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Case Report

Internal Medicine Section

Mucormycosis, Acute Necrotising Pancreatitis and Haemorrhagic Stroke Occuring Simultaneously in an Immunocompetent Male: The Unwarned Apocalypse

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ABSTRACT

Mucormycosis or zygomycosis is a life threatening invasive fungal infection, usually seen in patients with alteration of their immune system. It is a lethal and an aggressive fungal infection caused by the fungi of the order Mucorales. The angioinvasive property of mucormycosis can lead to fatal complications such as intracranial bleed. Acute pancreatitis refers to inflammation of the pancreas which presents mainly as acute pain in the abdomen and is a potentially fatal condition. The association of mucormycosis with acute pancreatitis is rare but dangerous. This case report highlights a case of 32-year-old male patient, with no co-morbidities, who was admitted to rural central Indian hospital with four days of abdominal pain and two days of headache. Patient appeared to be in good health prior to this event. He was ultimately diagnosed with mucormycosis of paranasal sinus with acute pancreatitis. The patient was treated with intravenous antifungals, antibiotics and fluid therapy along with other supportive measures. Patient later developed intracranial bleed five days after admission, and ultimately succumbed on day seven of admission. After an extensive review of literature, it was found that this is the first article to report mucormycosis, acute pancreatitis and intracranial bleed all occurring at once in an immunocompetent male.

Keywords: Intracranial bleed, Opportunistic infection, Zygomycosis

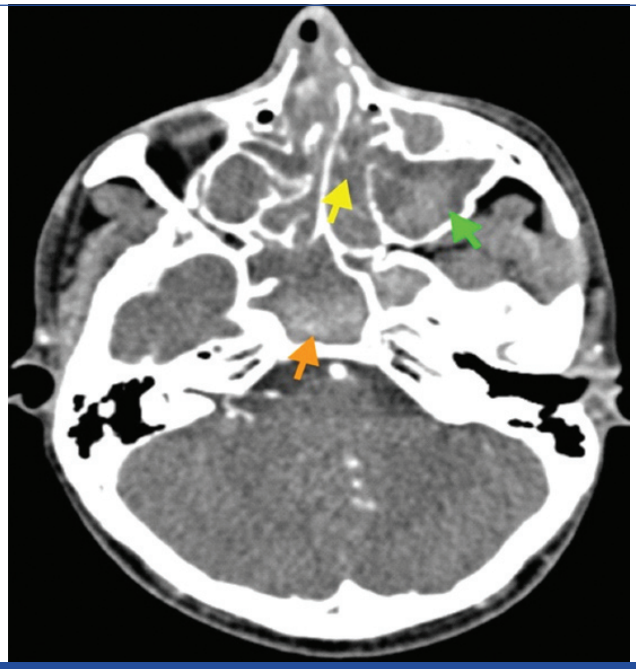
CASE REPORT

A 32-year-old male patient was admitted with complaints of abdominal pain for four days and headache for two days. No history of fever, cough or cold was reported. There was also no history of palpitations or chest pain, loss of consciousness, seizures, haematemesis, melena, yellowish skin or urine, oliguria, or swelling in the lower limbs. The patient was in good health four days prior to admission and had no history of hospitalisation. There was no history of diabetes mellitus, solid organ transplantation or Coronavirus Disease (COVID-19), and no history of use of steroids or immunomodulators. The patient had no habit of alcohol intake or any other substance abuse.

On examination, pulse rate was 86 beats per minute, and his blood pressure was 130/80 mm Hg in right arm supine position, Saturation of Peripheral Oxygen (SpO_2) was 96% on room air and respiratory rate was 28 breaths per minute. On systemic examination, he had tenderness in the epigastrium with a palpable spleen. Heart sounds were normal and chest was bilaterally clear. Patient was conscious and oriented.

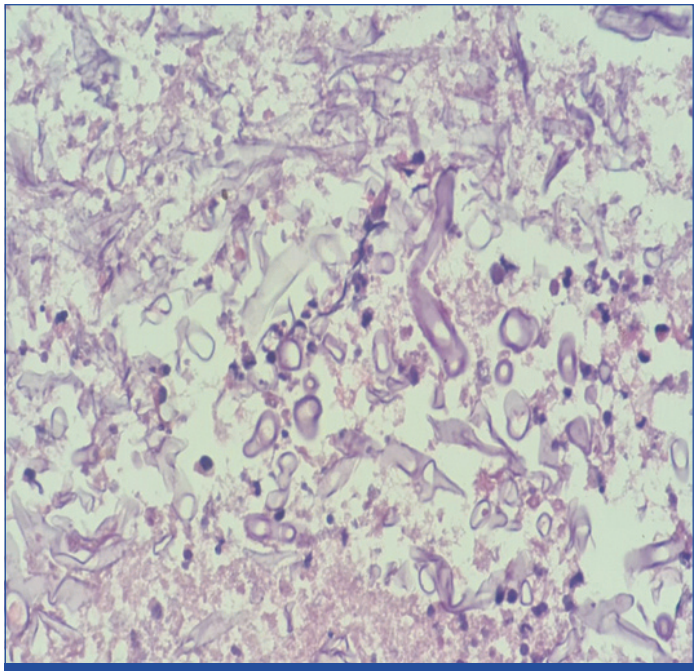
Patient was admitted in the medicine intensive care unit for further treatment. The laboratory findings were haemoglobin 8.4 gm%, Mean Corpuscular Volume (MCV) 91 fL, white blood cell count 21,200 per microlitre, platelet 3.71 per microlitre, International Normalised Ratio (INR) 1.2, Erythrocyte Sedimentation Rate (ESR) 60 mm/hour, amylase 300 units/litre, lipase 980 units/litre, urea 53 mg/dL, creatinine 1.7 mg/dL, sodium 133 mEq/L, potassium 3.8 mmol/L, Glycated haemoglobin (HbA1c) 6.8%, alkaline phosphatase 227 IU/L, Serum Glutamic Oxaloacetic Transaminase (SGOT) 43 U/L, Serum Glutamic Pyruvic Transaminase (SGPT) 20 U/L, albumin 3.2 g/L, globulin 3.9 g/L, total bilirubin 2.9 mg/dL, p-Antineutrophil Cytoplasmic Antibodies (p-ANCA) 2.7 AU/mL, calcium 8.5 mg/dL, magnesium 2.7 mg/dL, phosphorus 7.8 mg/dL and uric acid 8 mg/dL.

Computed Tomography (CT) scan of the head showed paranasal sinusitis [Table/Fig-1] for which functional endoscopic sinus surgery was performed, as the patient was having sepsis and opportunistic infection of the sinus was suspected. A biopsy sample was taken from maxillary sinus which showed growth of mucor species [Table/Fig-2].



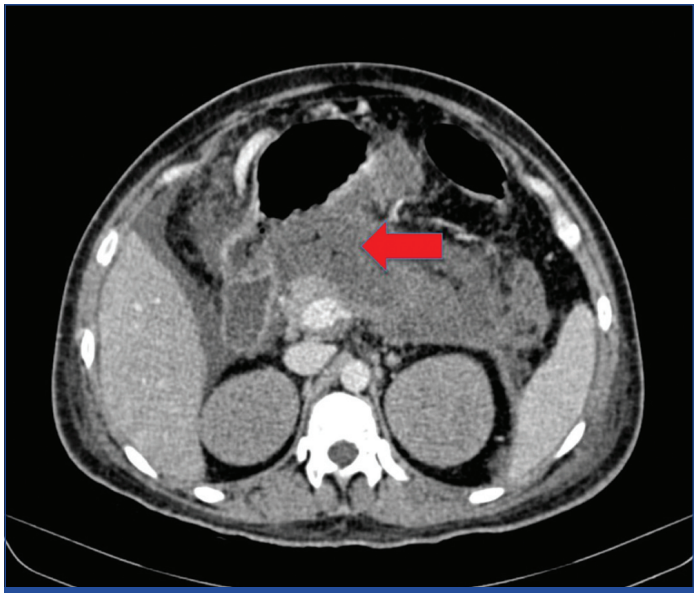
[Table/Fig-1]: Showing paranasal sinusitis.

Contrast-enhanced CT scan of the abdomen and pelvis revealed bulky appearance of head, body and tail parts of pancreas. There was diffuse hypodense attenuation and multifocal area of necrosis, involving more than 40% of pancreatic parenchyma associated with peripancreatic fat stranding and peripancreatic fluid collection. These findings were suggestive of necrotising pancreatitis [Table/Fig-3]. Acute necrotising pancreatitis was indicated by mild ascites with multifocal regions of bleeding in the left lumbar region and



[Table/Fig-2]: Biopsy from maxillary sinus showing growth of mucor species stain used is haematoxylin and eosin with 10X magnification.

minimal bilateral pleural effusion. The modified CT severity index was 10, on a scale of one to ten. A 2-dimensional (2D) echo was performed, which did not reveal any abnormality.

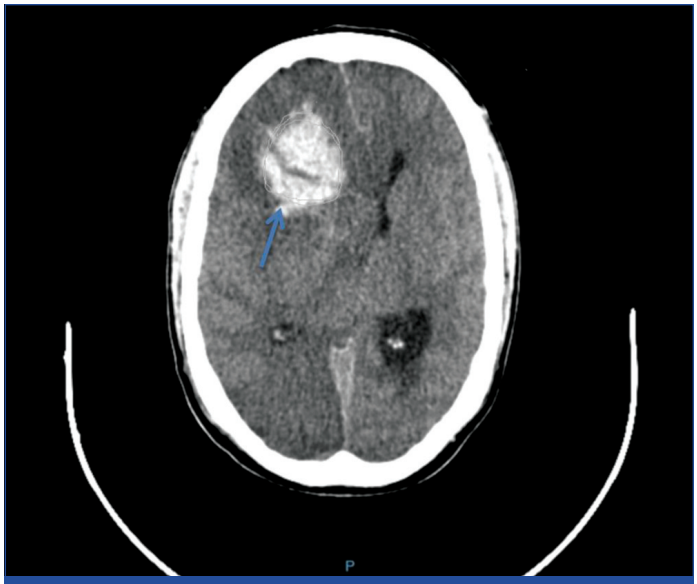


[Table/Fig-3]: Contrast-enhanced computed tomography scan of the abdomen showing necrotising pancreatitis (red arrow).

The patient was kept nil by mouth and managed with Intravenous (i.v.) fluids, antibiotics (injectable meropenem 500 mg i.v. thrice a day, injectable levoflox 500 mg i.v. once daily and injectable linezolid 600 mg i.v. twice a day), antifungal (injectable liposomal Amphotericin B 3 mg/kg), analgesics and other supportive measures.

On day five of admission, patient was intubated due to a drop in Glasgow Coma Scale (GCS) (from E3V4M5 on admission to E2V2M2). A CT brain scan revealed a massive intraparenchymal haemorrhage in the right frontoparietal region with subfalcine herniation, limited subdural haemorrhage, a subarachnoid component with intraventricular extension and diffuse cerebral oedema [Table/Fig-4].

A neurosurgical opinion was sought, and mannitol and 3% NaCl were recommended, instead of surgery as the patient was unfit for surgery. He was provided conservative therapy along with inotropic support (injectable vasopressin infusion) and antibiotics in view of septic shock. On day seven of admission, injectable noradrenaline infusion was added as the patient had persistent hypotension inspite



[Table/Fig-4]: Computed tomography scan of brain showing massive intraparenchymal haemorrhage in the right frontoparietal region (blue arrow).

of vasopressin support. Injectable colistin 3 million IU stat followed by 1 million IU thrice a day was added on day eight of admission, as white blood cell count increased from 21,200 cells/mm^3 on admission to 28,900 cells/mm^3 on day eight.

On day nine of admission, injectable dopamine infusion was added as patient was still having shock. However, the patient succumbed after 10 days of admission.

DISCUSSION

In recent decades, mucormycosis has emerged as a life threatening invasive fungal infection, particularly in immunocompromised patients with haematological malignancies and haematopoietic stem cell transplant recipients, solid organ transplant recipients, diabetes mellitus patients, surgical patients, patients with burns, injection drug users and trauma patients [1-4]. The infection rates of post-transplant fungal infections ranged from 2-14% [5]. Mucormycosis is linked to the longest hospital stay and the worst two year survival in Renal Transplant (RT) patients, although accounting for just 2-6% of all invasive fungal infections [6]. However, mucormycosis in immunocompetent young individuals with no prior co-morbidities is rare to find. Association of mucormycosis with intracranial bleed has been denoted to its angioinvasive properties and has been previously reported [7].

Necrotising pancreatitis is a rare manifestation of mucormycosis while rhino-orbital, pulmonary and cutaneous manifestations being more common [8-10]. Pancreatitis associated with mucormycosis is commonly found in gastrointestinal mucormycosis, presenting most commonly with ulcers in the intestine or stomach [11]. However, the incidence of gastrointestinal mucormycosis is rare with diagnosis being established only after endoscopy and biopsy.

Mucorales are saprophytic fungi that can be found in soil, air, and decomposed organic materials. Even though they have a low intrinsic pathogenicity, they can cause an aggressive and frequently fatal infection when the host's defences are weakened [12]. Mucormycosis, on the other hand, has rarely been reported in previously healthy people.

The index patient had no prior co-morbidities or history of steroid or immunomodulator consumption and was COVID-19 negative (reverse transcriptase polymerase chain reaction tested in nasopharyngeal swab, on admission). This ruled out common causes of immunosuppression and also ruled out drug induced immunosuppression. Patient developed acute pancreatitis with mucormycosis induced paranasal sinusitis. Whether it was as association or a chance finding, cannot be established as the patient

was not fit for conducting endoscopy. One school of thought states that disseminated mucormycosis could have caused involvement of the gastrointestinal tract leading to pancreatitis and another school of thought states that sepsis due to acute pancreatitis could have led to immunosupression leading to mucormycosis [13]. Absence of other risk factors for acute pancreatitis such as alcohol abuse or gall bladder stones supports the postulate of mucormycosis induced necrotising pancreatitis in the patient. Intracranial bleed, which led to further deterioration, can be explained by the angioinvasive property of mucormycosis.

The presence of mucormycosis in immunocompetent individuals has been reported earlier with chronic local insult being the key factor [14]. Immunocompetent patients developing mucormycosis seems to be related to the ability of this fungus of attacking the epithelium which was previously damaged by any prior infection, or agent which are cytotoxic or through direct trauma [14]. Proteases are certain toxins secreted by mucor sporangiospores which have the potential to destroy the mucosal membrane comprised of the endothelial cells [15]. The fungi causing mucormycosis might have invaded the damaged epithelium in order to enter the mucosal sinuses, spreading along vascular as well as neuronal structures and infiltrating the walls of blood vessels. Infection would have eroded bone through walls of the sinus area [16]. This infection could have then travelled through haematogenous route to various other sites leading to disseminated mucormycosis.

In the above scenario, it can be postulated that the patient developed fatal complications of mucormycosis, such as necrotising pancreatitis and intracranial bleed, even in the absence of any risk factors for mucormycosis.

CONCLUSION(S)

This case report highlights mucor infection in a person without any co-morbidities as well as without immunosuppresive drug history. There is a diagnostic dilemma, whether mucor caused pancreatitis or vice versa, which ultimately resulted in a fatal outcome. Therefore, it is important for the clinicians to be vigilant of the association between mucormycosis and pancreatitis as both can have a potentially lethal course, even in a young immunocompetent male.

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