MUCORMYCOSIS OF THE CENTRAL NERVOUS SYSTEM ASSOCIATED WITH HEMOCHROMATOSIS

REPORT OF A CASE *

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Human infection with fungi of the family Mucoracea is rare. Mucormycosis is not mentioned in the standard American works on pathology, although it is both described and illustrated in one German text.[1] Organisms of this group are referred to as potential pathogens in most works on medical mycology.[2-7] In others they are mentioned as contaminants [8] or "probable pathogens." [9] The literature is reviewed by Gregory, Golden, and Haymaker.[10]

The lungs are the organs most frequently involved, the central nervous system most rarely. The case of Paltauf [11] and the three reported by Gregory, Golden, and Haymaker [10] appear to be the only instances on record of involvement of the central nervous system.

The present case is reported chiefly because of its remarkable resemblance in clinical and pathological details to the three described by Gregory *et al.*[10]

Report of Case

E. A. (R 2104), a white male, 57 years of age, was admitted to the U. S. Veterans' Hospital, West Roxbury, Mass., on September 25, 1944. No adequate history was obtainable. He was semi-comatose, confused, and muttering. The breath had a strong odor of acetone. He did not move his left arm or leg. The right pupil was larger than the left. The right eye was inflamed, swollen, and exuded a purulent discharge. The urine showed 2.5 per cent sugar, a heavy trace of albumin, a few red and white cells, and 3 plus acetone. Blood sugar was 130 mg. per cent; leukocyte count, 12,400, with 84 per cent polymorphonuclear leukocytes, 10 per cent lymphocytes, and 6 per cent monocytes. Hemoglobin was 13 gm. Complement-fixation and precipitation tests for syphilis were negative.

The patient was given 40 units of insulin shortly after admission. The following day he received 100 units with 1000 cc. of 10 per cent glucose. No definite improvement was noted, and he was subsequently given 200 units of insulin with 2000 cc. of 10 per cent glucose. The patient failed to recover consciousness and died on September 27th.

Autopsy (no. 122) was performed by Capt. S. Balkin. The right upper eyelid was found to be markedly swollen and injected. The right pupil was irregular and measured 4 mm. in diameter, while the left one measured 2 mm. About 2000 cc. of clear pale yellow fluid was found in each pleural cavity and 300 to 500 cc. of similar fluid in the peri-

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toneal cavity. The heart weighed 450 gm. and appeared negative. The lungs were congested. The liver weighed 2100 gm., was a dusky reddish brown, and showed numerous small, knob-like elevations of its surface. On the cut surface islets of brown tissue were surrounded by depressed gray tissue. The lower end of the esophagus contained dilated veins. The brain showed congestion of the dura and pia, and there were petechial hemorrhages in the pons, medulla, and cerebellum.

Microscopically, the tissues showed the characteristic findings of hemochromatosis, with deposition of yellow pigment granules giving a positive reaction for iron in the liver, spleen, pancreas, adrenals, kidneys, and heart. There was a well marked cirrhosis of the liver.

The brain showed an acute meningo-encephalitis associated with an abundant large, branching fungus (Figs. 1 to 3). The organism consisted apparently of hyphae branching in a nonseptate or coenocytic manner and measuring about 10 to 14 μ in diameter and up to 200 μ in length. The walls of the hyphae were sharply defined and refractile, while the inner portion stained light blue with hematoxylin. The hyphae showed an extraordinary tendency to invade, infiltrate, and replace the walls of blood vessels and to grow within their lumina (Fig. 3). In many places there was an intense reaction of polymorphonuclear leukocytes associated with the presence of the fungus. In other regions, especially where the hyphae lay within the brain substance, as they occasionally did, the reaction was only slight (Fig. 1).

Unfortunately, no culture was obtained from the tissues at autopsy. Sections of the brain were sent to Dr. John E. Gregory, who stated: [12] "Examination of the sections sent to me by Dr. LeCompte reveals invasion by an organism apparently identical with that present in the three cases previously reported."

Slides and tissue were also sent to Dr. C. W. Emmons, Principal Mycologist of the U. S. Public Health Service, who replied: [13] "I concur in Dr. John E. Gregory's opinion that the fungus seen in these sections is probably Mucor because of the size of the hyphae, the infrequency of cross walls and the manner in which the hyphae branch. In the absence of the culture, I am unable to make any more definite identification of the organism."

Discussion

The association of the fungus infection with hemochromatosis in this instance is presumably accidental as far as the disturbed iron metabolism of that disease is concerned. In other respects, however, the case is remarkably similar to those described by Gregory *et al.*[10] All four cases have exhibited a definite triad, as follows: (1) uncontrolled diabetes;

(2) evidence of orbital infection; (3) meningo-encephalitis associated with the presence of a fungus having the characteristics described above. Another feature common to these cases and mentioned elsewhere in the literature is the extraordinary tendency of the fungus to grow in the walls and lumina of blood vessels. As noted by Gregory *et al.*, much of the necrosis and reaction must be attributed to ischemia produced by the involvement of blood vessels. A similar vascular involvement has been noted in infections with organisms of the Aspergillus group.[6,14]

It seems probable that the fungus gains access to the orbital tissues from the paranasal sinuses and thence invades the brain directly, although such a connection was not definitely demonstrated in the present case. Presumably these cases provide another example of the increased susceptibility of diabetic patients to fungus infections.

Summary

A case of mucormycosis of the central nervous system, apparently the fifth one on record, is described. All four cases reported from this country have had in common the following triad: (1) uncontrolled diabetes, with either coma or mental confusion; (2) evidence of orbital infection; and (3) meningo-encephalitis, with the presence of large, nonseptate, branching hyphae having a peculiar predilection for the walls of blood vessels.

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DESCRIPTION OF PLATE

PLATE 113

FIG. 1. A nonseptate branching hypha in the brain. In this instance the reaction of the tissue is relatively slight. Hematoxylin and eosin stain. × 500.

FIG. 2. Hyphae in the brain tissue, accompanied by a marked polymorphonuclear leukocytic reaction. Hematoxylin and eosin stain. × 500.

FIG. 3. Small meningeal vessel in a cerebral sulcus. The fungus has almost replaced the wall of the vessel and is growing in the lumen. Hematoxylin and eosin stain. × 500.

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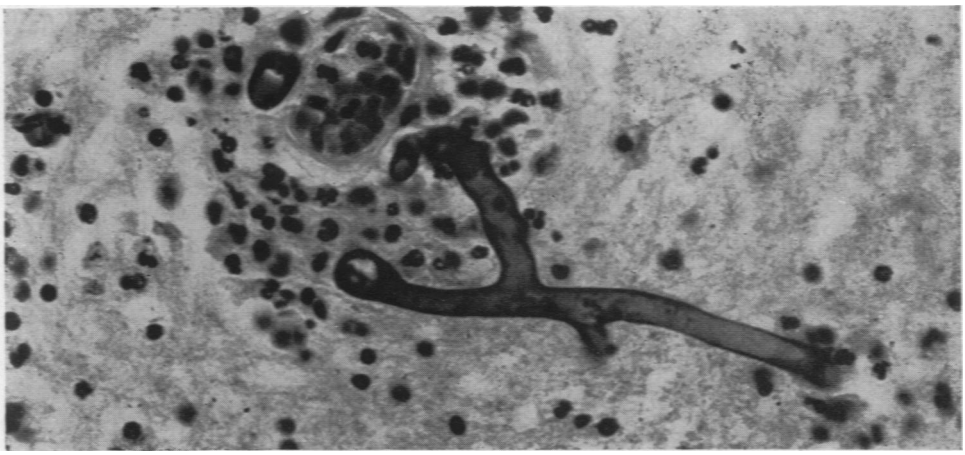

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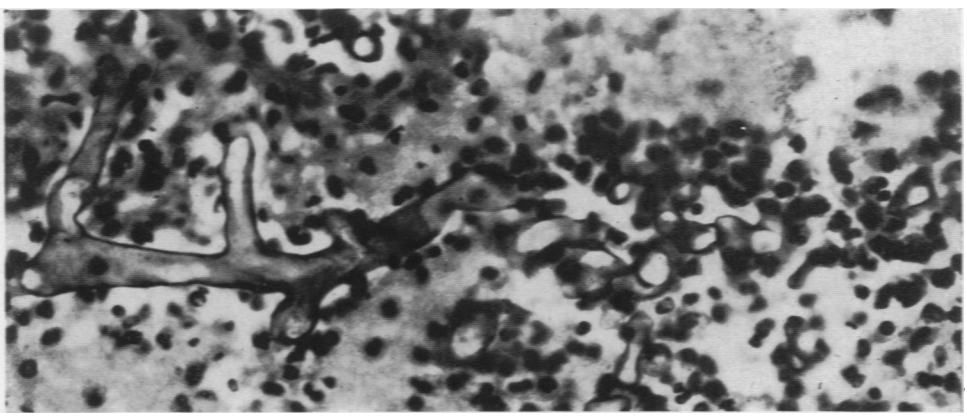

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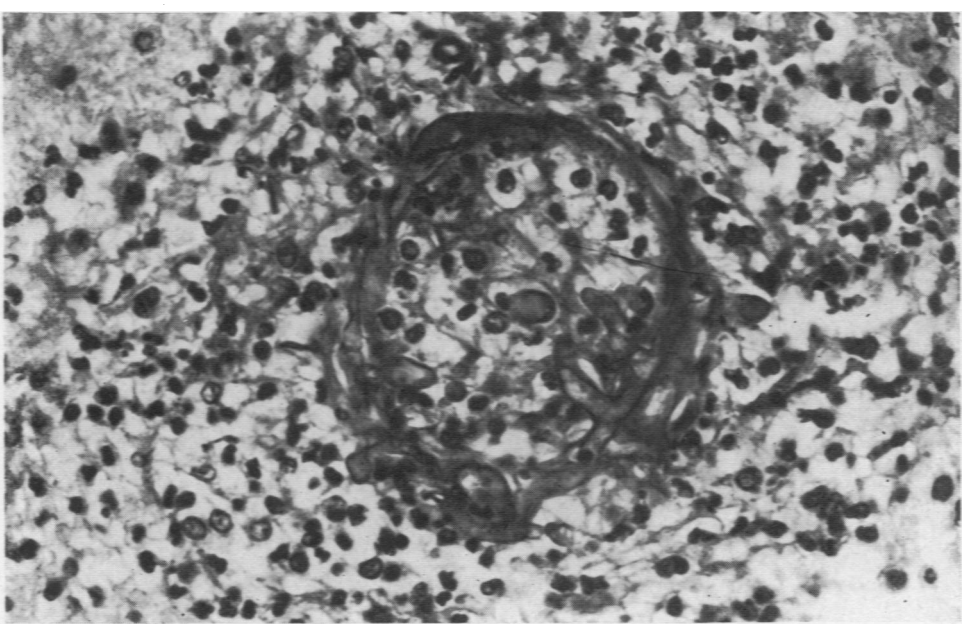

LeCompte and Meissner Mucormycosis with Hemochromatosis