Mucormycosis presenting as positional nystagmus and hydrocephalus

Case report

PATRICK J. SWEENEY, M.D., JOSEPH F. HAHN, M.D., MARTIN C. McHENRY, M.D., AND HIROSHI MITSUMOTO, M.D.

Departments of Neurology, Neurosurgery, and Infectious Disease, The Cleveland Clinic Foundation, Cleveland, Ohio

A case of mucormycosis presenting with signs of positional nystagmus and obstructive hydrocephalus is described. The authors believe that this presentation of *Mucor* is unique.

**KEY WORDS** hydrocephalus • mucormycosis • positional vertigo • positional nystagmus

**Mucormycosis** (phycomycosis) is a fulminating infection found almost exclusively in patients with compromised immunity. The best recognized clinical picture is seen in the diabetic patient with ketoacidosis presenting with a third-nerve palsy and orbital chemosis. Patients with chronic steroid therapy, immunosuppressive therapy, extensive burns, and those in renal failure are other populations at risk.

We have recently diagnosed and treated a patient from India, who presented with positional vertigo-nystagmus and obstructive hydrocephalus as the initial signs of mucormycosis of the central nervous system. We believe that this presentation is unique. The following case report illustrates some of the difficulties we encountered in diagnosing and managing this type of infection.

**Case Report**

This 37-year-old Indian woman from Calcutta presented for evaluation of positional vertigo. Her illness began several weeks before admission with the acute onset of positional vertigo, nausea, and emesis. Her vertigo was lateralized in that she could induce an attack by turning the head to the left lateral position, or by reclining on her left side. Her past medical history was completely unremarkable, without serious illness requiring medical or surgical treatment.

**Examination.** Germaine findings on admission included mild lethargy and loss of mental acumen. Vertigo, nystagmus, and emesis were induced when she turned her head to the left. Computerized tomography (CT) scanning demonstrated hydrocephalus (Fig. 1 left) with dilatation of the fourth ventricle (Fig. 1 right). On pneumoencephalography (PEG), air did not enter the ventricular system. Cerebrospinal fluid (CSF) findings at the time of PEG revealed normal parameters, with a protein content of 16 mg%, glucose levels of 89 mg%, and one white blood cell (WBC). Gram staining and india ink preparations were negative.

Subsequently, external ventriculostomy was performed; the opening pressure was 120 mm Hg and the CSF was cloudy. The ventricular fluid contained a protein value of 80 mg%, a glucose level of 89 mg%, 319 WBC's, and three red blood cells. Gram stain and india ink preparations were again negative. Cultures for bacteria and fungi were negative. Cytological examination of the CSF revealed numerous non-segmented hyphal forms.

**Operation.** Craniotomy of the posterior fossa was performed; the opening pressure was 120 mm Hg and the CSF was cloudy. The ventricular fluid contained a protein value of 80 mg%, a glucose level of 89 mg%, 319 WBC's, and three red blood cells. Gram stain and india ink preparations were again negative. Cultures for bacteria and fungi were negative. Cytological examination of the CSF revealed numerous non-segmented hyphal forms.
Mucormycosis with positional nystagmus and hydrocephalus

Postoperative Course. Treatment with intravenous amphotericin B produced gratifying results, and the patient returned to normal health. Extensive investigation of this patient for evidence of compromised immunity or underlying disease was unrewarding, and failed to reveal any abnormalities.

Discussion

Positional nystagmus (PN) is well recognized as a sign of posterior fossa disease. The presence, degree, and persistence of both vertigo and nystagmus have provided the basis for subdivision of PN into three types: PN I, II, and III. Clinical experience suggests, however, that despite subdivisions into types, the etiology of PN remains undiagnosed most of the time. In this particular instance, the clinical sign proved to be valid for the site of pathology.

Mucormycosis, a severe infection produced by a fungus of the class Phycomycetes, is regarded by many as the most acutely fatal of all fungal diseases. The clinical syndrome can take one of several forms (Table I). The best recognized disorder is the facial-rhino-cerebral form in association with uncontrolled diabetic acidosis. Typically, the disease produces pain and congestion in and about the nose and eyes. Necrotic bloody nasal discharge, dark turbinates, perinasal swelling, and orbital chemosis follow. Ultimately, ptosis, exophthalmos, ophthalmoplegia, and a fulminating encephalitis occur. Other patients prone to this infection are those with altered immunity from a wide variety of causes, such as steroid or immunosuppressive therapy. Malignancy of the lymphoma and leukemia are also associated conditions.

Diagnosis requires biopsy of involved tissue with demonstration of the characteristic hyphae in pathological sections. A caveat worthy of mention is the frequent inability to culture this organism from either brain tissue or CSF even when one applies expert mycological procedures and techniques. Fresh cerebral tissue known to harbor the characteristic mycelium is often negative on culture. This does not seem to be the case when one is dealing with paranasal sinus tissue. Here one of the more common fungi isolated is Rhizopus, one of the three genera, along with Mucor and Absidia, of the class Phycomycetes. The literature contains frequent examples of this inability to culture the organism successfully when one is dealing with cerebral material.

The pathophysiology of this disease relates to the malignant and invasive qualities of the hyphae once they are in tissue. They have a special affinity to invade the walls of blood vessels. Masses of the hyphae fill the lumina of vessels, producing thrombus.

TABLE 1

<table>
<thead>
<tr>
<th>Rhino-Orbital-Cerebral Type</th>
<th>Pulmonary-Disseminated Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>metabolic acidosis</td>
<td>immunosuppressed drugs</td>
</tr>
<tr>
<td>diabetes</td>
<td>malignant leukemia</td>
</tr>
<tr>
<td>renal disease</td>
<td>lymphoma</td>
</tr>
<tr>
<td>vomiting (in infants)</td>
<td></td>
</tr>
<tr>
<td>diarrhea (in infants)</td>
<td></td>
</tr>
<tr>
<td>tooth extraction</td>
<td>burns</td>
</tr>
<tr>
<td>penetrating head injury</td>
<td></td>
</tr>
</tbody>
</table>

FIG. 1. Computerized tomography scan demonstrating enlargement of the ventricular system (left) and enlargement of the fourth ventricle (right).

FIG. 2. Photomicrograph of the operative specimen. The organisms are visible in both cross and longitudinal section and appear as large, non-septate hyphae. H & E, × 400.
formation, necrosis, and ischemic infarction distally. The organism proliferates outward from the nose, paranasal sinuses, and orbital areas to invade the cribriform plate and pass upward into the cerebral leptomeninges and frontal lobe.

Therapy rests on the cornerstones of: 1) control of the associated metabolic disturbances; 2) extensive debridement of involved tissue, and 3) the administration of amphotericin B intravenously. Prior to 1958, surgical excision and debridement, together with supportive care, were the main treatment modalities. In 1958, Chick, et al., reported on the efficacy of amphotericin B treatment of Rhizopus in rabbits. Thereafter, amphotericin was considered essential in treating this infection. Given intravenously, the drug can be lifesaving; however, it is associated with numerous serious side effects, including nephrotoxicity and azotemia. These require close and constant monitoring.

To our knowledge, this patient is unique from several points of view. A rather extensive investigation for the presence of underlying associated disease or evidence of immunosuppression was unrewarding. As well as can be determined, this illness appeared against a background of normal health. Second, we believe that Mucor has never been reported as producing an obstructing hydrocephalus.

References

Address reprint requests to: Patrick J. Sweeney, M.D., Department of Neurology, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44106.