MUCORMYCOSIS OF THE LARGE BOWEL *

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Fungi of the family Mucoraceae, usually referred to as molds and commonly encountered as contaminants in routine culture and as saprophytes on dead or decaying vegetation, may occasionally produce infection in man. The genus Mucor has been responsible for a large number of lesions in man with perhaps *M. corymbifer* as the best known species. Gregory, Golden, and Haymaker [1] reviewed the literature and noted that in mucormycosis usually only a single organ or system is involved, most commonly the lungs or the ears. Superficial mucormycosis is not common, with only a few reported instances. Serious infection with Mucor likewise is rare although within recent years several instances have been revealed, including 4 in the central nervous system.[1,2]

The case herein reported appears to be unique in that it was characterized by mucosal inflammation and multiple ulcerative lesions of the large bowel. The lesions were infected uniformly by a fungus which appeared morphologically to be a Mucor. The involvement was extensive, actively inflammatory, and led to perforation of the bowel with death from generalized peritonitis. Although gastric ulcers infected with these fungi have been reported,[1] no previous record has been found of a widespread ulcerative colitis due to Mucor.

REPORT OF CASE

Clinical History.† The patient was a white woman, 37 years old, who was admitted to St. Joseph's Hospital, Milwaukee, complaining of generalized abdominal pain, nausea, and vomiting. Her symptoms began a week prior to admission with severe cramp-like pain in the left flank, followed by the passage of a hard mucus-covered stool. During the following days, the stools became looser, were tan, and contained large quantities of mucus. No gross blood was reported. The family physician made a diagnosis of "intestinal flu" and placed her on sulfonamide medication. The abdominal pain became generalized at the end of a week and was accompanied by nausea and vomiting.

The patient gave a history of having suffered from recurring attacks of transient gastro-intestinal disturbances during the previous 5 years. They occurred several times each year and were accompanied by the passage of mucus-covered stools. A physician had not been consulted. From her own experience she avoided greasy and fatty foods because of the distress that they caused. There was no clinical or laboratory evidence of diabetes mellitus.

On admission the patient was acutely ill. Her abdomen was noticeably distended

* Received for publication, June 4, 1948.

† We are indebted to Drs. E. G. Collins and W. Casper for the clinical information on this case.

and tender. Bowel sounds were absent. The white blood cell count was 13,300, with 21 per cent band cells, 56 per cent segmented neutrophils, 14 per cent lymphocytes, and 9 per cent monocytes. The urine contained occasional leukocytes, 1 or 2 red blood cells per high-power field, and a few crystals. A roentgenogram of the abdomen revealed a ladder-like arrangement of the loops of the small bowel and suggested intestinal obstruction or ileus. The impression after physical examination was that an acute, spreading peritonitis was present, due to a ruptured appendix or diverticulum. Surgical procedures were not attempted and a conservative course of treatment was instituted, consisting of chemotherapy, intravenous fluids, blood transfusions, and Wangensteen suction. The patient's condition rapidly became worse and she expired 8 days after admission to the hospital.

NECROPSY FINDINGS

At necropsy, 3 hours after death, the abdomen was still greatly distended but contained no palpable masses. The omentum covered the abdominal viscera and was bound firmly within the pelvis. When the omentum was released, thick, gray fluid, amounting to approximately 500 cc., welled upward into the abdominal opening. Other localized areas containing lesser amounts of purulent exudate were found throughout the abdominal cavity. A large pocket of purulent material, lying between the spleen and diaphragm, extended upward behind the pleura into the chest wall. The small bowel was dilated and its loops were bound together by recent fibrinous adhesions. The serosal surfaces of all abdominal organs were dull and appeared thickened. The appendix was not ruptured. A small rounded perforation, measuring 0.4 cm. in diameter, was discovered in the inferior surface of the cecum. The large bowel displayed numerous small, shallow, irregular, mucosal ulcers. The ulcers were present throughout the entire length of the colon and varied from approximately 0.5 to 2.0 cm. in diameter. The bases of the ulcers were pinkish white and were comparatively free from exudate. One of the ulcers had extended completely through the wall of the cecum, forming the small perforation noted above.

The spleen was soft and its capsule was thickened, especially where it formed the floor of an abscess. The pulp was soft and easily scraped from the cut surface. The remaining abdominal organs and tissues showed no significant abnormalities.

The left lung was partially collapsed and the pleural cavity contained approximately 500 cc. of clear yellow fluid. A retropleural abscess was found in the left posterior thoracic wall. It communicated with the abdomen by passing beneath the diaphragm.

Permission was not granted to examine the central nervous system.

Microscopic Examination

On microscopic examination, the epicardium was thickened and infiltrated with lymphocytes and plasma cells. A similar change was noted

in the visceral pleura, which was covered also with a thin coat of fibrin. The pulmonary alveolar spaces and the small bronchioles contained pink-staining fluid and occasional polymorphonuclear leukocytes. The splenic capsule was greatly thickened and infiltrated with plasma cells and lymphocytes. The splenic pulp was congested and contained numerous neutrophilic leukocytes. No pertinent changes were found in the liver, adrenals, kidneys, pancreas and internal genitalia.

Gastro-intestinal Tract. Multiple sections taken through the shallow ulcers of the colon presented identical microscopic appearances. The serosa was edematous, infiltrated with leukocytes, and its surface was covered with a thick, inflammatory exudate consisting of interlacing strands of fibrin and entrapped degenerating leukocytes. Lymphocytes, plasma cells, and occasional neutrophils were found scattered through the muscularis. The submucosa was three times its usual thickness, due to intense edema and an accumulation of mononuclear cells. The mucosa was edematous and in many areas necrotic. The glands and stroma in many areas were broken up into a granular mass of débris. Scattered among the necrotic tissues and in the bases of the ulcerative area were large accumulations of polymorphonuclear leukocytes and filaments of a fungus. Disruption of the muscularis mucosae and extension into the submucosa frequently were found. The same inflammatory changes encircled the fungus in the submucosa. At several points the fungus had invaded the small vessels of the submucosa and could be seen within their lumina. The vessel walls showed early necrotic changes and were infiltrated with polymorphonuclear leukocytes. In most areas extension did not occur more deeply than into the submucosa. Careful microscopic examination failed to reveal the fungus in the peritoneal exudate, in the lungs, or in other organs.

Mycologic Findings

The Mucors in general, like the Aspergilli and the Penicillia, are considered to be the weeds of mycology. They are found as saprophytes growing on dead or decaying plants or animals. Since these organisms produce numerous spores which are easily disseminated by the wind—air-borne—it is not uncommon to find them on food that we ingest or in the air that we breathe. Occasionally, these fungi may become parasitic or pathogenic as primary agents of disease in man. Usually, however, they attack man as secondary invaders, being dependent upon a preceding alteration of the tissues by infection by other organisms, chiefly bacteria, as in the case of tuberculosis; by general or constitutional disorders; by various tumefactions, notably neoplasms; or by direct trauma.

In the routine cultivation of skin lesions of various types and of sputa, it is not unusual to find these organisms as contaminants. On occasion one may feel reasonably sure that these fungi play a rôle, either major or minor, in pathogenesis. Aspergillus is the most frequent culprit, followed closely by Penicillium. Mucor is not a frequent offender but appears in a sufficient number of sputum cultures to harass the mycologist. When found producing single isolated colonies, they are usually passed over lightly. When found in abundance, however, they should be considered seriously.

It is unfortunate that cultures of the fungus responsible for the lesion described in this case were not made before the material had been placed in a fixative. The diagnosis of mucormycosis may be established with a degree of certainty on the basis of characteristics both of the tissue reaction and of the various morphologic variations of the fungus in its parasitic phase in tissue. Under these circumstances, in the absence of actively growing cultures, the organism can be identified only as to genus and not as to species. Several cases of mucormycosis, with and without the cultivation of the fungus on artificial media, have appeared in the literature. The authors agree on the general morphologic properties of the fungus in tissues, which are those of a species of Mucor; namely, that the organism has a comparatively large diameter, varying in different tissues; branching of the filaments, either abundant or not; lack of septa—coenocytic hyphae; and large accumulations of filaments in the affected tissue.

The appearance and location of the fungus in the tissue are closely linked to the state and degree of tissue reaction. The general picture of mucormycosis as observed in the sections of this case was that of an intense inflammatory process with massive areas of edema and necrosis (Fig. 1). At the periphery of the inflammatory zone was a sharp demarcation between normal and affected mucosa. Here the fungi were not seen until the area was reached where the mucosa began to show a reaction. The fungous filaments were few, appeared isolated, and were enlarged, irregular, or sclerotic. In the distinctly inflamed and hyperplastic zone the fungi were of a smaller diameter and seemed to penetrate the tissue toward the unaffected region. The filaments appeared to be very active, showing numerous branching forms which had little regard for barriers since they had invaded the lumina of the glands and had branched freely (Fig. 2). The same held true for the blood vessels, with the filaments having branched within the lumina (Fig. 4).

In the necrotic areas the filaments were abundant either as isolated large forms or as freely branching growths (Fig. 5). The hyphae ap-

peared uniform in size with actively growing, lightly staining tips indicative of young protoplasm. Cross-wall formation or septa were not seen. The presence of lightly stained areas in the filaments—vacuoles—adjacent to intensely stained segments gave at times the appearance of septum formation. In the sections, groups of filaments could be seen which on cross section gave the appearance of spores (Fig. 7). This peculiar picture was due in many cases to the irregular branching and kinking of the filaments. This characteristic was particularly noted in nodular growths in which the fungous filaments were intertwined and matted together with various inflammatory tissue cells (Figs. 3 and 6).

In summary, it may be said that although cultures of the fungus were not obtained, thus making absolute identification impossible, a sufficient number of characteristics were readily visible to suggest a close relationship to the Mucoraceae. The large size of the filaments, both in diameter and length, the method of free and irregular branching, and the absence of cross-wall formation all point to Mucor. To strengthen this view, one may refer to the publications of others in which it was stated that cultures were obtained, and that the organism, in addition to possessing the above properties, produced similar tissue changes with invasion of the lumina of the intestinal glands and of the blood vessels.

Summary

In a patient with acute colitis due to a fungus, there were ulcerative colonic lesions, perforation of the bowel, and death from generalized peritonitis. The morphologic features of the fungus, as found in the lesions produced by it, indicated that it was in all probability a species of Mucor.

REFERENCES

1. Gregory, J. E., Golden, A., and Haymaker, W. Mucormycosis of the central nervous system. A report of three cases. *Bull. Johns Hopkins Hosp.*, 1943, 73, 405–419.
2. LeCompte, P. M., and Meissner, W. A. Mucormycosis of the central nervous system associated with hemochromatosis. Report of a case. *Am. J. Path.*, 1947, 23, 673–677.

[*Illustrations follow*]

DESCRIPTION OF PLATES

All photomicrographs were made from sections stained with hematoxylin and eosin.

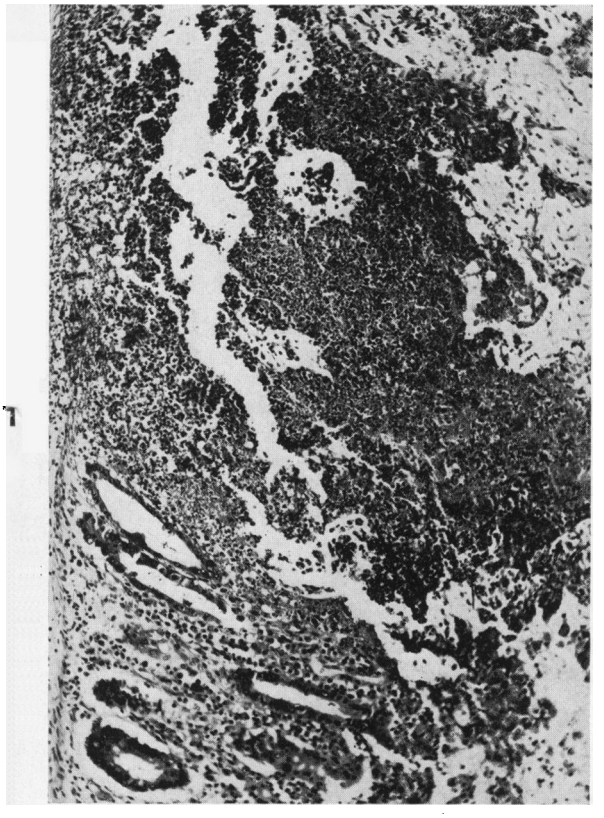
PLATE 83

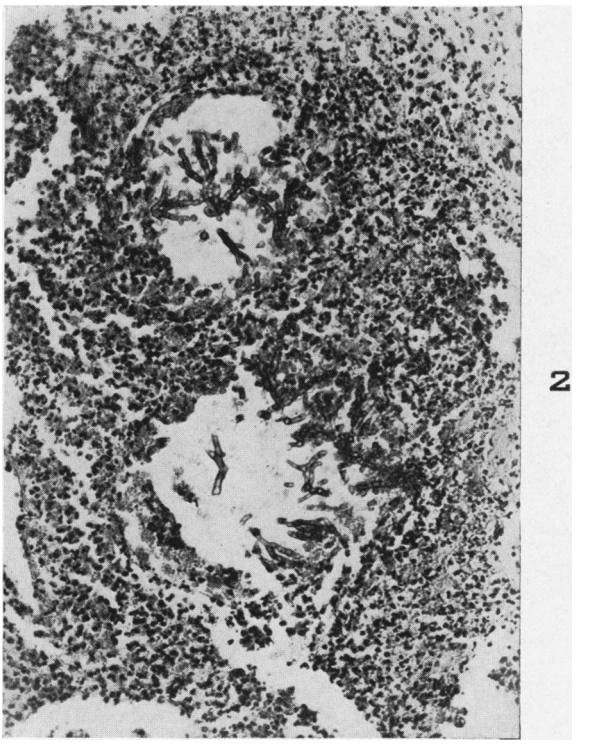
FIG. 1. Section through an inflammatory and necrotic zone of the mucosa. × 90.

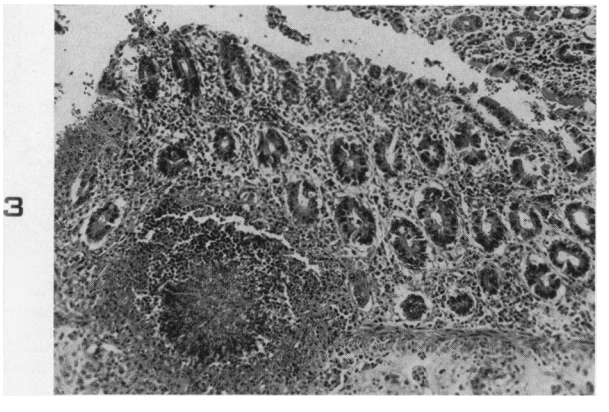
FIG. 2. An inflammatory and necrotic area, showing branching fungous filaments in the lumina of the destroyed glands. × 165.

FIG. 3. Nodule of intertwined filaments and inflammatory cells in the submucosa. × 50.

FIG. 4. Blood vessel invaded by the fungus, which has branched. × 715.







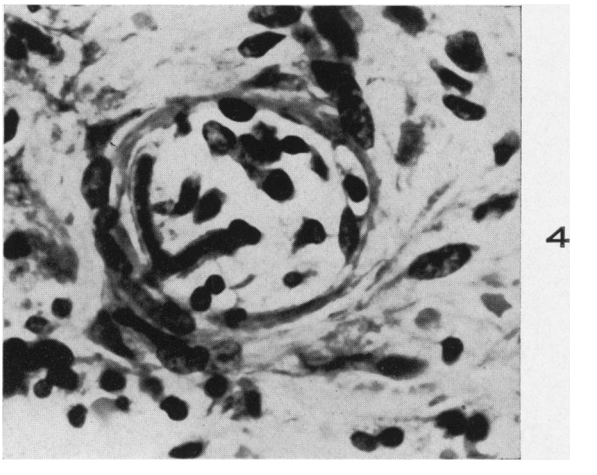


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PLATE 84

FIG. 5. Freely branching forms of the fungus in a necrotic area, showing vacuolar structure and young, growing tips of filaments. × 515.

FIG. 6. Nodule of an intertwined mass of fungous filaments and inflammatory cells. Many of the hyphae appear in cross-sectional form. × 120.

FIG. 7. Fungous filaments seen in cross section. Their resemblance to spores may be noted. × 545.

FIG. 8. Young filament invading the tissue. Intense tissue response is absent. × 685.

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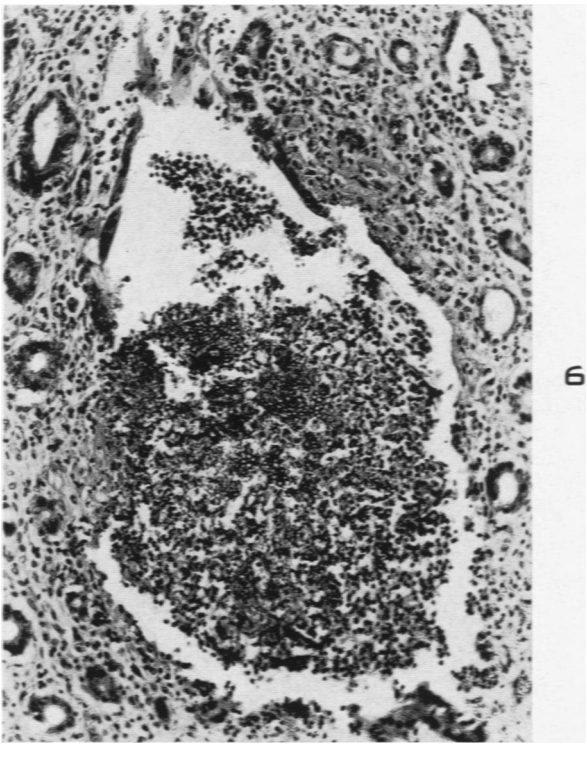

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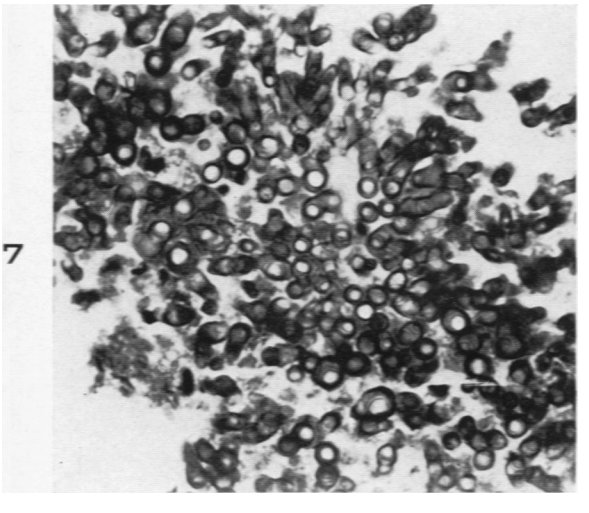

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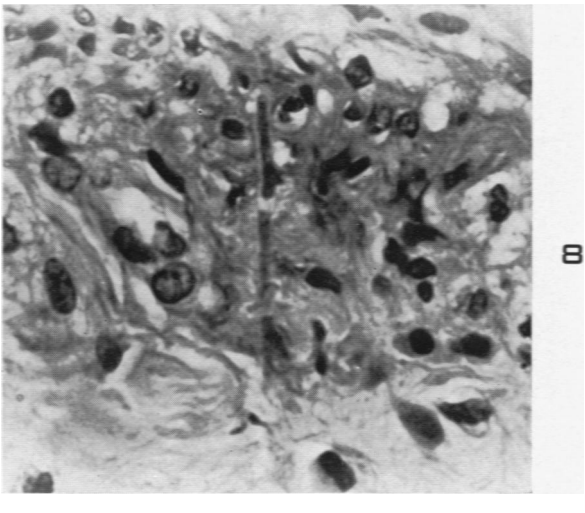

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