FATAL PERFORATIONS OF THE STOMACH DUE TO MUCORMYCOSIS OF THE GASTRO-INTESTINAL TRACT

I. ABRAMOWITZ, M.B., B.CH. (RAND), F.C.S. (S.A.), F.R.C.S. (EDIN.), *Coronation Hospital, Johannesburg, and University of the Witwatersrand**

Certain fungi belonging to the *Mucoraceae*, including *Mucor*, one of the common bread moulds widely distributed in air and food, may under certain conditions assume pathogenic qualities in man, resulting in inflammatory and necrotic changes. The regions commonly involved are the head and neck, the central nervous system, the lungs, and the gastro-intestinal tract. This paper reports its occurrence in the digestive tract, resulting in multiple gastric perforations and mucosal ulceration in the colon, with fatal outcome.

CASE REPORT

The patient, a Bantu male (E.K. 3211/8) aged 35 years, was admitted to Coronation Hospital on 7 April 1958. He gave a 4-day history of abdominal pain commencing in the epigastrium and later generalized. During this period he had passed melaena stools and on the morning before admission he had vomited blood-stained material. During the past year he had complained of vague abdominal pains occurring after meals. There was no suggestion of diabetes or any other debilitating condition.

On examination the patient was found to be markedly shocked and dehydrated. The abdomen was distended and there was generalized abdominal tenderness and rigidity, with absence of normal bowel sounds. A clinical diagnosis of generalized peritonitis was made, probably due to perforation of a viscus. This was confirmed on radiological examination, which revealed the presence of gas shadows under the diaphragm on both sides.

Laboratory findings (blood specimens taken on admission). Blood urea 137 mg./100 ml. Serum Na 124 mEq./l., serum K 5 mEq./l., serum Cl 95 mEq./l. CO_2 combining power 21 mEq./1. Blood agglutination tests, Widal, Malta fever, Weil-Felix and Vi: all negative. Urine: S.G. 1025, albumin trace, sugar nil, acetone nil. Blood culture: no organisms cultured.

In view of the patient's poor condition and the duration of his symptoms he was treated conservatively with continuous gastric suction and intravenous fluid therapy, including the administration of plasma. Hydrocortisone and antibiotics were also administered, the latter including penicillin, streptomycin, and at a later stage intravenous tetracycline. In spite of a favourable initial response to these measures, the patient subsequently deteriorated and died 9 days after admission.

Autopsy report. Generalized peritonitis present. 8 pints of foul-smelling dark fluid removed from the peritoneal cavity. 4 gastric ulcers associated with marked gastritis; 2 of the ulcers had perforated, one into the greater sac through the anterior stomach wall, the other into the gallbladder. Areas of superficial ulceration throughout the colon.

Histopathology. Histological sections of the stomach at the sites of the perforations and of the bowel at the areas of colonic ulceration showed a marked haemorrhagic and inflammatory reaction, with large branching non-septate fungal hyphae suggesting origin from the mucoraceae (Fig. 1)—particularly marked in the mucosal and submucosal areas.

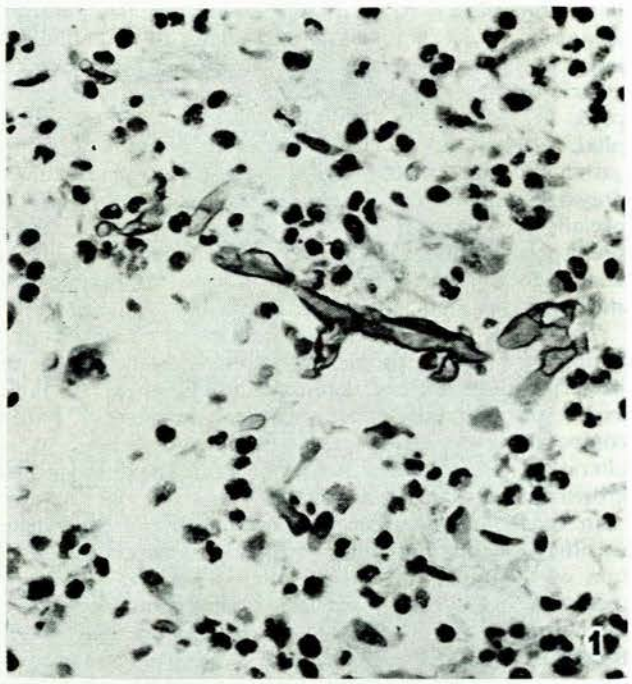

Fig. 1. Section through wall of stomach adjacent to perforation, showing inflammatory infiltrate and fungal hyphae (haematoxylin and eosin, ×480).

DISCUSSION

Pathogenesis

Mucormycosis is infection with a fungus belonging to a genus of the family *Mucoraceae* (order *Mucorales*, class *Phycomycetes*), characterized by long, wide hyphae branching in a non-septate manner and bearing terminal spores. These ubiquitous saprophytes are found abundantly in nature and assume pathogenic properties when the resistance of the host is broken down by some debilitating illness, particularly diabetes. Other factors facilitating this invasion of the tissues include leukaemia, uraemia, tuberculosis, and chronic malnutrition.[1-3]

In man, three genera of the *Mucoraceae*—*Rhizopus*, *Mucor* and *Absidia*—appear to be causal agents producing an acute inflammatory reaction.[4,5] This process is characterized by the invasion of the bloodvessels by the fungal elements, which grow rapidly and multiply along the course of the vessel, producing thrombotic reactions, often referred to as mucorthrombosis. This results in infarction and necrosis of surrounding tissues. Infection is thought to be due to inhalation or ingestion of the spores and 3 clinical forms are described:

1. *Involvement of structures of the head and neck and the central nervous system.* Bauer *et al.*,[1] and Baker,[2] have drawn attention to a pathognomonic clinical syndrome, characterized by retinal-artery thrombosis, periorbital infection, ophthalmoplegia, blindness, and meningoencephalitis. Neame and Rayner[6] have suggested that this form follows a primary infection of the paranasal sinuses, probably due to inhalation.

*Present address: 6 Silwood Road, Bramley Reserve, Johannesburg.

2. *Pulmonary infection,* associated with pneumonic changes.

3. *Gastro-intestinal mucormycosis,* characterized by mucosal ulceration and often perforation.

The literature indicates that the form involving the head and neck is the commonest presentation. Case reports from South Africa, however, suggest an apparently greater incidence of the gastro-intestinal form.[6-8] The majority of these cases have occurred among Bantu subjects, especially infants. Neame and Rayner[6] found mucormycosis in 0·68% of all necropsies in a Durban hospital, the majority of cases showing involvement of the gastro-intestinal tract. They and other workers[8] have drawn attention to the association of malnutrition, especially kwashiorkor, with this fungal infection. Other predisposing factors they refer to include gastroenteritis and acidosis. Isaacson and Levin[8] suggest that the acidotic state may favour proliferation of mucor.

There has been widespread support for the view that antibiotics favour fungal infections by destroying the bacterial flora of the intestinal tract, which normally exerts an inhibiting effect on fungal elements.[9] Steroid compounds have also been incriminated, operating by an alteration of the host-tissue response facilitating the growth of saprophytic organisms.[10]

In the present case there was no evidence of diabetes or other debilitating condition, nor was there any suggestion of malnutrition. The possibility that the mucor elements were tissue contaminants must be entertained, but this would make it difficult to explain the gastric perforations and mucosal ulceration. Antibiotics and steroids used in the treatment of this patient might have been contributory factors, but it must be stressed that his illness had commenced before these drugs were administered. It is therefore concluded that mucormycosis was the cause of the patient's illness, though the possibility of an associated debilitating illness, not recognized at the time, cannot be ruled out altogether.

Prognosis, Diagnosis and Treatment

Infections involving the head and neck offer the best prognosis and several survivals have been reported.[11] With mucormycosis of the lungs and of the gastro-intestinal tract, most published case reports indicate that the patients usually die in spite of all measures.

In the majority of cases diagnosis is extremely difficult because the condition is not suspected. There have been reports of success with direct microscopic examination of infected material;[11] culture of the fungus has also proved possible; and some help has been obtained from specific intradermal and complement-fixation tests.[11] In the majority of the reported cases, the diagnosis has been made from microscopic examination of postmortem specimens.

Treatment. With the exception of cases presenting with characteristic symptoms of the involvement of cranial structures, the presence of this infection, as indicated above, is in most cases unsuspected, and consideration of treatment is therefore somewhat hypothetical. Nevertheless the possibility of this condition in debilitating illnesses should be borne in mind. No treatment for mucormycosis is known. Amphotericin B,[12] griseofulvin and nystatin[11] have been used, with doubtful results. Anticoagulant therapy has been suggested by Bank *et al.*[11] as a possible means of countering the thrombotic processes that characterize mucor infections. The treatment of the predisposing disease and adequate supportive measures appear therefore to be of chief importance in the management of patients suspected to be suffering from mucormycosis.

SUMMARY

Mucor, a common bread mould, may assume pathogenic qualities resulting in inflammatory and necrotic lesions in the cranial region, the central nervous system, or the pulmonary or gastro-intestinal systems. From case reports, the gastro-intestinal cases appears to be commoner in South Africa, especially among the Bantu people.

A case of mucormycosis of the gastro-intestinal tract in an adult Bantu male, with fatal outcome, is described. The pathogenesis, prognosis, diagnosis and treatment are considered with particular reference to the literature. The poor prognosis of the gastro-intestinal form is contrasted with the more favourable syndrome in head-and-neck involvement.

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Obituary

JAMES T. LOUW, CH.M. (CAPE TOWN), F.R.C.O.G.

We regret to announce that Dr. James T. Louw, Professor of Obstetrics and Gynaecology at the University of Cape Town, died suddenly on 27 January 1964. An obituary article will be published in a later edition.