

## INSECT BITE CAUSING MUCORMYCOSIS REPORT OF TWO CASES

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Mucorales are ubiquitous fungi in nature, but disease is limited in most cases to immunocompromised hosts. Different forms of mucormycosis are described as per the anatomical locations. The most commonly reported form, rhinocerebral, is seen primarily in diabetics, especially those with ketoacidosis, following airborne inhalation of spores.<sup>1</sup> Acquisition via the cutaneous or percutaneous route also occurs with traumatic disruption of skin barriers, burns, biopsy, direct injection or catheters<sup>2</sup>. We report two cases of mucormycosis which occurred following insect bites.

### CASE -1

A 23-year-old healthy young man was admitted elsewhere in February 2007 with sudden onset development of right-sided ear pain, facial swelling, numbness and vision loss. On enquiry, history revealed accidental entry five days prior of an insect into the right ear. The insect was removed after two days. Based on the clinical findings and computerized tomography (CT); the symptoms were attributed to right-sided malignant otitis externa with orbital cellulitis and cavernous sinus thrombosis. Despite antibiotics, there was no improvement. Nine months later in November 2007, he was admitted to our institution with headache and right-sided hearing-loss, facial swelling and proptosis (Fig. 1). Neurological examination revealed proptosis of right eye with complete blindness as documented by inability to perceive light; palsies of cranial nerves II, III, V, VI, VII and VIII on the right. CT imaging revealed right cavernous sinus thrombosis (Fig. 2) with a right internal carotid artery (ICA) aneurysm. He underwent right orbital exenteration and clipping of the right ICA aneurysm. Histopathology showed broad aseptate hyphae with occasional right angle branching consistent with mucormycosis (Fig. 3). He was treated with amphotericin B at a dose of 1 mg/kg/day which was later changed to lipid formulation of L Amphotericin B (LAmB) at 5 mg/kg/day in view of worsening renal insufficiency. The patient recovered satisfactorily and was discharged in January 2008. He remains healthy two years after the treatment.

### CASE REPORT-2

A 58-year-old man, known case of type-2 diabetes for 15 years, well controlled on treatment, presented four months ago with complaints of pain in the left ear and left sided facial weakness which occurred five days after removal of an insect from his left ear by an ENT specialist. CT scan was suggestive of erosion in the inferior meatal wall without any intracranial complications. He was treated elsewhere for malignant otitis externa and was started on meropenem and levofloxacin. However he developed induration and diffuse swelling over ipsilateral infraclavicular area with rising fever. A repeat CT scan after four days showed diffuse facial and neck swelling for which he underwent debridement. Specimen on histopathological examination was consistent with mucormycosis and he was started on LAmB and caspofungin at 70 mg/day as an adjuvant therapy.



Fig1



Fig2



Fig3

Multiple debridements were done regularly. As his condition worsened, partial parotidectomy and retro auricular radical debridement was done. Histopathological examination again showed mucor and although the culture was done without homogenization,

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no growth was obtained. The patient was discharged after receiving caspofungin for 14 days and LAmB for 42 days. After 15 days he was readmitted with complaints of discharge from the same ear. By this time he had developed left eye proptosis, bilateral VI nerve palsy and restricted neck movements. Magnetic Resonance Imaging (MRI) of the brain and skull base revealed marked fullness of the soft tissue along the posterior nasopharynx extending on either side (Fig. 4) which had increased when compared with previous imaging along with atlantoaxial dislocation (Fig. 5). As almost all vital areas near the base of skull were necrotic and extensive debridement was impossible, he was treated with LAmB 5mg/kg, hyperbaric oxygen and iron chelator deferasirox 20mg/kg/day. Despite aggressive therapy, the patient's condition deteriorated, and he died two months after the second admission.

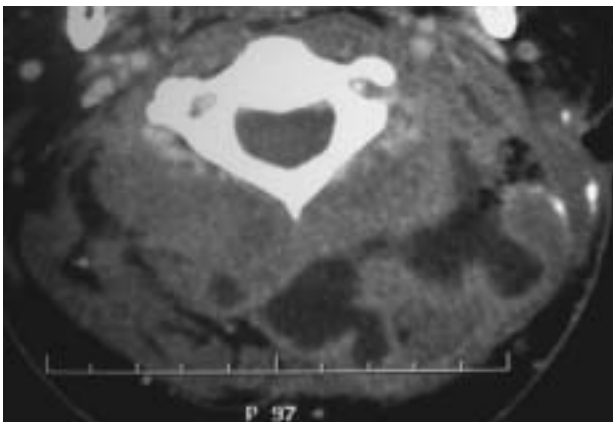


Fig4

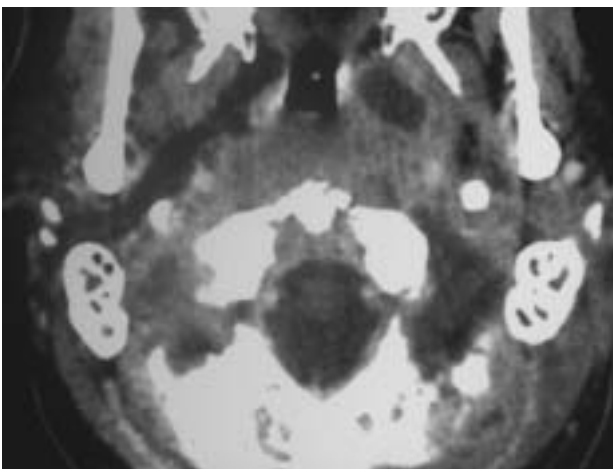


Fig5

## DISCUSSION

Mucormycosis is caused by fungi of the order of Mucorales and Entomophthorales<sup>3</sup>; Mucorales (*Rhizopus*, *Mucor*, or *Absidia*) are more common than Entomophthorales. Agents of mucormycosis are ubiquitous in the environment that are commonly found in decaying organic substrates, including bread, fruits, vegetable matter, soil, compost piles and animal excreta.<sup>3-4</sup> There is some evidence that they are present in the gastrointestinal and respiratory tracts of healthy individuals.<sup>3</sup> These fungi are characterized by broad (10 to 20  $\mu$ m diameter), ribbon-like hyphae with only occasional or sparse septae with right angle branching which is distinct from *Aspergillus* species.<sup>5</sup>

Mucormycosis may be seen histologically with hematoxylin and eosin staining, Grocott-Gomori methenaminesilver nitrate staining, and occasionally periodic acid-Schiff (PAS) staining whereas the hyphae of entomophthorales are readily visible on routine hematoxylin and eosin staining but, in contrast to most other fungal pathogens, are not as well demonstrated by PAS or silver staining.<sup>5</sup> The role of fungal cultures in establishing the diagnosis is more limited as cultures for the organism may not be positive despite the presence of widespread and aggressive disease.<sup>6</sup> The organisms show little regard for tissue barriers and cross fascial planes readily in the course of infection. They invade tissue with a particular affinity for blood vessels, leading to thrombosis and tissue ischemia.<sup>1,7</sup> Mucormycosis mainly presents in 5 locations: the sinonasal tract, lungs, gastrointestinal tract, central nervous system, and skin.<sup>4</sup> Atypical presentations of mucormycosis like nasopharyngeal mucormycotic osteitis,<sup>8</sup> isolated central nervous system involvement<sup>8</sup> and primary cutaneous mucormycosis in a healthy young girl following an insect bite<sup>9</sup> on an extremity have also been reported. The most common underlying risk factors for invasive mucormycosis include poorly controlled diabetes-mellitus, metabolic acidosis, high dose glucocorticoid therapy, penetrating trauma, persistent neutropenia, and chelation therapy with deferoxamine in patients on dialysis or chronically transfusion dependent.<sup>4</sup> Less commonly, it occurs in the setting of renal failure, diarrhea, and malnutrition in low birth infants and in HIV patients.<sup>4</sup>

The first case of mucormycosis was reported by Platauf in 1885<sup>4</sup>, but it was not until 1955 that Harris reported the first survival from mucormycosis.<sup>6</sup> Use of amphotericin B, wide and perhaps, multiple surgical debridements, and control of the underlying metabolic disease are the three most important factors in improving outcome in mucormycosis, resulting in survival rates of up to 85%.<sup>8</sup> Adjuvant therapies include hyperbaric oxygen<sup>10</sup>, deferasirox, an iron chelating agent<sup>11</sup>, caspofungin<sup>12</sup> and salvage or step down treatment with posaconazole.<sup>13</sup> In contrast to deferasirox, desferrioxamine functions as a siderophore and enhances risk of mucormycosis

These two cases of mucormycosis are reported for the following reasons. The unusual mode of infection through insect bites the slower pace of the illness than what is commonly thought, lack of suspicion of diagnosis in the initial stages and use of novel adjuvant therapy as deferasirox, especially if complete surgical debridement is not possible

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