Phycomycosis (Mucormycosis) of the Central Nervous System

Report of a Case*

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Phycomycosis is a fungus infection characterized by the proliferation in tissue of broad, branching, rarely septate hyphae. Species of the genera mucor, rhizopus, absidia, Mortierella, and basidiobolus, all of the class phycomycetes, have been observed as pathogens in the relatively few cases reported in which cultures have been obtained.¹ For this reason the now generally accepted term “phycomycosis” was suggested by Lie and his co-workers⁷ as a more appropriate designation for this group of infections, in which sections of tissue reveal a fungus of the phycomycete morphology.

These fungi are ubiquitous molds in nature, common as laboratory and household contaminants, and not ordinarily considered pathogenic. Ultimate diagnosis depends on the histopathologic demonstration of the characteristic hyphae invading tissue and cannot be based solely on the isolation by culture of such saprophytic organisms. On the other hand, culture is necessary to establish the toxonomic status of the etiologic agent. Phycomycosis of the orbit and central nervous system is generally caused by species of mucor, rhizopus, or absidia.⁴

Phycomycosis appears to be on the increase. Prior to 1948 only 30 cases were collected from the literature, involving the central nervous system.⁹ In a comprehensive review, Straatsma and his co-workers¹² reported 163 cases in the 19 years from 1943 to 1962. One third of these involved the nasal and paranasal sinuses, orbit, and central nervous system. The infection is principally a complication of other diseases, of which diabetes is the most common.⁸ In a recent series 42 per cent of the patients were diabetic. Other predisposing situations are leukemia, depression of bone marrow, and generalized malignancy. As with other mycoses, increased incidence in recent years seems related to the therapy with antibiotics, steroids, or antimitabolites.

The portal of entry is usually a superficial lesion of the mucous membrane of the nose, paranasal sinuses, bronchopulmonary tree, or alimentary tract. Mycosis has also occurred in the eyes, central nervous system, lungs, gastrointestinal tract, and subcutaneous tissues. In susceptible individuals the organism propagates in a unique manner, invading and proliferating within the muscular walls of arteries, and to a lesser extent veins and lymphatics, giving rise to purulent arteritis, thrombosis, and consequent infarction. Phycomycosis of the orbit and central nervous system begins in the para-nasal sinuses and spreads along vascular channels, leading to orbital and cerebral complications by producing thromboarteritis of the branches of the ophthalmic and internal carotid arteries. Only 6 survivors of cerebral phycomycosis have been reported and all of these individuals had residual neurologic deficits.⁹

Case Report

History. A 30-year-old woman who had recognized diabetes mellitus for the last 6 years experienced episodes of nausea and vomiting on January 14, 1951. These were followed by soreness of the throat and the following morning by confusion. She had been taking 30 units of insulin daily. The diabetes, which was thought at first to be the cause of her trouble, was found to be under control. Because of her sore throat, it was believed she was suffering from an upper respiratory infection.

Within a few days her confusion cleared. However, she became drowsy and showed impaired movements of the left eye, particularly on lateral gaze with weakness of the left side of the face and left arm. The spinal fluid pressure was normal and there were only 12 white cells in the spinal fluid. On one occasion the blood leukocyte count was 37,000 and on another, 24,000. Blood cultures taken prior to her hospitalization were negative. A mild sinusitis was observed on the roentgenographic films. There had been no headache.

Examination. Because of the development of coma, she was referred by her personal physician for hospitalization and diagnostic study on January 20th. The history was obtained from her husband and her physician. Except for her pallor and comatose state, a slight injection of the nasopharynx was the only general physical abnormality found. There was startling pallor of the optic fundi, as though the vessels had been obliterated or drained of their blood. An ophthalmological consultant interpreted this as indicative of complete obstruction of both central retinal arteries, possibly due to an embolus. There was a left external rectus paresis. Babinski’s sign was positive bilaterally and the abdominal and epigastric reflexes were absent. She had little movement of the right arm and leg.

Medical consultation led to the impression of a prob-

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Fig. 1. Broad branching nonseptate hyphae proliferating within the wall of an ophthalmic artery and into the septic thrombus with the arterial lumen. H. & E., X1100.

The diabetes was under control so that the coma could not be attributed to that condition. A viral infection leading to encephalitis with the secondary development of a thrombotic process was thought to be unlikely because of the elevated leukocyte count. The white blood cells were not leukemia and showed simply a prominent left shift of the neutrophils. The cardiac picture did not suggest an embolic process.

Course. She remained deeply comatose. Because of a suspected septic process, she was given substantial amounts of antibiotics. On the day of her death necrosis of the lids of the left eye was noted, as well as destruction of the globe of the left eye and collapse of its anterior chamber. The necrosis involved all the soft tissues of the orbit and extended to the lateral aspect of the bridge of the nose. It was believed this represented a retrograde thrombosis of the ophthalmic artery bilaterally. She died 2 days after admission.

Post-mortem Findings. The gross anatomic findings were basilar fibrinopurulent leptomeningitis with bilateral cavernous sinus thrombosis, as well as thromboses of the left anterior and middle cerebral arteries, the intracranial portion of the left internal carotid artery, and both ophthalmic arteries. There was also an acute suppurative left otitis media, suppurative ethmoiditis, suppurative sphenoiditis, plus bilateral cellulitis of the orbits, retro-orbital tissues and periorbital skin. No other visceral lesions were encountered. Bacteriologic cultures of material obtained from the necropsy were inconclusive. Fungus cultures were not taken.

Microsections of the thrombosed vessels revealed massive proliferation of large nonseptate branching hyphae, which stained clearly with hematoxylin and less intensely with the periodic acid-Schiff reaction and the methenamine silver method. A striking picture was produced by the profuse proliferation of the hyphae beneath the endothelium and the internal elastic lamella of arteries, lifting these structures from the media, destroying the endothelium, and initiating a purulent inflammatory response with subsequent thrombosis (Figs. 1 and 2). The fungus was identified as phycomycete by the staff of the Armed Forces Institute of Pathology (AFIP Acc. 691893).11

Discussion

Awareness of the clinical features of mucormycosis of the central nervous system can lead to its diagnosis and treatment.3,9 The possibility should be borne in mind in patients with debilitating disease, in those receiving antibiotics, steroids, or antimetabolic agents, and particularly in those with diabetic acidosis. Even with an aroused clinical suspicion, in a diabetic patient with symptoms of sinusitis, orbital cellulitis, ophthalmoplegia, and neurological abnormalities suggestive of meningoencephalitis, the progression of the disease is often so rapid that institution of fungicidal therapy at this time may not lead to recovery; or recovery, if achieved, would be at the expense of disabling sequelae. Amphotericin B is the most effective therapeutic agent and the prognosis which had been uniformly discouraging has at least brightened with its use.2,3 The importance of establishing the diagnosis and carrying out early treatment is clear. It might even seem wise to begin treatment on the basis of clinical findings without prior verification by culture.

Smith and Kirchner10 have emphasized the diagnostic value of the presence of a black nasal turbinate in nasal phycomycosis. Biopsy of accessible lesions such as those occurring in the nasal mucosa or skin produces conclusive evidence.