transmitted by long-term asymptomatic cyst-excreters or by those who excrete cysts for a short period of time. The infectious dose of cysts is also unknown.

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Pathogenesis and pathology

Bowel: excystation occurs in the intestine and trophozoites invade the large bowel. Lectin-mediated cell adhesion is the first step in the pathogenesis. Mucin from the gut may protect against this process by binding to the lectin, but amoebae ingest mucus, reducing its protective efficacy. Colonic bacteria have glucosidases, which may alter mucus to increase susceptibility. Amoebae move between cells and kill them by inserting a large, permanent ion channel (amoebapore) into the host cell membrane. Individual amoebapore units polymerize to form the channel. The three amoebapores exhibit 25–30% sequence homology with the perforin molecule of natural killer cells and cytotoxic T cells. Within amoebae, these proteins kill bacteria phagocytosed as nutrient sources. It is unknown how the amoebae avoid destroying themselves with amoebapore. Parasite cysteine proteinases disrupt host cell adhesion, aiding invasion and movement through tissue.

Humoral and cellular responses are demonstrable in invasive disease and *in vitro*, but the extent to which they signify protection is questionable. Effective host responses might be protective in the small proportion of individuals who are asymptomatic excreters of *E. histolytica*. It is currently unknown what would be seen at colonoscopy in these cyst-excreters. Necrosis is the hallmark of invasive amoebiasis, producing flask-shaped, undermined ulcers with amoebae in the base and advancing margins.

Amoebic liver abscess: amoebae enter blood vessels and spread haematogenously via the portal vein, reaching the liver and producing an abscess by the cytotoxic effect described above; this begins focally when a single or perhaps a group of amoebae gain access to the liver and reproduce asexually. As the number of amoebae increases, the necrotic focus expands irregularly outwards. Lysed liver cells, RBCs and serum produce amoebic pus, but neutrophils are absent despite peripheral blood neutrophil leucocytosis. These neutrophils may undergo contact-mediated lysis with amoebae in the advancing edge of the abscess. Embolization of amoebae to several foci produces multiple abscesses. Metastasis from the liver to cause brain abscess can occur.

Clinical features

Dysentery: Figure 1 describes the typical history in intestinal amoebiasis, which does not begin with a febrile illness and acute watery diarrhoea. The extent of colonic involvement can vary; the greater the extent, the more severe the clinical manifestations. Patients with greater mucosal ulceration suffer more significant bleeding and protein loss into the gut lumen, and bacteraemia may contribute to systemic upset.

The typical appearance is of discrete ulcers with slough in the base and surrounding erythema scattered over an otherwise normal mucosa, but there is a range of appearances, and diffusely inflamed, bleeding mucosa may be seen. Symptoms and signs are listed in Figure 2. Toxic dilatation, perforation and haemorrhage are complications of severe amoebiasis; occasionally, a length of mucosa may be sloughed off and passed per rectum – an illustration of the extent to which amoebae undermine the surface mucosa. Strictures can occur during the course of amoebic dysentery, and cutaneous amoebiasis can develop in the perianal and perineal areas and on the genitalia.

Examination of faecal smears shows motile trophozoites. These are also seen in material scraped from inflamed or ulcerated

Case history

Mr K had been travelling in South East Asia for 3 months. About 6 weeks into his journey, he noted a change in bowel habit, with stools of variable consistency, and observed flecks of bloodstained mucus on the outside of the stools. There was no pain or systemic upset. Physical examination of the abdomen and rectal examination were normal. On sigmoidoscopy, scattered haemorrhagic areas were seen on the tops of mucosal folds. A scraping of these areas, mounted on a slide covered with saline and a cover slip, showed motile trophozoites with ingested RBCs. An amoebic indirect fluorescent antibody test was negative.

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mucosa on endoscopy and mounted in saline for direct microscopy. Biopsies (Figure 3) show amoebae in sections stained with H and E or periodic acid-Schiff. With increasing extent of colonic involvement, albumin levels decline and C-reactive protein (CRP) increases. Amoebic serology is positive in two-thirds of cases; therefore, negative serology does not exclude intestinal amoebiasis. Barium studies show ulcerated mucosa.

Amoeboma is a late colonic complication of previous amoebic dysentery. The clinical finding is a tender mass lesion that is usually single, often in the caecum, but occasionally multiple. The differential diagnoses are appendix abscess, carcinoma, tuberculosis and pericolic abscess. Amoebae may be difficult to find in the lesion on colonoscopy. Histology shows granulation tissue. Amoebic serology is always positive.

Amoebic liver abscess: symptoms and signs relate to the site and size of the abscess. Patients with a small abscess may exhibit only fever, anorexia and night sweats. With increasing abscess size, pain is a constant feature. Occasionally, multiple abscesses are seen, causing fever, chills and rigors with hepatic pain. Sometimes, fever

Clinical features of amoebic dysentery

• Duration	‹ 4 weeks 85%, › 4 weeks 15%
• Diarrhoea	100%
• Dysentery	99%
• Abdominal pain	85%
• Low back pain	66%
• Previous dysentery	33%
• Fever	38%
• Abdominal tenderness	83%
Localized	42%
Generalized	41%
• Distension	5%
• Dehydration	3%

Source: Adams E B, McCleod I N. *Medicine (Baltimore)* 1977; **56:** 315–23.

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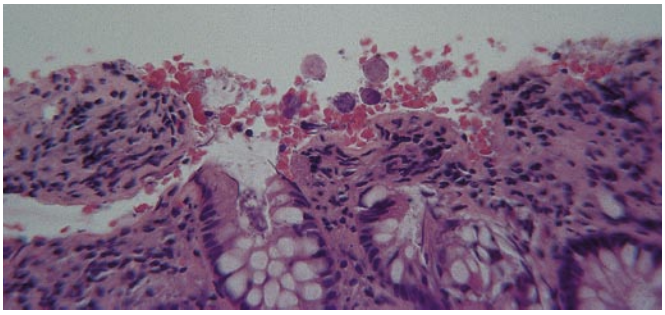

3 Amoebiasis. This colonic biopsy shows ulceration, with trophozoites of *Entamoeba histolytica* on the surface and invading the mucosa.

and night sweats are absent and the presentation resembles that of malignant disease affecting the liver. Pain may be continuous, or may be pleuritic when the abscess is close to the chest wall or referred to the right shoulder region when it is beneath the hemidiaphragm. Jaundice is uncommon.

When examining the patient, it is important to explore the intercostal spaces with a fingertip to seek point tenderness, which indicates that the abscess is close to the skin at this site. The right lobe is the most common site, but multiple abscesses affecting right and left lobes are also seen. Left lobe abscess is the least common. Involvement of the liver beneath the diaphragm leads to signs at the right lung base, including collapse, collapse–consolidation and pleural effusion. The abscess can rupture into the pleural space or lung, in which case amoebic pus is coughed up. Rarely, there is haematogenous spread to the brain. Differential diagnoses are listed in Figure 4.

Investigations

Amoebic serology is positive in 99% of patients with amoebic liver abscess. Tests in the first week of illness may be negative, but are positive if repeated 1 week later. Amoebic cysts are often not present in stools.

Imaging of the liver is important; ultrasonography is the most convenient and readily available technique. A single cavitating area extending irregularly into surrounding liver tissue is seen, often with areas of solid liver tissue within it; occasionally, multiple abscesses are seen.

Neutrophil leucocytosis is seen with mild anaemia. Low albumin, raised CRP, ESR and alkaline phosphatase, more modest elevation of transaminases and, rarely, raised bilirubin are found. Blood cultures are sterile. If the abscess is aspirated, the pus may exhibit the anchovy sauce colour described in textbooks, but it can be cream or yellow; it does not have a foul smell, which would suggest anaerobic bacterial sepsis, and pus cells are not seen. Gram-staining is negative, and amoebae are found only in material aspirated from the very edge of the cavity.

Management

Drug treatment of amoebiasis is shown in Figure 5. Individuals excreting *E. dispar* cysts do not require treatment with diloxanide furoate, provided it is confirmed that the cysts are not those of *E. histolytica*. Tests to differentiate the two are available in some laboratories; when these are not routinely available or strains are not typable, the author's preference is to administer diloxanide furoate. This drug is well tolerated, though flatulence is a common