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CASE REPORT

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SIADH secondary to rhino-orbito-cerebral mucormycosis: A case report

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Key Clinical Message

Invasive fungal mucormycosis and its outcome as SIADH and orbital apex syndrome is uncommon. Mucormycosis in paranasal sinuses can even lead to intracranial invasion and its treatment with the use of amphotericin B can cure improve the prognosis of the disease. Early diagnosis and prompt treatment with antifungal, endoscopic surgery, and controlling of diabetes can be beneficial.

Abstract

Mucormycosis is an opportunistic invasive fungal infection which is rare and fatal and can even cause intracranial invasion leading to SIADH. The infrequency with which mucormycosis with SIADH is encountered makes it a formidable diagnostic challenge. 70-year-old women uncontrolled diabetes mellitus presented with bilious vomiting and persistent headache with ptosis, proptosis, absence of extraocular movement, pupillary light reflex, and light perception of left eye. Radiographic investigation, KOH mount, and Biopsy showed mucormycosis in sinus with intracranial extension leading to SIADH. Further investigation revealed hyponatremia, decreased plasma osmolality. Then, when diabetes was controlled and hydrocortisone and amphotericin was given along with Endoscopic sinus debridement, SIADH was well controlled. This case illustrates the potential of mucormycosis in paranasal sinuses can even lead to intracranial invasion and its treatment with the use of amphotericin B can cure improve the prognosis of the disease. Prompt diagnosis through clinical history, radiological investigation, and laboratory parameters are important and its treatment is crucial for the better prognosis.

KEYWORDS

amphotericin B, diabetes mellitus, hyponatremia, mucormycosis, rhino-orbital-cerebral

1 | INTRODUCTION

Mucormycosis is an uncommon severe and life-threatening systemic infection that is caused by fungi of the Order Mucorales.[1] Mucormycosis is a life-threatening fungal infection caused by Mucorales, thermotolerant opportunistic fungi characterized by broad aseptate hyphae. Rhizopus arrhizus is the most common species causing mucormycosis globally.[2] It commonly presents in rhino cerebral, pulmonary, or disseminated forms, with rhino cerebral being the most frequent. The infection can spread rapidly, causing complications such as orbital cellulitis, meningo-encephalo-vasculitis, and thrombosis of cerebral vessels.[3] Histopathology finding includes broad, ribbon-like, and pauciseptate with right-angled branching.[4] The clinical presentation of mucormycosis has been reported frequently as the rhino-orbito-cerebral type.[5] Rhino-Orbito-Cerebral-Mucormycosis (ROCM) refers to the infection that infects the nasal cavities, paranasal sinuses, neck spaces, orbits, and intracranial structures. ROCM occurs in an acute situation, comparable to sinusitis.[6] The causes of Syndrome of Inappropriate Antidiuretic Harmone (SIADH) includes tumor, infection, stroke, space-occupying lesion, carcinoma, metastases, and drugs induced.[7] CNS infection when lead to SIADH can be due to "reset Osmo stat."[8] SIADH is defined by euvolemic hyponatremia, as well as urinary hyperosmolarity which is the result of the release of ADH when there is no suitable stimulus.[9] In SIADH, AVP over stimulates water reabsorption with consequent water diuretic insufficiency though the patient is hyponatraemic.[10] Due to the vasopressin activity, the level of urine osmolarity will be increased (often >100 mOsm/L) is one of the characteristics diagnoses of the SIADH.[11]

Here, we present the case of 70-year-old female having uncontrolled diabetes mellitus and hypertension with diagnosis of SIADH which is a rare complication of invasive mucormycosis. This case shows that the presentation of rhino cerebral mucormycosis is life-threatening and leads to intracerebral invasion, so prompt diagnosis and treatment is required to save the patient.

2 | CASE HISTORY/EXAMINATION

A 70-year-old female, a known case of type II diabetes mellitus and hypertension patient for 22 years presented with, 3–4 episodes bilious vomiting which was nonprojectile with undigested food particles in vomits for the past 15 days. In addition, persistent unilateral dull aching headache for 30 days, worse at night associated with nausea for 2 days. The patient had a significant history of left nodal tuberculosis 14 years back for which she took ATT therapy for 6 months. There was no associated history of fever, altered sensorium. The patient also described having drooping and swelling of the left eyelid for 8 days. She denies the consumption of alcohol whereas she is a chronic smoker. The patient had a significant history of left nodal tuberculosis 14 years back for which she took ATT therapy for 6 months. Her all-vital parameters were within normal limits except her blood pressure, which was raised that is, 140/80 mm of Hg. Her ophthalmic examination included bilateral periocular swelling, on the left eye there were ptosis, proptosis, absence of extraocular movement, pupillary light reflex, and light perception whereas right eye and pupil were normal.

3 | METHODS

When she presented to the hospital, Investigation for Diabetes was done and found Hba1C level to be high that is, 8.3% (Normal: 4.5%–6.4%). Other laboratory values were remarkable with sodium of 121 mEq/L (Normal: 135–146 mEq), potassium with 3.43 mEq/L (Normal: 3.5–5.2 mEq) and serum osmolality of 254.6 mOsm/kg (Normal: 275–295 mOsm/kg). Her biochemical profile includes alanine aminoTransferase (ALT) 16 U/L (Normal: 7 to 56 units per liter), alkaline Phosphatase (ALP) 91.6 IU/L (Normal: 44–147 international units per liter), aspartate amino transferase (AST) 17.5 U/L (Normal: 8–33 U/L), triiodothyronine (fT3): 2.24 pmol/L (2.4–6.0), thyroxine (fT4): 11.95 pmol/L (9–18), TSH: 0.761 uIU/mL (0.35–4.94), cortisol: 19 ug/dL (3.7–19.4), HDL Cholesterol (Direct): 1.4 mmol/L (0.8–1.6) and LDL Cholesterol (Direct): 0.7 mmol/L (less than 4). Laboratory tests revealed leukocyte count of 14,900/cmm (Normal: 4000–11,000/cmm) with neutrophil predominance, C-reactive protein (CRP) level of 48.89 mg/dL (Normal: 0–6 mg/dL), high ESR (Capillary Photometric) of 84 mm/h. (Normal: 0–22 mm/h) and low hemoglobin level of 10.9 gm% (Normal: 12.5–15.0 gm%). Further investigation was done where Urine osmolarity of 304.5 mOsm/kg [Normal: 295–800] and Urine sodium of 66 mEq/24 h [Normal: 43–217 mEq/24 h]. Pus culture suggested culture sterile and the KOH mount of left middle meatus revealed hyaline branched hyphae.

A Plain and Contrast CT scan of the Nose and Paranasal sinuses was done which suggested mild enhancing soft tissue density with branching hyperdense content in the left maxillary, ethmoid, and bilateral sphenoid sinus with feature of bony erosion and intracranial spread (Figure 1). T2 weighted MRI of Brain and Orbit with contrast revealed lesions in the left maxillary sinus extending to the osteo-meatal complex with less

defined involvement in the central part of the sphenoid sinus, most possibly parasagittal region of both sphenoid sinuses.

4 | CONCLUSION AND RESULTS

Based on the clinical history, examination, laboratory and radiological investigations, provisional diagnosis of invasive fungal mucormycosis with orbital apex syndrome with SIADH was made. Amphotericin B was given intravenously in the dose of 50 mg once daily after 5 days of admission for 1 week. Per operative finding revealed fungal debris on the left maxillary sinus and whitish fungal unhealthy tissue on the sphenoidal sinus, vault of nasopharynx, floor of sphenoidal sinus, orbital apex, and nasal septum. Tissue specimens were sent for histopathological examination. The biopsy findings suggested fungal infection consistent with mucormycosis which on examination showed dense inflammatory infiltrate predominantly of neutrophil with necrosis and aseptate fungal elements with broad base and wide angle branching in maxillary sinus. (Figure 2).

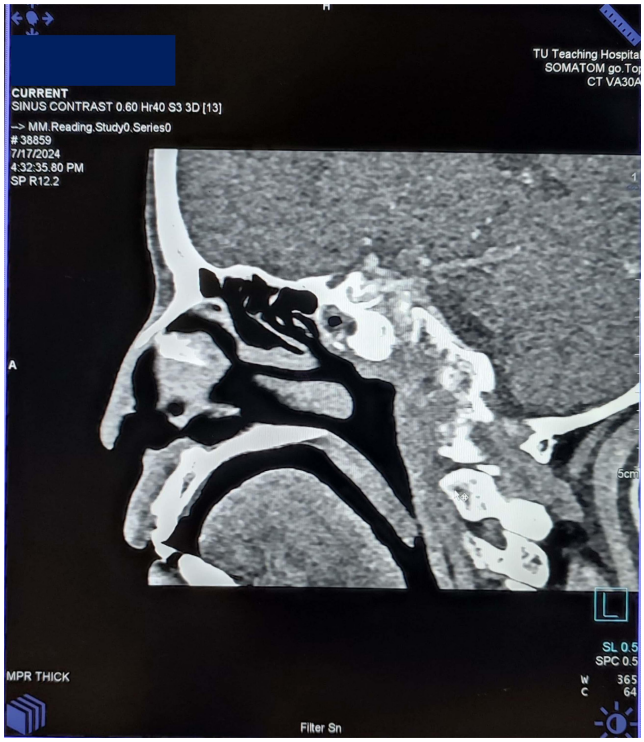

FIGURE 1 Nose and paranasal sinus CT scan showing bony erosion and intracranial extension.

On the first postoperative day, Subcutaneous Insulin Glargine 16 Units along with Subcutaneous Lispro 6 Units was started for Uncontrolled Diabetes. IV Hydrocortisone 100 mg, IV KCl 40 mEq was administered for electrolyte imbalance. On the second postoperative day, she was under Oral Spironolactone 25 mg, IV KCl 40 mEq. Sodium and potassium were monitored 12 h a day and Urea, Creatinine, Magnesium were monitored daily. Her SIADH had resolved and on subsequent investigation, sodium level was in normal range within 4 days after endoscopic sinus debridement surgery. Following the normal sodium level, her headache and vomiting were also resolved.

5 | DISCUSSION

This case highlights the rare cause of SIADH which has improved with administration of antifungal treatment. Mucormycosis is a rare, and emerging fungal infection having high morbidity and mortality which is caused by mucoromycetes species.[11] Fungal infection invasion in the pituitary gland and leading to SIADH is rare.[12] The most common presentation of mucormycosis is rhino-orbito-cerebral, pulmonary, cutaneous, and disseminated.[5] CNS infection leading to SIADH can be due to "reset Osmo

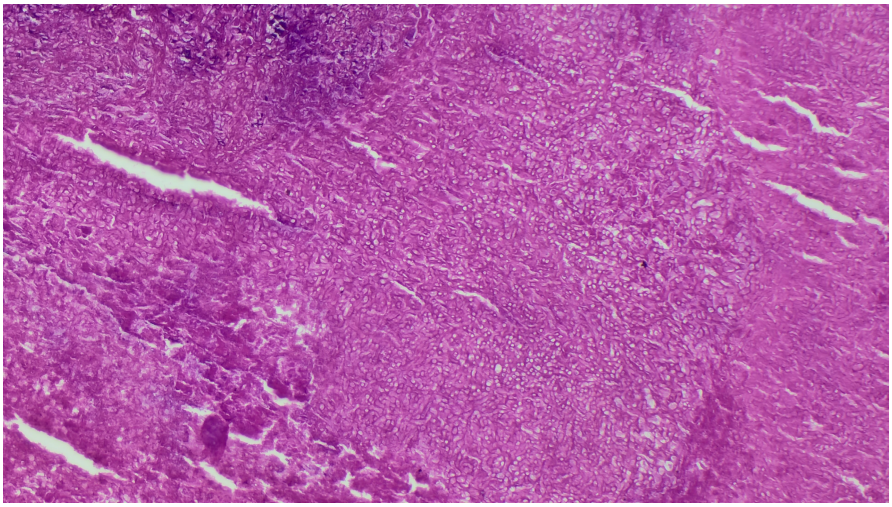

FIGURE 2 Biopsy of Maxillary sinus showing aseptate fungal elements with broad base and wide angle branching in maxillary sinus.

stat." This is explained as when the brain resets its Osmo stat to maintain sodium plasma level at a lower concentration than normal and is facilitated by increased release of ADH.[8]

Syndrome of inappropriate antidiuresis (SIAD) is a disorder in which there is unsuppressed release of antidiuretic hormone leading to impaired water excretion and hyponatremia.[11] The diagnosis of SIADH includes Bartter and Schwartz criteria which includes a decreased plasma osmolality of <275 mOsm/kg increased urine sodium ranging >20–40 mOsm, increased urinary osmolality >100 mOsm/kg, euvolemia, and no other identifiable cause.[13] It is well known that SIADH is a diagnosis of exclusion. Hyponatremia is the common electrolyte balance disorder in clinical practice and SIADH is the common cause. However, it is a common electrolyte disorder, optimal prompt treatment can improve the prognosis.[9] In this case, our patient had hyponatremia and after endoscopic debridement and antifungal treatment, it has resolved.

Invasive rhinosinusitis is mainly caused by Aspergillus and mucormycosis species whereas, the most invasive is Aspergillus (80%). Mucormycosis is a potentially lethal infection, which occurs in a patient with poorly controlled diabetes and immunocompromised patient through inhalation of fungal spores so infection spreads from the sinuses to intracranial structure.[14] The patient in this case had comorbid conditions of uncontrolled diabetes, hypertension, and tuberculosis. Orbital apex syndrome is one of the serious and rare outcomes of invasive mucormycosis especially in diabetic patients.[15] It mainly presents with ophthalmoplegia and vision loss due to involvement of cranial nerves.[16] Our patient had restriction of extraocular movement, absence of pupillary light reflex, ptosis, and loss of vision of left eye which suggests orbital apex syndrome secondary to Invasive mucormycosis.

The CT scan finding includes thickening of the mucosa in one or more paranasal sinuses which mimic malignant tumor along with destruction of sinus wall and extension.[17] In this case, CT of Paranasal sinus was done and revealed branching hyperdense content within the left maxillary, ethmoid, and bilateral sphenoid sinus with features of bony erosion and intracranial extension. In MRI, signal strength on T1 and T2 decreases, and sinus wall shows irregular bone destruction or sclerotic change.[18] In this case as well, MRI was done which revealed lesions in the left maxillary sinus extending to the osteo-meatal complex with less defined involvement in the central part of the sphenoid sinus, most possibly parasagittal region of both sphenoid sinuses.

Endoscopic debridement is effective for managing invasive mucormycosis with the provision of excellent visualization and access to affected areas.[17] In this case Endoscopic sinus surgery with debridement of invasive fungal aspergillosis was done and revealed fungal debris on the left maxillary sinus and whitish fungal unhealthy tissue where tissue was sent for biopsy. The biopsy report suggested fungal infection consistent with mucormycosis. Mucormycosis species are resistant to most antifungal including Voriconazole however Amphotericin B has shown promising results.[19] The patient was treated with Amphotericin B, as an intravenous infusion at 50 mg OD postoperatively and it has improved hyponatremia. This case report, however, has its limitations. Due to financial constraints to the patient, repeat radiological investigations was not done, however repeated plasma sodium level was done and was found to be normal after antifungal and endoscopic sinus debridement.

AUTHOR CONTRIBUTIONS

Bibek Shrestha: Conceptualization; data curation; formal analysis; methodology; project administration; visualization; writing – original draft; writing – review and editing. **Prabin Shrestha:** Investigation; supervision; validation. **Pradeep Shrestha:** Conceptualization; data curation; investigation; resources; supervision; validation. **Sudip Bastakoti:** Investigation; supervision; validation. **Shiva Ram Ale Magar:** Data curation; formal analysis; writing – original draft. **Prahlad Gupta:** Data curation; formal analysis; writing – original draft.

FUNDING INFORMATION

None declared.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The Institutional Review Board of the Institute of Medicine, Nepal, does not mandate ethical approval for the writing or publication of case reports, and patient consent was obtained.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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