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Case report

Isolated cerebral mucormycosis: A case discussion

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ABSTRACT

We report a case of a 32-year-old male with a history of type 1 diabetes, inhaled drug use, and alcohol use disorder, who presented with encephalopathy, holocranial headaches, neck pain, confusion, and generalized tonic-clonic seizures. The patient initially presented at a rural community hospital with a fever and was found to be in diabetic ketoacidosis (DKA). He was also hemodynamically stable but stuporous, prompting intubation to protect his airway. Despite initial treatment measures, his neurological condition worsened and he remained ventilator-dependent. Key findings include a high glucose level, presence of ketones, and evidence of drug use. Blood cultures showed no growth, but his febrile state persisted. Cerebrospinal fluid (CSF) analysis revealed mild pleocytosis, hyperglycorrhachia but normal protein, with no growth. Neuroimaging showed right hemispheric slowing on EEG and diffusion restriction in the right frontal lobe on MRI. The patient's neurological status worsened on the second day of admission, manifesting as sluggish pupillary reflexes, right third nerve palsy, and decerebrate posturing. Emergent MRI suggested cerebral edema, leading to initiation of hypertonic saline. This case highlights the diagnostic challenges and critical management considerations in a patient with multiple comorbidities presenting with unexplained neurological deterioration, emphasizing the importance of a comprehensive and timely approach to diagnosis and treatment.

Introduction

Mucormycosis, an opportunistic fungal infection, typically affects individuals with severe immunosuppression or uncontrolled diabetes mellitus [1]. It is commonly associated with pulmonary and rhino-orbital-cerebral involvement, but isolated cerebral mucormycosis (ICM) is an exceedingly rare manifestation [2]. We report an unusual case of ICM in a 32-year-old male with a history of type 1 diabetes, inhaled drug use, and alcohol use disorder, who presented with encephalopathy, seizures, and diabetic ketoacidosis. This case highlights the unique challenges of diagnosing and treating this rare and often fatal disease entity. The report underscores the necessity of maintaining a high index of suspicion in vulnerable patient populations and emphasizes the importance of early detection and management for improved patient outcomes.

Case

A 32-year-old male with a history of type 1 diabetes, inhaled drug use and alcohol use disorder was transferred to our facility from a rural community hospital for encephalopathy. Prior to his admission, the patient had experienced two days of holocranial headaches, neck pain and confusion followed by multiple generalized tonic-clonic seizures (GTCS) while working in his garden. The patient presented to the nearest Emergency Department with a fever of 101.2 °F but hemodynamically stable via ambulance. He was stuporous on exam, unable to protect his airway and therefore was intubated. Pertinent blood work revealed a blood glucose of 750 mg/dL, sodium 127 mmol/L, ESR and CRP were normal. His urinalysis showed 4 + ketones, with beta-hydroxybutyrate of 1.22 mmol/L, indicating diabetic ketoacidosis (DKA). His urine drug screen was positive for benzodiazepines and amphetamines. As he had a neutrophil-predominate leukocytosis and fever, blood cultures were drawn, and broad spectrum antimicrobials (acyclovir, ampicillin, ceftriaxone, and vancomycin) were initiated along with insulin drip. A noncontrast CT head was unremarkable. He was loaded and started on fosphenytoin 100 mg IV every 8 h then transferred to our hospital. On admission to the Neuro Intensive Care Unit, he was stuporous, with intact brainstem reflexes, localizing with his right upper and lower

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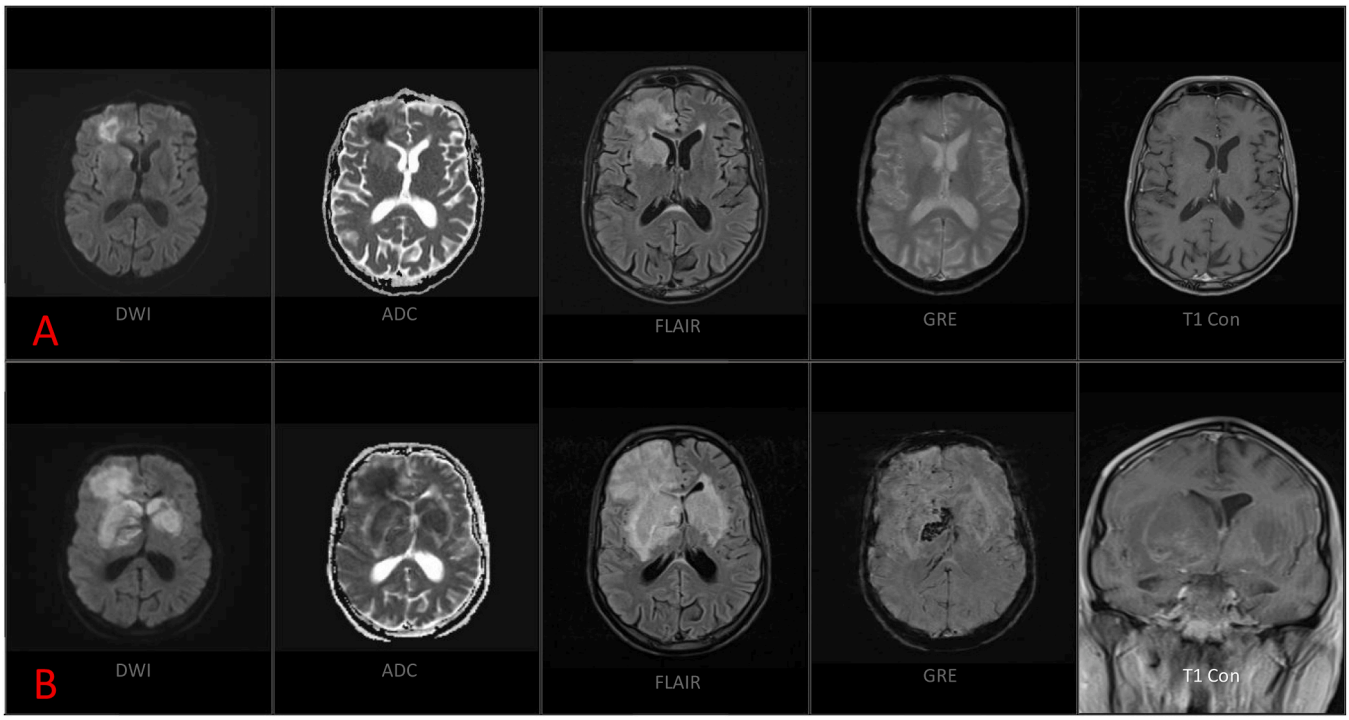

Fig. 1. A: MRI Brain w/wo Contrast: Diffusion restricting lesions in right frontal lobe with FLAIR signal abnormality in the right basal ganglia and anterior limb of internal capsule and associated small foci of petechial hemorrhage. Associated local mass effect with sulcal effacement, partial effacement of right lateral ventricle, and minimal right-to-left midline shift without pathologic intracranial enhancement. B: New diffusion restricting lesions in left basal ganglia. Marked progression of right frontal lobe cytotoxic and vasogenic edema with worse leftward midline shift (9 mm), effacement of the third ventricle, obstructive hydrocephalus, and subfalcine herniation without intracranial enhancement.

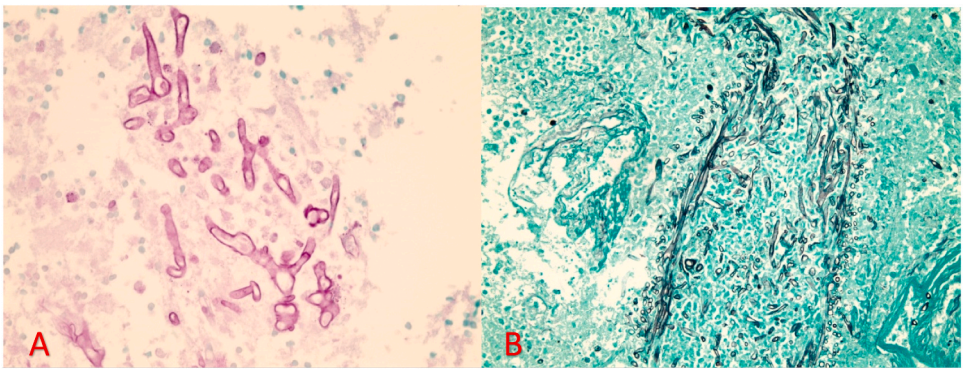

Fig. 2. A: High-power magnification of brain tissue stained with Periodic Acid-Shiff (PAS) showing characteristic pauciseptate ribbon-like hyphae with wide angle branching, suggestive of mucormycosis. B: Medium-power magnification of brain tissue stained with Grocott's Methenamine Silver (GMS) showing black colored Mucor hyphae.

extremities and flaccid on the left side. An EEG was performed shortly upon arrival revealing a moderate right hemispheric generalized slowing without epileptiform discharges. An MRI brain was obtained, promptly after, showing diffusion restriction in the right frontal lobe, see Fig. 1 A. During his hospitalization he remained obtunded and ventilator dependent. Despite blood cultures revealing no growth, he remained febrile thus a lumbar puncture was obtained showing CSF WBC count of 15 cells per mm^3, RBC 12 cells per mm^3, CSF glucose of 397 mg per dL (Serum 144 mg per dL), CSF protein 49 mg per dL, however no growth on CSF cultures. On day 2 of his admission, the patient deteriorated neurologically, developing sluggish pupillary reflexes, right third nerve palsy and decerebrate posturing. Hypertonic saline was initiated for suspected cerebral edema and an emergent MRI brain with and without contrast was obtained, see Fig. 1B.

The MRI revealed a new contralateral subcortical lesion with obstructive hydrocephalus. Neurosurgery was consulted and the patient underwent an External Ventricular Drain. Given the CSF profile coupled with the new MRI findings, the patient was started on IV Amphotericin B and underwent a flexible fiberoptic endoscopy of the nasal cavity and paranasal sinuses, which did not show evidence of fungal invasion. Subsequently, a stereotactic-guided biopsy of his right frontal lesion was performed and sent for pathologic analysis, see Fig. 2.

Discussion

Mucormycosis is a sporadic but tenacious fungus that predominantly affects patients with uncontrolled diabetes mellitus or severe immunosuppression. With an annual global prevalence of 910,000 cases predominately arising in Asian countries, it has an estimated prevalence of 1.73 cases per million [1]. While the most common risk factor in Asia is

diabetes mellitus, in Europe and the United States hematological malignancies or immunosuppression linked to organ transplantation are among the significant risk factors [1]. Mucormycosis can spread from the nasal cavity to the adjacent paranasal structures commonly involving the septum, middle meatus, and turbinate. Depending on the disease severity and host immunity, the mucosa and bone can become infected via angioinvasion or bony erosion [2]. Mucormycosis is prefixed rhino-orbital-cerebral (ROCM) when the invasive fungus invades the nasal sinuses, orbit, and brain [2]. In ROCM, the sphenopalatine and internal maxillary arteries are involved leading to the invasion of the brain or orbit. The typical presentation of these patients is usually a unilateral headache, facial swelling, or nasal/sinus congestion. In rare cases, seizures and encephalopathy leading to stupor can be seen [2]. Isolated Cerebral Mucormycosis (ICM) is an exceedingly rare presentation of the fungal infection affecting only 16 % of patients [2]. We present a rare case of mucormycosis presenting as ICM highlighting the diagnostic challenges and treatment.

Although diabetes and an immunocompromised state are risk factors for mucormycosis, these are classically associated with pulmonary and ROCM and have rarely been reported in ICM. This entity typically results from intravenous drug abuse as was the case in our patient. It is presumed that ICM results from an episode of fungemia secondary to intravenous drug abuse [3]. Since the fungal spores are inoculated directly into the blood through contaminated illicit drugs, some microspores might escape pulmonary capillary filtration, and then enter the brain through arterial circulation [3].

Patients with ICM typically present with subacute onset of headache (44 %), fever (41 %), hemiparesis (38 %), and altered mental status (21 %) [4]. The majority cases of ICM tend to involve the basal ganglia due to the specific size of mucor sporangiospores, thought to facilitate distribution through the striatal arteries to the heavily vascularized basal ganglia [5]. The predilection of mucor for the basal ganglia may also be due to high levels of iron in this region, since iron has been shown to stimulate growth of mucor [6]. CSF analysis generally reveals lymphocytic pleocytosis with low glucose and elevated protein. In diabetic patients, serum glucose should be measured at the time of lumbar puncture so CSF glucose can be interpreted correctly. In addition to standard CSF analysis, recent studies have suggested that India ink staining of CSF and PCR-based analysis of RNA isolated from CSF may facilitate early detection of mucormycosis [7]. MRI features may include an irregular abscess cavity wall, intracavitary projections, and an abscess cavity with prominent diffusion restriction. MR spectroscopy may demonstrate presence of lipids, lactate, and amino acids, with a depleted N-acetyl aspartate [8]. While stereotactic biopsy has been effective in some cases, it may provide insufficient tissue to diagnose ICM. As a result, open surgical biopsy may be advisable depending on clinical scenario.

Treatment of ICM should be prompt and requires a certain level of clinical suspicion [5]. Lesions in the basal ganglia, rapidly progressive symptoms, and a history of intravenous drug abuse should raise suspicion for the early initiation of treatment and tissue sampling as delayed treatment is associated with poor survival [6]. Mortality of ICM exceeds 60% and outcomes are also dependent on the degree of immunosuppression, extent of infection, presence of other comorbidities such as renal disease, presence of hemiparesis, and type of treatment provided [5,6,9]. Patients who received amphotericin and underwent tissue sampling had double the chances of survival [10]. The standard treatment of ICM includes surgical debridement and amphotericin B. The lipid formulation of amphotericin (liposomal amphotericin B) with a starting dose of 5 mg/kg/day up to 10 mg/kg/day is generally preferred over amphotericin deoxycholate as it is less nephrotoxic [11]. While the intrathecal administration of amphotericin B has been employed with variable success, it is not currently considered standard of care [12].

Surgical staining of this patient's right frontal lobe lesion with methenamine silver and PAS showed an organizing fungal abscess with hyphal organisms and focal chronic brain tissue inflammation with gliosis, morphologically consistent with mucormycosis and clinically consistent with the suspected diagnosis of ICM, see Fig. 2. Despite the projected poor prognosis, his family pursued all measures. He was continued on IV amphotericin B, a tracheostomy and percutaneous endoscopic gastrostomy were performed, and he was eventually discharged to a Long-Term Care Facility in a ventilator-dependent state.

CRediT authorship contribution statement

Harneel Saini: Conceptualization, Investigation, Writing-Original Draft, Writing-Review & Editing, Visualization. **Harinoor Mann:** Investigation, Writing-Original Draft. **Ishveen Saini:** Investigation, Writing-Review & Editing, Visualization. **Nitin Bhanot:** Conceptualization, Investigation, Writing-Original Draft, Writing-Review & Editing, Visualization. **Kevin Kelly:** Conceptualization, Investigation, Writing-Original Draft, Writing-Review & Editing, Visualization. **Sandeep Rana:** Conceptualization, Investigation, Writing-Original Draft, Writing-Review & Editing, Visualization, Project administration.

Ethical approval

Not applicable.

Consent

Written informed consent for publication of the clinical details and/or clinical images was obtained from the patients mother.

Conflict of interest

I confirm that I nor other authors on this manuscript have a financial or other interest in the subject/matter of the work that may be considered as constituting a real, potential or apparent conflict of interest.

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