

Isolated cerebral mucormycosis in a patient with diabetic ketoacidosis and intravenous drug use

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Abstract

Background: Isolated Cerebral Mucormycosis is an uncommon fatal infection caused by Mucor, an opportunistic micro-organism. Patients in increased risk for infection are intravenous drug users, immunocompromised and uncontrolled diabetics. Imaging findings are non-specific and the definitive diagnosis requires tissue sampling. Rapid induction therapy with amphotericin B may improve patient's prognosis in early stages of the infection.

Case report: A 31-year-old male with past medical history of Diabetes Mellitus type 1, intravenous drug use and insulin treatment non-compliance was found unresponsive by his girlfriend at home. The patient was taken to the emergency room by the emergency medical services where he was found to be in Diabetic Ketoacidosis. Physical exam revealed fever, altered mental status and left hemiparesis. Magnetic Resonance Imaging (MRI) of the brain was requested revealing a lesion in the frontal lobe on the right side with severe surrounding edema. Patient underwent urgent decompressive craniectomy with subsequent biopsy of the right frontal lobe lesion reporting Mucormycosis. The patient presented with progressive neurological exam deterioration and subsequently died secondary to cardiopulmonary failure.

Conclusion: Cerebral Mucormycosis is a rare life threatening condition associated with intravenous drug use and uncontrolled Diabetes Mellitus. Imaging findings are non-specific and histopathological examination is the gold standard test for diagnosis. The infection requires prompt antifungal medication administration with amphotericin B and neurosurgery intervention for debridement of the affected tissue.

Keywords

Mucormycosis; intravenous drug user; diabetes mellitus; magnetic resonance imaging; spectroscopy.

Introduction

Cerebral Mucormycosis is an uncommon infection with high morbidity and mortality rate caused by opportunistic microorganisms such as *Mucor* and *Rhizopus* which belong to the Fungi kingdom and Mucorales order [1]. The first case of Mucormycosis affecting the central nervous system was reported by Paltauf in 1885 [1,2]. Predisposing factors include intravenous drug use, immunosuppression and uncontrolled Diabetes Mellitus [1,2]. Most cases of intracranial Mucormycosis extend from sinus disease resulting in Rhinocerebral Mucormycosis [1,2]. Isolated Cerebral Mucormycosis refers to infection confined only to the cerebrum, brainstem or cerebellum in the absence of other primary sites of infection [1]. We describe a case of Isolated Cerebral Mucormycosis in an intravenous drug user with decompensated Diabetes Mellitus type I complicated by Diabetic Ketoacidosis resulting in a fatal outcome.

Case History

A 31-year-old male with past medical history of Diabetes Mellitus type 1 with multiple episodes of Diabetic Ketoacidosis, intravenous drug use and insulin treatment non-compliance was found unresponsive by his girlfriend at home. The patient was taken to the emergency room where he was found to be in Diabetic Ketoacidosis with altered mental status, leukocytosis and fever. On Physical examination the patient was difficult to arouse and demonstrated left hemiparesis. MR of the brain revealed a heterogeneous lesion with two hemorrhagic rings and restricted diffusion involving the frontal lobe on the right side compromising the basal ganglia (Figure 1). MR spectroscopy of the brain lesion revealed elevated choline (Cho), myoinositol (mI), lactate (Lac) and lipids with depleted N-acetyl aspartate (NAA) (Figure 2). The patient was noted to have fixed and dilated pupils and subsequently underwent decompressive craniectomy. Biopsy of the frontal lobe lesion revealed reactive neutrophils with perivascular lymphocytes, acute inflammation and macrophages with multinucleated giant cell formation associated with fungal infection consistent with Mucormycosis (Figure 3).

The patient experienced increasing intracranial pressure despite hypertonic saline administration and his neurologic status progressively deteriorated over a 3 days period. The neurosurgery team discussed the poor prognosis with family, who elected to withdraw care on day 7 of hospitalization. The patient subsequently died secondary to cardiopulmonary failure.

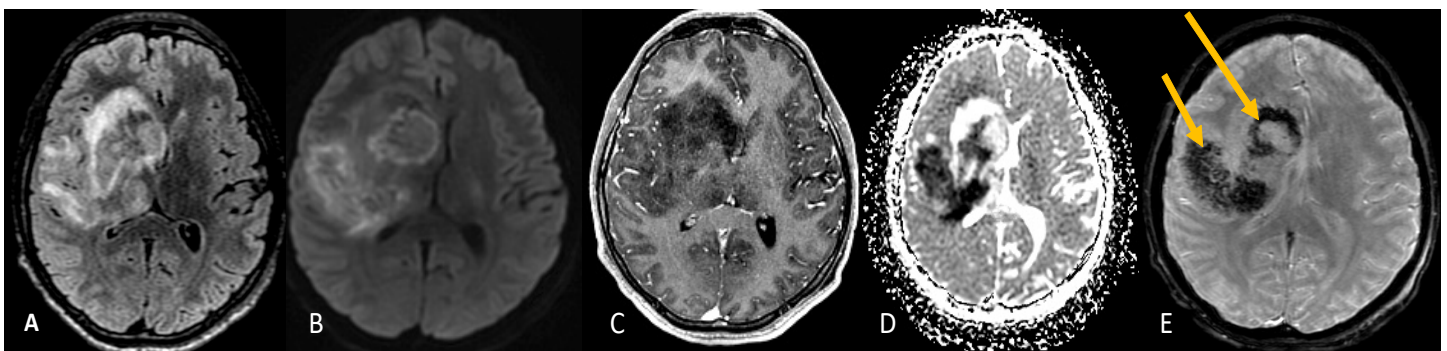


Figure 1: Brain MR, Axial views. (A) T2-weighted FLAIR, (B) diffusion-weighted imaging, (C) T1-weighted post-gadolinium, (D) apparent diffusion coefficient map and (E) susceptibility weighted imaging reveal a non-enhancing heterogeneous mass with two hemorrhagic rings (arrows) and restricted diffusion involving the frontal lobe on the right side compromising the basal ganglia.

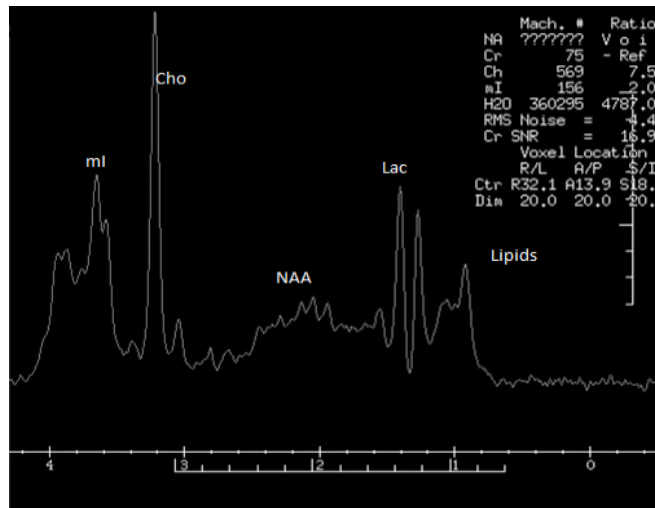


Figure 2: MR Spectroscopy with voxel placed over the right basal ganglia lesion shows markedly elevated choline (Cho), elevated myoinositol (ml), lactate (Lac) and lipids; depleted N-acetyl aspartate (NAA). The spectroscopy profile corresponds to a pyogenic abscess.

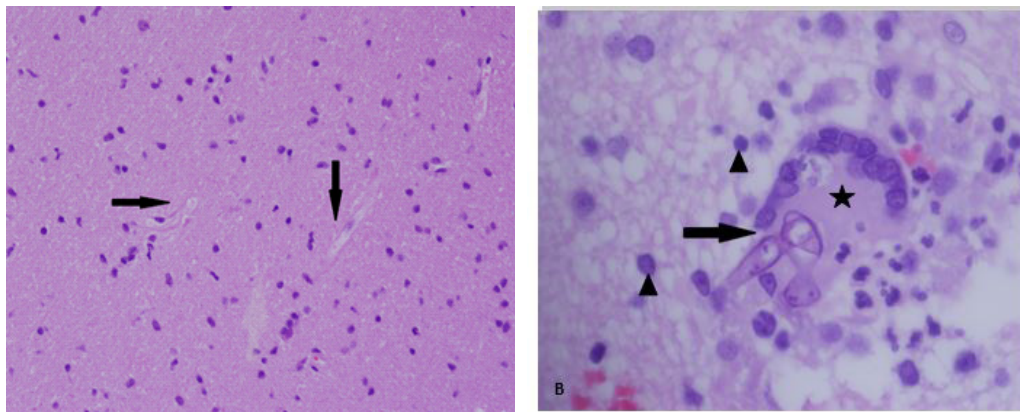


Figure 3: Hematoxylin and Eosin stain of biopsy specimen at (A) x400 and (B) x600 magnification demonstrate tangential cut hyphae (arrows). Findings were consistent with Mucormycosis infection. Multinucleated giant cell (star), lymphocytes (arrowshead).

Discussion

Mucormycosis is a fungal infection most commonly caused by *Rhizopus* and *Mucor* micro-organisms. The most common affected sites by Mucormycosis are skin, lung and sinuses [1,2]. The majority of intracranial Mucormycosis cases extend from sinus disease resulting in Rhinocerebral Mucormycosis. Imaging findings of this condition include opacification of the nasal cavity and maxillary, sphenoid, ethmoid and frontal sinuses; periorbital cellulitis with stranding of the extraconal adipose tissue and frontal lobe involvement secondary to the extension of the Mucormycosis infection through the cribriform plate [3].

The central nervous system is affected in about 30% of the cases of which only about half have isolated involvement [4]. Isolated Cerebral Mucormycosis is a rare and often fatal condition that infects the cerebrum, brainstem and cerebellum. Mortality rates exceed 60% in reported cases [1,4,5], if not treated promptly. Predisposing risk factors include intravenous drug use and in less proportion, uncontrolled diabetes and immunosuppression [4,6,7]. Symptoms in a patient with Isolated Cerebral Mucormycosis include headache (44%), fever (41%), hemiparesis (38%), and altered mental status (21%) [4,8].

Imaging diagnosis of this condition is challenging and requires a group of imaging modalities such as diffusion weighted images, apparent diffusion coefficient map and magnetic resonance spectroscopy to increase accuracy.

Computed tomography of the head may demonstrate an enlarging heterogeneous mass and ring appearing lesions with severe surrounding edema [1]. MR Imaging findings include a heterogeneous irregular lesion or lesions with intracavitary projections and restricted diffusion [1]. Our patient presented with a large heterogeneous mass with two hemorrhagic rings and restricted diffusion involving the frontal lobe on the right side compromising the basal ganglia. MR spectroscopy may reveal decreased N-acetyl aspartate with presence of lactate, amino acids and lipids [4,9,10]. Our patient's MR spectroscopy with voxel placed on the frontal lobe lesion showed necrosis with increased lipids and lactate plus negligible N AA indicating neuronal loss. MR spectroscopy also demonstrated a 10-fold increase in choline corresponding to a high proliferative index. Cerebral Mucormycosis usually involves the basal ganglia because the sporangiospores of the causative micro-organism facilitates its distribution to the vascularized basal ganglia [4,5].

Differential diagnoses of Cerebral Mucormycosis include Aspergillosis, Cryptococcosis, Histoplasmosis and neoplastic process such as Lymphomas. Aspergillosis may present as a solid enhancing lesion referred to aspergilloma or multiple areas of ischemia demonstrating several hyperintensities on T1 weighted imaging (T1WI). Cryptococcosis shows cryptococcomas, (chronic granulomas) as masses that are low intensity on T1WI and high intensity on T2 weighted imaging (T2WI). Histoplasmosis reveals lesions that are hyperintense on T2WI and hypointense on T1WI with perilesional edema and ring enhancement. Lymphomas usually demonstrate hypointense signal on T1WI, iso to hypointense signal on T2WI and avid homogeneous enhancement in post contrast studies [11,12]. Definitive diagnosis of Isolated Cerebral Mucormycosis requires surgical biopsy of the brain lesion [4]. Broad, non-septate hyphae, and wide angles may be seen on Hematoxylin and Eosin stain of the biopsied tissue [4].

The medication of choice for isolated Cerebral Mucormycosis is Amphotericin B dosed between 0.5 mg/kg/day and 1.0 mg/kg/day which decreases reported mortality from 92% to 41% [4,13]. In Cerebral Mucormycosis the treatment of choice is radical surgical debridement with concomitant pharmacological management [14].

Conclusion

Isolated Cerebral Mucormycosis is an uncommon life threatening condition that requires a high degree of clinical suspicion. Patients with history of intravenous drug use and uncontrolled Diabetes Mellitus presenting with fever, vomit, severe headaches and hemiparesis suggest fulminant Cerebral Mucormycosis. Imaging findings in such patients are not specific for Mucormycosis. A group of imaging modalities are required to increase accuracy. Large abscesses involving the basal ganglia in intravenous drug users should raise awareness of Isolated Cerebral Mucormycosis.

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