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Case Report

Cerebral Mucormycosis without Rhino-Orbital Involvement in a Patient with Chronic Kidney Disease

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ABSTRACT

Isolated cases of cerebral mucormycosis demand high clinical suspicion and prompt diagnosis and treatment. In the present case, the patient was a young diagnosed case of chronic kidney disease (CKD) for two years on maintenance hemodialysis, presented with symptoms of headache and increased intracranial pressure, which necessitated both emergency surgical and medical management and was both diagnosed and managed efficiently. Early recognition of clinical and radiological cues with early institution of a medico-surgical approach, with proper containment of underlying predisposing conditions, is vital for managing mucormycosis. The case elucidates that mucormycosis can present as an isolated cerebral abscess without rhino-orbital involvement. CKD should be considered as a possible immunocompromised state predisposing to mucormycosis.

KEYWORDS: Cerebral abscess; Kidney diseases; Mucor

INTRODUCTION

Mucormycosis represents a wide spectrum of diseases caused by a ubiquitous fungi, 'mucor'. The last couple of years have witnessed a tremendous surge in the cases of Mucorales, especially with the ongoing COVID-19 pandemic contributing to significant morbidity and mortality. Having a predilection to affecting immunocompromised patients, the disease is primarily seen in uncontrolled diabetics, patients on corticosteroids or other immunosuppressive therapy, transplant recipients, and patients undergoing radiotherapy or chemotherapy.[1] Mucormycosis has been described in three major forms, rhino-orbital and systemic are the more common forms, and isolated cerebral mucormycosis is an infrequent presentation, mainly affecting immunocompromised patients or patients with a history of intravenous drug abuse.[2]

Chronic kidney disease (CKD) leads to impairment of the normal reaction of the innate and adaptive immune systems, which predisposes patients to an increased risk of infections, virus-associated cancers, and a diminished vaccine response.[3] Infections are a significant cause of morbidity and mortality among patients at all stages of CKD and constitute the second most common cause of death.[4]

Here, we report a case of a young patient of CKD on maintenance hemodialysis (HD) who presents with isolated cerebral mucormycosis.

CASE REPORT

A young man in his 20s presented with a severe holocranial headache for 15 days. He was diagnosed with CKD two years ago and was on maintenance HD. There was no history of intravenous drug abuse or significant exposure to fungal spores. Headache was

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associated with multiple episodes of non-bilious, on-projectile vomiting. The patient did not report any complaints of fever, seizures, altered sensorium, or loss of consciousness.

On presentation to the Emergency Department, the patient had signs of increased intracranial pressure, including bradycardia, raised blood pressure, and blurred vision. A general physical examination revealed no abnormality except bilateral symmetrical painless pitting edema.

An urgent non-contrast computed tomography (NCCT) head was done that revealed well-defined, discrete to coalescent, centrally hypodense lesions with hyperdense rim, the largest measuring 3.1x2.7×1.5 cm^3 with surrounding edema in the right posterior temporoparietal lobe causing a mass effect in the form of effacement of ipsilateral sulcal spaces with a midline shift of 12.2mm towards the left side (Fig 1A-B). Other investigations are detailed below in Table 1.

FIGURE CAPTIONS

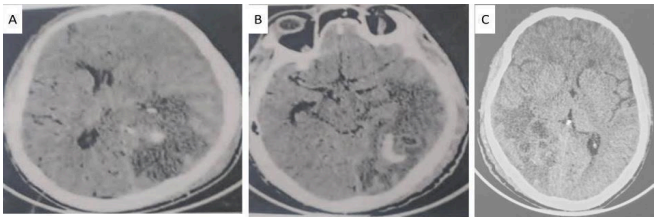

Figure 1. Computed tomography (CT) images of the patient in different time intervals. A and B: NCCT head of the patient at the time of admission. Image showing multiple hypo dense lesions with surrounding edema in the right temporal parietal lobe with midline shift of 12.2 mm towards left side. C: NCCT head of the patient after burr hole surgery and 14 days of Liposomal Amphotericin B therapy. Image shows decrease in the midline shift to 7 mm.

The pus extracted from the brain abscess was sent for Gram stain, culture, and KOH analysis. Gram stain was negative, and the culture turned out to be sterile. However, the KOH mount revealed broad, aseptate fungal hyphae suggestive of mucorale.

Cerebral abscesses in immunocompromised patients can be due to various etiologies, including protozoal, fungal, tubercular, and viral. Even vasculitic and neoplastic lesions like brain tumors or metastasis can present with symptoms like a cerebral abscess in immunocompromised individuals, chronic kidney disease being one of them. Detailed history and radiological imaging, including NCCT head and MRI brain, are needed in the initial diagnosis. Further, confirmatory diagnosis requires microbiological evidence, including specific staining techniques and culture. In our case, the presence of an immunocompromised state and clinical features suggestive of raised intracranial pressure necessitated NCCT head, which was suggestive of multiple cerebral abscesses. Aspirate cytology with KOH mount revealed thin hyaline aseptate hyphae suggestive of mucorale as the pathogenic organism. Gram stain was negative, and bacterial culture was sterile, but fungal culture couldn't be performed due to technical limitations.

Table 1: Major investigations of the patient during hospitalization

Investigations (with reference range)	At Admission	At discharge	Other Investigations
Hb (13-17 g/dL)	10.9	10.8	Anti-HIV Ab/HBsAg/Anti-HCV Ab: Non-reactive Urine Routine and microscopy: Protein: 500 mg/dL Glucose: 50 mg/dL HbA1c (%): 5.4 USG W/A: Bilateral small echogenic kidneys with loss of corticomedullary differentiation
Leucocyte count (4000-10000/µL)	11.39	10.8	
Differential Count (N/L)	70/25	66/28	
Platelet Count (150000 - 450000/µL)	214000	190000	
Total Bilirubin (0.3 - 1.2 mg/dL)	0.7	0.64	
Direct Bilirubin (< 0.20 mg/dL)	0.3	0.2	
AST (0 - 50 U/L)	45	52	
ALT (0 - 50 U/L)	48	50	
Alkaline phosphatase (30-120 U/L)	108	110	
Gamma-glutamyl transferase (0-55 U/L)	35	29	
Serum Total protein (6.4 - 8.3 g/dL)	5.6	5.4	
Serum Albumin (3.5 - 5 g/dL)	3.4	3.2	
Serum Globulin (2.5 - 3.5 g/dL)	2.2	2.2	
Serum Urea (5 - 20 mg/dL)	102	85	
Serum Creatinine (0.7 – 1.2 mg/dL)	8.65	4.2	
Serum Sodium (136 - 145 mmol/L)	123	133	
Serum Potassium (3.5 – 4.5 mmol/L)	5.3	4.9	

The patient was managed in lines of isolated cerebral mucormycosis. A Neurosurgery opinion was sought for

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further management of the case. The patient underwent urgent burr-hole surgery to remove the pus. The postoperative period was uneventful. The patient was started on liposomal amphotericin-B (LAB) therapy with close monitoring of serum electrolytes and renal function while continuing his maintenance HD. ENT opinion was sought to rule out rhino orbital involvement. An endoscopic examination done by the ENT team did not reveal any blackish discoloration or crusting, suggesting rhino-orbital involvement.

Moreover, an MRI of the brain at the presentation and during follow-up did not reveal any intra-orbital extension. A repeat NCCT head 14 days after initiating antifungal therapy showed a decrease in the size of the cerebral abscess and a reduction in the midline shift by 5 mm (Fig 1C). The patient was continued on LAB and was improving symptomatically regarding the resolution of raised intracranial pressure and reduction in the frequency and intensity of headache. LAB was continued at a dose of 5 mg/kg every alternate day post-hemodialysis sessions for 11 weeks. One day during his 6th week of hospitalization, the patient reported an aggravation of headaches. On examination, the patient had a BP of 200/120 mm Hg, PR of 45/min, and RR of 22/min. An urgent neurosurgery opinion was taken, and the patient was subjected to right parieto-occipital craniotomy with excision of the abscess. The second surgery was done because of the worsening of symptoms, following which the patient improved symptomatically, and the course of antifungal therapy was completed. He received a cumulative dose of 6 grams LAB. He was continued on maintenance HD thrice per week during his hospital stay.

The patient reported a tremendous improvement in symptoms following the completion of his antifungal therapy and neurosurgical interventions. Repeat imaging showed a decrease in the number and size of the cerebral abscesses and a decrease in the midline shift. On OPD follow-up for six months, the patient reported no further symptoms and could perform his daily activities without significant discomfort.

DISCUSSION

Mucorale is a ubiquitous fungus prevalent in the tropical and subtropical regions of the globe. Most cases of mucormycosis result from inhalation of fungal sporangiospores that have been released in the air or direct inoculation of organisms into disrupted skin or gastrointestinal tract mucosa.[5-6] Seasonal variations affect the incidence of mucormycosis, with most infections occurring from August to November.[7] In our case, the patient presented the symptoms mentioned above to the Emergency Department around October.

CKD with uremia is associated with immune deficiency, contributing to increased mortality among ESRD patients. Studies have shown that loss of renal function causes a preferential loss of the number and function of lymphoid cells, loss of thymic function, attrition of telomeres, and expanded memory T-cell population, leading to premature immunological aging.[8] The patient, in this case, was diagnosed with CKD on maintenance HD, leading to a relatively immunocompromised state, which acted as a risk factor in the development of mucormycosis.

The most common underlying diseases in developed countries are hematological malignancies and transplantation. The epidemiology of mucormycosis is evolving as new immunomodulating agents are used to treat cancer and autoimmune diseases and as modern diagnostic tools lead to the identification of previously uncommon genera/species such as *Apophysomyces* or *Saksenaea* complex. In addition, new risk factors are reported from Asia, including post-pulmonary tuberculosis and chronic kidney disease.[9] Post-covid isolated mandibular mucormycosis was seen in a case of chronic kidney disease.[10]

Rhino-orbital mucormycosis is the most common manifestation of the disease. Cutaneous, pulmonary, and renal are the less common variants. Cerebral mucormycosis is extremely rare and may result in abscesses, infarcts, or hemorrhage, usually in the basal ganglia and frontal lobes, unlike this case, had temporoparietal lobe involvement.[11] Most of the cases of isolated cerebral abscesses have been reported in intravenous drug abusers, unlike this case.[12]

The diagnosis of mucormycosis remains challenging, as the clinical approach needs more sensitivity and specificity. Due to the high fatality associated, the disease warrants early diagnosis and prompt management without any delay. Microscopy (direct and histopathology) and culture are the cornerstones of diagnosis. The young patient was diagnosed based on KOH mount, which revealed aseptate hyaline septa in this case.

Several approaches have been developed, such as immunohistochemistry (IHC) that can confirm the histopathologic diagnosis of the invasive mold infection, polymerase chain reaction (PCR) on formalin-fixed paraffin-embedded (FFPE) or fresh

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tissue, body fluids such as bronchoalveolar fluid (BAL), and detection directly from serum/blood. Other evolving technologies include serologic tests, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF/MS), metabolomics, and metagenomic shotgun sequencing.[13] Mucorales qPCR tests targeting the Mucorales genera Lichtheimia, Rhizomucor, and Mucor/Rhizopus revealed a sensitivity of 85.2%, specificity of 89.8%, and positive and negative likelihood ratios of 8.3 and 0.17, respectively in this prospective study.[14] The sensitivity and specificity of 28S rDNA PCR compared to culture were found to be 85.71% and 27.78%, respectively, while for ITS-based PCR, they were 42.86% and 77.78%, respectively in a study in a COVID-19 setting.[15]

Successful treatment of mucormycosis requires a multimodal approach involving timely clinical suspicion and diagnosis, control of the underlying predisposing condition, administration of LAB, surgical removal and debridement of all infected tissues, management of raised intracranial pressure using prompt neurosurgical intervention in a case of cerebral mucormycosis as required in the case mentioned above. Due to its rare presentation, the exact course and prognosis of isolated cerebral mucormycosis remain uncertain. However, recent studies have shown some positive results with early prompt diagnosis and treatment initiation.[2,11-12] Control of predisposing factors plays an instrumental role in preventing invasive fungal infections; chronic kidney disease is the risk factor in our case.[16]

CONCLUSIONS

Mucorales can present as an isolated cerebral abscess without any rhino-orbital involvement. CKD is a possible immunocompromised risk factor resulting in cerebral mucormycosis. Isolated cerebral mucormycosis can present as a temporoparietal lobe abscess. Considering the rise in CKD in the community, mucormycosis in this entity should be suspected in isolated brain abscess cases.

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CONFLICTS OF INTEREST

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ETHICS STATEMENT INCLUDING PATIENT CONSENT

Informed consent was obtained, but there is no ethical approval required as per institute protocol.

AUTHOR'S CONTRIBUTION

All authors qualified for authorship as per ICMJE criteria. They approved the manuscript.

AI DECLARATION

No AI tool was used to generate research data, perform data analysis, interpret findings, formulate scientific conclusions, or make editorial decisions. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript.

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