Amoebiasis: A Neglected Diagnosis

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Those doctors whose diagnostic acumen is based on the adage 'Common things commonly occur' can happily dismiss amoebiasis as unlikely to upset the statistics of their diagnostic accuracy. However, they will be directly responsible for the considerable morbidity, mutilation or even death of the occasional patient. Amoebiasis is a very treatable disease; from the patient's point of view a better diagnostic adage is 'Consider the treatable diseases first', and on this basis amoebiasis should be high on the list of differential diagnoses for any abdominal or hepatic complaint.

The purpose of this article is to draw attention to the importance of considering amoebiasis in the differential diagnosis of gastrointestinal and hepatic conditions, and to advise that amoebic serology should be done on all patients in whom a diagnosis of ulcerative colitis or Crohn's disease has been made or who have abdominal or hepatic symptoms for which no cause has been found.

PREVALENCE OF AMOEBIASIS IN THE UNITED KINGDOM

For various reasons it is not possible to make an accurate assessment of the prevalence of amoebiasis in the United Kingdom: it is not a notifiable infection; even expert faecal protozoologists will find only about 50 per cent of the true number of positives if they examine three consecutive stools from each patient; all too often the diagnosis is not even considered and the patient learns to live with an unstable bowel habit after his doctor has given him the label of 'functional diarrhoea' or 'irritable colon'; in an analysis of 30 deaths in England and Wales certified as caused by amoebiasis during the period 1963-73 it was found that 12 were diagnosed only at necropsy (Stamm, 1975).

Parasitological surveys have shown that about 3 to 5 per cent of the population of the United Kingdom are asymptomatic carriers of Entamoeba histolytica (Morton et al., 1951). A 10 per cent sample hospital inquiry in England and Wales made by the statistical section of the DHSS showed an annual discharge from hospitals of about 200 patients with a diagnosis of amoebiasis (personal communication).

That the figures for deaths from amoebiasis and discharges from hospital with a diagnosis of amoebiasis must be a considerable underestimate of the true position is shown by the high proportion diagnosed only at necropsy. But even if these figures were approximately correct, they do not represent the whole picture.
Among the 30 deaths analysed, there were 6 patients on whom a laparotomy was performed and on 5 of them the correct diagnosis was still not reached as a result of the operation; it is certain that in addition to those who die, a considerable number of patients have parts of their anatomy unnecessarily removed or opened, and survive with varying degrees of mutilation.

INDIGENOUS AMOEBIASIS
An assessment of the prevalence of amoebiasis acquired while resident in the United Kingdom is even more difficult than the assessment of the overall prevalence. Patients are often not asked whether they have ever been abroad or the answer is not recorded in the clinical notes. Of the 30 patients who died from amoebiasis in the period 1963-73 (Stamm, 1975) 16 were white and born in the United Kingdom; 11 of these had a history of residence or visits overseas; there was no record on this point in the others’ clinical notes.

In the series of eight patients with amoebiasis seen in Oxford and reported by Wright (1966), one patient had never been abroad and one had only paid a visit to Calais, 18 years previously. Apart from one patient who was a Pakistani and the patient who had never been abroad, the time interval between the onset of clinical symptoms and the probable time of infection was over 15 years.

In view of this long incubation or latent period, the lack of a recent history of travel abroad should be given little weight in excluding the diagnosis, although a history of travel to a highly endemic area should call for careful investigation.

COMMON MISDIAGNOSES
Amoebiasis can mimic almost any abdominal or hepatic condition, and the incorrect diagnoses often call for surgical interference or medication with steroids, both of which are likely to have disastrous results in a patient with amoebiasis.

In Wright’s (1966) series, two patients had intestinal amoebiasis and six had an amoebic liver abscess. Of the two patients with intestinal amoebiasis, one was diagnosed as ulcerative colitis and caecal carcinoma; a laparotomy was performed. On the other, an emergency laparotomy with total colectomy and ileostomy was performed; at necropsy he had gross amoebic ulceration of the gut mucosa and a small liver abscess. Of the patients with an amoebic liver abscess, two were diagnosed only after laparotomy for cholecystitis and peritonitis, two revealed the true diagnosis by coughing up the contents of their abscess, one died with a diagnosis of secondary carcinoma of the liver, and the sixth, a Pakistani, was only correctly diagnosed on his second admission with a pyrexial illness.

Of the 30 patients who died from amoebiasis in the period 1963-73, 9 had been given steroids at some stage in their illness and their condition had thereafter rapidly deteriorated. The wrong diagnoses on the 12 patients who were correctly diagnosed only at necropsy were carcinoma (3), ulcerative colitis (1), acute colitis (1), portal pyaemia (1), pyogenic liver abscess (1), kala-azar (1), no diagnosis (4).
Eight other patients were correctly diagnosed too late for effective treatment; one of these had been diagnosed as fulminating ulcerative colitis and one as Crohn’s disease.

In the last two years I have been concerned with two patients suffering from an amoebic cerebral abscess secondary to an amoebic lung abscess; in both cases amoebae in the original lung biopsy were missed. Similarly, in two cases diagnosed as Crohn’s disease, the amoebae were missed in the biopsy specimens and the correct diagnosis was made only at the necropsy that followed treatment with steroids.

Tucker et al. (1975) reported eight patients diagnosed as suffering from ulcerative colitis and two as suffering from Crohn’s disease who were eventually considered to have amoebiasis and recovered on anti-amoebic treatment. One of the patients, on whom seven faecal examinations had been reported as negative, was put on steroid therapy; he developed multiple liver abscesses.

Pittman et al. (1973) reported eight cases of acute amoebic colitis. They concluded ‘It is imperative that studies be carried out to establish or exclude the diagnosis of amoebiasis in all patients who present with a clinical and sigmoidoscopic picture of colitis’.

INVESTIGATION OF SUSPECTED AMOEBIASIS
Clinicians should be more aware of amoebiasis as a possible and very easily treatable cause of most abdominal and hepatic symptoms. A few years ago it could be argued that the diagnosis of amoebiasis was difficult and time-consuming; to eliminate it in every case where it was a possible candidate would be uneconomical and out of the realm of practical medicine.

In most hospital laboratories the staff have neither the time nor the expertise to carry out adequate examinations of faecal specimens and the specimens submitted are rarely fresh or well selected. Even the presence of amoebae in faeces does not prove a causal relationship to the symptoms.

Recent developments in the field of serology have radically altered the situation and numerous different techniques have been developed; they vary in their sensitivity and specificity and they do not all test for the same antibodies (Maddison et al., 1965). The indirect haemagglutination (IHA) and latex agglutination (LA) tests are sensitive but may remain positive for years after the patient has been cured (Stamm et al., 1973). The indirect immunofluorescent antibody (IFA) test is not quite so sensitive but is much less persistent although it may remain positive to low titre for several months or even up to three years. The gel diffusion precipitin (GDP) test is less sensitive, becomes positive at a later stage of the disease but returns to negative within a few weeks of successful treatment. For clinical purposes, a combination of the IFA and the GDP provides the most useful information (Stamm et al., 1976). If the IFA test is positive at a titre of 1 : 64 or higher and the GDP test is positive, the patient almost certainly has
invasive amoebiasis. If the IFA test is positive at a titre between 1 : 64 and 1 : 256 but the GDP test is negative, the result can be interpreted only in the light of the clinical findings; there may be a past history of amoebiasis that accounts for the positive IFA test, or symptoms may be of very recent onset, which accounts for the negative GDP test. The IFA test is positive in 95 to 100 per cent of sera from patients with an amoebic liver abscess and in 60 to 80 per cent of sera from patients with intestinal amoebiasis. In severe intestinal amoebiasis the percentage of positives is probably very much higher. If, therefore, amoebic serology is done on all patients in whom a diagnosis of amoebiasis is a possibility, the vast majority of those in danger of mutilating surgery or dangerous medication will be recognised.

In many of the reports on the sensitivity and accuracy of serological tests the main criterion for diagnosis of an amoebic liver abscess has been response to therapy with amoebicides, which in recent years has usually meant response to treatment with metronidazole. This may have led to the assessment of serological accuracy being lower than the true figure, because metronidazole is very effective against anaerobic organisms; some of the liver abscesses with negative serology but a good therapeutic response may in fact have been caused by anaerobic streptococci.

It is my belief that all patients diagnosed as suffering from ulcerative colitis, Crohn's disease and other abdominal or hepatic conditions where no proved diagnosis has been made, should have serum examined for amoebic antibodies.

The principles underlying the IFA test can be applied to specific staining of trophozoites in culture, faeces, pus or histological specimens (Parelkar et al., 1971; Parelkar and Stamm, 1973). All biopsy specimens where a diagnosis of amoebiasis is suspected should be screened for amoebae by the immunofluorescent staining technique; this is done on ordinary routine formalin fixed, paraffin embedded sections.

Serological tests and the immunofluorescent staining of amoebae require some experience both in technique and in interpretation; positive and negative controls are necessary; large numbers of sera can be tested with very little more technical staff than is required to test a few. For these reasons centralisation is both more economical and more clinically helpful than having the occasional test done in a hospital or regional laboratory. It is with this in view that the Amoebiasis Diagnostic and Research Unit has been established at St Giles's Hospital, as a national diagnostic unit. For serological tests, a minimum of 2 ml of clotted blood or, preferably, 1 ml of serum should be sent to the unit; for histological examination one section stained with haematoxylin and eosin and 6 unstained sections from formalin fixed, paraffin embedded tissue should be sent; for examination of pus, unfixed, unstained smears are required. Faecal specimens are accepted for confirmation of the identity of objects thought by the local laboratory to be amoebic trophozoites or cysts; the specimens should be either
stained smears with the suspected objects marked, or faeces emulsified in polyvinyl alcohol or in Schaudinn's fixative for trophozoites, or in 4 per cent formol-saline for cysts. Full clinical details should be included with all requests; a follow-up card is sent with each report, so that the unit can check on the validity of the results. When speed in getting the result is important, the request should be marked 'urgent', when the result will be given by telephone and confirmed by post.

Since the formation of the St Giles's Unit at the end of 1973, the clinicians in the King's group of hospitals have become aware of its existence. Over 60 sera have been tested from the King's group; 6 have been positive and all these have proved to have active amoebiasis; 4 of them would almost certainly not have been diagnosed correctly if serology had not been done.

To those who have read this article and have found nothing new and have never mistaken amoebiasis for some other disease, I apologise for having wasted their time.

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