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AMOEBIASIS – ENTAMOEBA HISTOLYTICA INFECTIONS – A REVIEW

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SUMMARY

Many populations of Entamoeba histolytica, identified by enzyme electrophoresis, are non-pathogenic, and as infections are frequently self limiting, treatment of asymptomatic cyst passers may often be unnecessary. Tissue (invasive) amoebiasis remains a diagnostic challenge, but the advent of improved serology and, for liver abscess, scannning techniques, particularly ultrasound, has made it easier to come to a reasonably certain diagnosis before starting treatment. Where facilities are limited, a therapeutic trial with a nitroimidazole such as metronidazole in an adequate single daily dose for 3 days is safe and rapidly effective.

PATHOGENIC/NON PATHOGENIC STRAINS LABORATORY DISTINCTION

Perhaps the most important contribution in recent years to the understanding of amoebiasis has been Robinson's introduction of a reliable culture technique (1). Initially used as an improvement in diagnosis, many more infections with Entamoeba histolytica can be recognised than by microscopic examination alone, it has been fundamental to the distinction of pathogenic Entamoeba histolytica from non-pathogenic forms in the laboratory (2).

The early history of amoebiasis was confused by the finding of amoebae in patients with and without disease. Walker and Sellards in a classical experiment (3) in which amoebic cysts were fed to patients, demonstrated that *E. coli* were harmless but *E. histolytica* were sometimes pathogenic. There have been many explanations put forward to account for this variable pathogenicity of *E. histolytica.* The natural course of events for the trophozoites of Entamoeba histolytica seemed to be to live in the lumen of the caecum without giving rise to symptoms, and, with the passage of the amoebae down the lumen of the colon to the anus, to form quardrinucleate cysts. Diarrhoea, whatever the cause, resulted in the trophozoites being swept out in the unformed stool without the opportunity for cysts to form. But sometimes E. histolytica invaded, causing ulceration of the wall of the large bowel, particularly in the caecum and in the rectum, giving rise to the clinical syndrome of amoebic dysentery. Colonisation of the liver, often unassociated

with dysentery, led to the formation of amoebic abscesses in the liver.

Sargeaunt and colleagues in a series of reports starting from 1978 (2), have demonstrated electrophoretic differences between pathogenic and non-pathogenic *E. histolytica*. Entamoeba histolytica from all over the world (4), but not apparently from East Africa, have been cultured in Robinson's medium, harvested, lysed and then subjected to enzyme electrophoresis. The patterns obtained on electrophoresis have formed the basis for the identification of 18 zymodemes of E. histolytica so far. Eleven of these have been obtained from asymptomatic cysts passers, and the remaining 7 (II, VI, VII, XI, XII, XIII, XIV) have been asosciated with invasive amoebiasis as well as being found in asymptomatic subjects. Patients with invasive amoebiasis have had either intestinal ulceration, accompanied by haematophagous trophozoites in their faeces, or E. histolytica cultured from pus aspirated from liver abscesses. The majority of patients with invasive amoebiasis and also asymptomatic subjects harbouring pathogenic E. histolytica have antibodies to E. histolytica in the blood, whereas those harbouring non-pathogenic E. histolytica are serologically negative (5). This finding supports Sargeaunt's classification of pathogenic and non-pathogenic zymodemes of E. histolytica, and also provides an indirect method of determining whether or not a cyst passer is harbouring a potential pathogen.

A major implication of Sargeaunt's work is that a great number of asymptomatic cyst passers can be safely left without treatment. In India, for example, only 1 of 4 zymodemes isolated is pathogenic, and in Kuwait the only zymodeme isolated so far has been non-pathogenic. A zymodeme map of East Africa might prove interesting, and might explain riddles such as the importance of invasive amoebiasis in Moshi compared with its relative infrequency in Nairobi.

Similar conclusions based on clinical observations on the significance of asymptomatic cyst passers have come from India (6). No correlation was found between cyst passers and symptoms in patients attending a gastroenterology clinic, except that diarrhoea was actually worse in patients without cysts. All of 15 cyst passers who were followed for up to 18 months stopped passing cysts without treatment, and none developed invasive amoebiasis.

DIAGNOSIS

The diagnosis of invasive amoebiasis has always been difficult, yet crucial, for a missed diagnosis coupled with inappropriate treatment so often results in an otherwise avoidable disaster. An occasional presentation of amoebic dysentery in a practice where ulcerative colitis is the usual cause of chronic bloody diarrhoea can be difficult to spot, with steroid therapy compounding the problem. With severe amoebic dysentery, the rectum is almost invariably involved so that a proctoscope is all that is needed to see the characteristic patchy involvement of the mucosa. The sigmoidoscope is potentially dangerous and is rarely needed to distinguish inflammatory disease of the

large bowel, especially in the tropics. Amoebiasis, ulcerative colitis and *schistosomiasis manson* all involve the retum, and on the few occasions that the rectum is spared, the sigmoid is likely to be spared also. In addition, the paucity of pus cells in the stools together with the surprising profusion of bacteria will help to alert the clinician to the possibility of amoebiasis even if trophozoites are not seen.

Amoebic liver abscesses are perhaps the most notorious diagnostic pitfall in tropical medicine. The development of various serological tests has been of some help, as they are also in amoebic dysentery and other forms of invasive amoebiasis such as amoeboma. The major danger is failure to consider the possibility of a liver abscess at all. Once the possibility has been thought of, it is usually not difficult to decide whether or not a therapeutic trial would be worthwhile, but it should be stressed that the presence or absence of E. histolytica cysts in the stool is irrelevant to such a decision. Scanning techniques, particularly ultrasound, are very useful, and will increasingly replace the occasional need for diagnostic aspiration, with its risks of haemorrhage, secondary infection and the perforation of an unsuspected hydatid cyst. With the development of low cost portable ultrasound there is a strong case for its deployment in district, let alone provincial/ regional, hospitals throughout East Africa.

TREATMENT

Therapeutic trials were less easy to justify when emetine was the mainstay of treatment, for the toxicity of emetine had to be balanced against the probability of a liver abscess. The efficacy and safety of nitroimidazoles have made it sensible to initiate a therapeutic trial if a liver abscess, or for that matter any form of invasive amoebiasis, seems a possibility and cannot be excluded with the available facilities. Early on, physicians at KCMC (Kilimanjaro Christian Medical Centre), Moshi established the value of the large (1.4g) single daily dose of metronidazole (Flagyl) for 3 days, but unfortunately did not publish their results widely, so that in many areas of the world metronidazole is still used in relatively extravagant and ineffective regimens of 400mg or 800mg three times a day for 5 to 10 days. At these dosage levels, failure of metronidazole is sometimes reported. When tinidazole was being developed, a physician working on the project told me that with doses below 1g, even if given three times a day, there sometimes appeared to be no effect on the trophozoites in acute amoebic dysentery, whereas with doses over 1g, symptomatic and objective improvement was immediate and invariable. Unfortunately again these findings were never widely published, but when tinidazole (Fasigyn) was marketed it was at a single daily dose of 2g. Metronidazole and tinidazole are, of course, structurally very similar. Several other nitroimidazoles are also available. All of them are effective tissue amoebicides, but poor luminal amoebicides. Entamizol is a combination drug of metronidazole and diloxanide furoate (Furamide) recognising this weakness of the nitroimidazoles, though many will still

prefer to give a short high dose course of a tissue amoebicide when that is what is needed, and a protracted course of a luminal amoebicide when that is appropriate. Diloxanide furoate, 0.5g three times daily for 10 days, is usually effective in clearing amoebae from the lumen of the caecum, but diphetarsone is probably the most effective luminal amoebicide (7). It also clears almost all the other amoebae such as *E. coli* from the lumen of the bowel, and has the added quality of being the most effective agent against *Trichuris trichiura*, another parasite sheltering in the large bowel and thus protected from potentially potent agents that are largely absorbed before they pass the ileocaecal junction.

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