venous infusion of secretin and pancreozymin were identical in normal people and patients with pancreatic disease. The studies were not strictly comparable, however: Worning measured amylase but not trypsin; assessed enzyme responses to a combined infusion of two different secretin and two different pancreozymin preparations rather than to pancreozymin alone; compared the output of enzyme after exogenous stimulation with the concentration of enzyme after a meal rather than using the same criterion for both tests; and included several different disease entities in the pancreatic malfunction group rather than restricting the consideration to patients with CP alone.

MTA in duodenal juice after a test meal depends not only on the amount of cholecystokinin-pancreozymin released from the intestinal mucosa but also on dilution of pancreatic enzymes by gastric, biliary, and intestinal secretions. Until these other factors have been carefully assessed the disproportionate reduction in tryptic response to endogenous compared with exogenous cholecystokinin-pancreozymin should not be taken to imply impairment of release of this hormone in CP. Whatever the explanation for this unreported phenomenon our observations validate the practical clinical usefulness of the Lundh-Borgström test (which is within the resources of most hospitals) when a diagnosis of CP is suspected. The SP test, which is better suited to specialist centres, provides valuable additional information about gall-bladder function and the presence of obstruction in pancreatic or biliary ducts¹⁸ and ideally will still be required for a more complete appraisal in individual cases.

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Corticosteroids and liver amoebiasis

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Summary and conclusions

Patients with amoebiasis who receive steroid treatment may suffer adverse effects including acute amoebic dysentery and exacerbation of the amoebiasis. In some cases the presenting symptoms are initially misdiagnosed and steroids prescribed, which provokes fulminating progression of hepatic amoebiasis. Repeated stool examinations often yield negative results.

Any patient being considered for treatment with corticosteroids who has lived in the tropics should be investigated for amoebiasis serologically and by repeated stool examination. Even after negative results the possibility of amoebiasis should be reconsidered if diarrhoea or fever develops during or after steroid treatment.

Introduction

One of the lesser-known complications of high-dose corticosteroid treatment is the superimposition of parasitic infections.¹

Steroid treatment is hazardous and may be disastrous, particularly in patients with amoebiasis. The adverse effects of corticosteroids in amoebic colitis have been documented, though only sporadically.²⁻⁷ The question arises whether deaths are more common than is generally realised, since patients with "colitis" are, rightly or wrongly, often treated with corticosteroids at some stage. Probably even in patients who pass amoebic cysts but are asymptomatic steroids applied locally or systemically may precipitate acute amoebic dysentery.⁸

The hazards of corticosteroids in amoebiasis, however, are not limited to the colon. The following cases show the risk of fulminating progression of hepatic amoebiasis during treatment with corticosteroids.

Case histories

CASE 1

A 26-year-old German sailor was treated in Portugal with prednisone, 20 mg, daily, for pain in the right shoulder. On arrival in Rotterdam 10 days later his condition had worsened considerably. He had severe bloody diarrhoea and had lost 10 kg in weight, and the pain in his shoulder was worse. He was extremely ill, with a high fever. At physical examination tenderness was noted below the right costal margin, but there were no other abnormalities. Erythrocyte sedimentation rate (ESR) was 84 mm in the first hour and white cell count (WBC) $21.4 \times 10^9/l$ ($21\,400/mm^3$) with 17% band forms. Results of liver function tests and chest radiograms were normal. Vegetative forms of *Entamoeba histolytica* were found in the stools. On a liver scan a large defect was seen in the right lobe. An amoebic abscess of the liver was diagnosed. At aspiration of the abscess 200 ml of brownish,

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bacteriologically sterile pus was collected. After treatment with emetine injections and metronidazole and phanquone by mouth the patient made an uneventful recovery.

Comment—The pain in the shoulder was initially misdiagnosed as a rheumatic disease, but this unusual presenting symptom was probably referred pain from the diaphragm caused by hepatic amoebiasis, which under steroid treatment progressed rapidly and evolved into a clinically overt liver abscess. At the same time fulminating amoebic colitis, initially latent, developed.

CASE 2

A 43-year-old Dutch labourer was admitted because of fatigue, anorexia, and pain in the right upper abdomen. Physical examination showed no abnormalities. ESR was 56 mm in the first hour and WBC $9.7 \times 10^9/l$ with 5% band forms. Alkaline phosphatase activity was twice normal, and transaminase concentrations were normal. Stools contained no cysts or vegetative forms of *E histolytica*. Results of cholecystography and barium-meal examination were normal. Liver biopsy showed chronic active hepatitis. The patient had two periods of fever. Since the clinical picture did not accord with chronic active hepatitis prednisone was withheld and he was followed up as an outpatient. During the next 10 weeks his temperature remained normal and there were no other developments apart from an increase in serum gammaglobulin concentration from 11.3 to 24 g/l (1.1 to 2.4 g/100 ml). He began treatment with prednisone, 60 mg daily. After improving initially he suddenly deteriorated. Within a few days a large swelling developed in the right upper abdomen, with intercostal oedema. He was severely ill, with a high fever. He mentioned that while in Indonesia 25 years previously he had suffered from bloody diarrhoea. ESR had increased to 100 mm in the first hour, and WBC was $13.5 \times 10^9/l$ with 42% band forms. Liver function tests yielded the same values as during the first admission. The diagnosis was changed to imminent perforation of an amoebic abscess. Prompt aspiration was carried out, and 3000 ml of pus containing vegetative forms of *E histolytica* was evacuated. A culture for bacteria was negative.

Treatment with emetine, chloroquine, and phanquone was started. Aspiration had to be repeated twice, and altogether 7000 ml pus was removed. With this treatment the patient recovered quickly and all biochemical abnormalities returned to normal. He was followed up for several years, and chronic active hepatitis was ruled out.

Comment—On reviewing this case we found that the pathological features of the hepatic tissue that had suggested chronic active hepatitis could be explained by necrosis and repair processes in the vicinity of a small dormant liver abscess. During the steroid treatment this small lesion must rapidly have given rise to an enormous liver abscess that was about to perforate.

CASE 3

A 32-year-old Dutch woman was unsuccessfully treated with several antibiotics for a febrile illness in Indonesia. Prednisone, 30 mg daily, was tried. Her temperature became normal but only temporarily, and she returned to Rotterdam for further evaluation. She had lost 12 kg in weight in a month and complained of pain in the right shoulder. Apart from the fever no physical abnormalities were found. ESR was 125 mm in the first hour, there was moderate normochromic anaemia, and WBC was $5.8 \times 10^9/l$ with 2% band forms. Stools contained no cysts or vegetative forms of *E histolytica*. Extensive analysis gave negative results. The results of liver function tests were normal except for a temporary marginal increase in transaminase concentrations. Because of a positive response to the latex test for rheumatoid factor and minor perivascular infiltration with mononuclear cells in a biopsy specimen from the dermis, vasculitis was provisionally diagnosed and the patient again put on prednisone, now 60 mg daily. Her temperature became normal, she felt better, and the pain in the right shoulder disappeared. As soon as the prednisone dose was reduced to 25 mg daily the fever returned. After a month she began to cough and to produce bloody, chocolate-coloured sputum. Chest radiography showed a pulmonary abscess above the right hemidiaphragm. The liver was not enlarged, but a liver scan showed a defect in the right lobe. The immunofluorescent antibody (IFA) titre against *E histolytica* was strongly positive (above 1/160). The diagnosis was changed to an amoebic abscess of

the liver complicated by a pulmonary abscess, she was treated successfully with emetine, metronidazole, and phanquone.

Comment—The pain in the right shoulder, a rare symptom of liver amoebiasis, was initially misdiagnosed. After perforation of the abscess into the lung and bronchi the correct diagnosis was made based on the defect shown by the liver scan and the positive IFA test.

Discussion

Using corticosteroids entails many serious risks. We have drawn attention here to the provocation and rapid progression of an *E histolytica* infection during systemic treatment with corticosteroids. In these three patients amoebic abscess of the liver developed rapidly during such treatment. In case 1 not only the liver abscess but also severe amoebic colitis became manifest; in case 2 the steroid treatment led to an enormous abscess under high pressure; and in case 3 the abscess ruptured into the lung and bronchi.

During the past six years 25 patients with an amoebic abscess of the liver have been admitted to our hospital. Three, the cases described here, received corticosteroids. Since these patients showed a fulminating downhill clinical course during steroid treatment a causal relation seems clear. Apparently the amoebae become more aggressive and invasive after corticosteroids have been given. Although the reason for this is less obvious, we suggest that suppressing the inflammatory and immunological responses interferes with the host-parasite equilibrium.

Since liver amoebiasis is clinically protean clearly it must be considered in the differential diagnosis of undefined illnesses in patients who have been in the tropics. This is most clearly shown by case 2, in which the patient had left the tropics 25 years before the amoebic liver abscess became clinically apparent.

If amoebiasis is suspected stools should be investigated for vegetative and cystic forms of *E histolytica*. This can be difficult, however, even for experienced parasitologists. Furthermore, results of repeated stool examination may be negative in both intestinal and extraintestinal infections, as in cases 2 and 3. In our series of 25 patients with liver amoebiasis positive results were obtained in only 12.

Useful adjuncts to the diagnosis of extraintestinal amoebiasis, particularly hepatic amoebiasis, are the various serodiagnostic methods that indicate the presence of circulating antibodies to *E histolytica*. These serological tests are reliable, being positive in almost all cases of amoebic abscess of the liver.^{8,9} All our patients with hepatic amoebiasis tested by indirect immunofluorescence had positive and high IFA titres. Serological tests are, however, less helpful in patients with active intestinal amoebiasis and of little use in those who pass cysts but are asymptomatic.

Clearly, any patient who has lived in the tropics and who is being considered for corticosteroid treatment should be carefully investigated for amoebiasis. The best laboratory procedure is serological investigation together with repeated stool examinations. But even if these tests give negative results the possibility of amoebiasis should be reconsidered in patients who develop diarrhoea or fever during or after treatment with corticosteroids.

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