Functions of phagocytic cells in chronic mucocutaneous candidiasis

Chronic mucocutaneous candidiasis (CMC) is a group of uncommon immunodeficiency disorders characterised by chronic infection of the skin, nails, and mucosal surfaces caused by Candida albicans. There are few reports about the functions of phagocytic cells in CMC. This led us to investigate phagocytosis and intracellular killing of C. albicans by granulocytes and monocytes in CMC with a recently developed technique.

Patients, methods, and results

Leucocyte functions were tested in five patients (two men (cases 2 and 5) and three women (1, 3, and 4)) with CMC. In four of these patients the candida infection was limited to the skin, nails, and mucosal surfaces (affecting the respiratory tract) and had the most severe candidiasis. Case 4 also suffered from hypoadrenalism and hypoparathyroidism affecting the respiratory tract) and had the most severe candidiasis. Case 4 also suffered from hypoadrenalism and hypoparathyroidism.

The method for measuring phagocytosis and intracellular killing by C. albicans has recently been briefly documented. Suffering from hypoadrenalism and hypoparathyroidism.

In all patients phagocytosis of C. albicans by granulocytes was normal in the presence of both normal serum and the patient’s serum. Phagocytosis by monocytes of cases 1, 2, 4, and 5 was in a normal range (93.8-98.9%), whereas the monocytes of case 3 showed slightly diminished phagocytosis (90.0%). The intracellular killing by granulocytes in the presence of normal serum or patient’s serum was normal in all patients. In the presence of normal serum the intracellular killing by monocytes was normal in two patients (cases 1 and 2), whereas two patients (4 and 5) showed no intracellular killing (>70% at 60 minutes) (see figure). Case 3 showed a slightly diminished killing. When patient’s monocytes were used together with patient’s serum, however, both cases 1 and 2 showed diminished intracellular killing and the results for cases 3, 4, and 5 were not altered (see figure). When normal monocytes were used together with patient’s serum, serum of case 2 showed increased intracellular killing, whereas with the serum of case 1 the intracellular killing was still diminished (see figure).

Comment

Concerning the functions of phagocytic cells in CMC Valdimarsson et al reported normal intracellular killing by granulocytes in five patients using the dye exclusion method. This method has the disadvantage of subjective microscopic judgment of candida cells being stained. Phagocytosis and intracellular killing of bacteria by leucocytes was normal in a child with recurrent pyogenic infections, CMC, and defective neutrophil chemotaxis.

We found that phagocytosis and intracellular killing by granulocytes were normal in all patients, and that phagocytosis by monocytes...
was slightly diminished in one (case 3). Intracellular killing by monocytes showed a heterogeneous picture: either the monocytes were hyperactive or defective in this respect. The hyperactive killing might be explained as a compensatory mechanism in chronic candida infection. The slightly decreased killing by monocytes in case 3 was probably also due to diminished phagocytosis as our killing assay measures the overall result of phagocytosis and intracellular killing.

In cases 1 and 2 the killing defect was remarkable because this defect is serum-dependent. The conclusion that only the disturbance of intracellular killing is serum-dependent is justified, because the phagocytosis assay showed no difference between normal and patient's serum. The question of whether the serum of these two patients contains an inhibitor or lacks a stimulant is under investigation. In two patients with CMC an inhibitor of intracellular killing of candida by granulocytes has been reported.1

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Prophylaxis with deglycyrrhizinised liquorice in patients with healed gastric ulcer

Recurrence of gastric ulceration after medical treatment is common, with recorded rates of 40%1 and 60%2 in the first two years. The use of ulcer-healing drugs that prevent relapse has received relatively little attention, though carboxbenzoxolone has been used, but with little success.3 An acceptable prophylactic drug would be of considerable value in the management of gastric ulceration, and we undertook a trial of deglycyrrhizinised liquorice (DGL) to assess its merit in this respect.

Patients, methods, and results

Forty-one patients (23 men, 18 women) with benign chronic gastric ulceration whose ulcer healed had been shown both radiologically and endoscopically within the previous four weeks, were selected for this study. All were aged under 75, and women of child-bearing age were excluded.

The trial was a double-blind controlled study, in which participants received five capsules a day, each containing either 450 mg of DGL (Ucelad) or an identical placebo. A normal diet was allowed and alcohol and tobacco were permitted in moderation. Antacids were taken as required. We reviewed the patients monthly for recurrence of symptoms, and a full haematological and biochemical profile was taken at each visit. Gastroscopy and barium-meal examinations were performed at six-monthly intervals, or earlier if dyspeptic symptoms arose in the meantime. Patients were followed up for at least two years or until the ulcer recurred.

On completion of the study eight patients had withdrawn, leaving 33 patients for analysis, of whom 22 had received placebo and 11 DGL. The composition of these groups and the ulcer recurrence rate on DGL and placebo is shown in the table. Eighteen patients developed a further gastric ulcer: five were receiving DGL and 13 placebo. This represents a relapse rate during follow-up of 45% for DGL and 59% for placebo. This difference is not significant. Seventy-eight per cent of the total recurrences occurred within the first 10 months of prophylaxis.

Reasons for withdrawal from the trial were deflection from follow-up (five patients) and intercurrent illness (three patients). No clinical, biochemical, or haematological abnormality was detected during treatment and no evidence of long-term toxicity was found.

Comment

A compound capable of preventing the recurrence of gastric ulceration would have considerable medical, social, and economic importance. Because the mechanism of gastric ulcer recurrence is unknown, the choice of a suitable test compound cannot be entirely rational. We chose DGL because of its reputed effectiveness in healing peptic ulceration1 (although this has been disputed3) and its lack of side effects. It has not previously been used prophylactically in man, but has been shown to protect against gastric ulceration in pylorus-ligated rats. DGL in the dosage used in our study is not an effective prophylactic of chronic gastric ulceration, though the recurrence rate was lower in the treated patients than in the placebo group. Nevertheless, the patients' acceptance of treatment combined with regular endoscopy and barium-meal studies was extremely good, which suggests that prolonged treatment and follow-up could be acceptable to informed patients.

Without precise information on the aetiology of gastric ulceration, the choice of further agents as potential prophylactics must be partly intuitive. Indeed, we cannot be certain that ulcer-healing agents will have any pharmacological activity as prophylactics. Nevertheless, we believe that the search for an effective prophylactic should continue, and suggest that the ideal characteristics of such a drug should be infrequent dosage, low cost, lack of side effects, and absence of long-term ill effects, tolerance, or teratogenicity.

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1 Veterans Administration Co-operative Study on Gastric Ulcer, Gastroenterology, 1971, 61, No 4, Part 2, 567.

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