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Case Report

A rare case of aggressive invasive fungal sinusitis with multidrug resistant *Pseudomonas aeruginosa* co-infection in immunocompromised: a therapeutic challenge

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ABSTRACT

Mucormycosis is known to be rapidly progressing and fulminant fungal infection which has the ability to cause significant morbidity and mortality, especially in immunocompromised patients. *Pseudomonas aeruginosa* commonly co-isolated bacterial species from chronic wounds are likely to interact and compete with Mucorales spores.We report a 70 years old female who presented to us initially with left facial swelling with a cheek ulcer. She had initially denied the necessary investigations but later presented to us with flared up symptoms. She was a known case of type 2 diabetes mellitus, hypothyroidism and dilated cardiomyopathy on medication with permanent pacemaker implant. She was found to have left maxillary mucormycosis with left sided cheek wound having superinfection with *Pseudomonas aeruginosa.* Patient was started on injection Amphotericin B (lipophilic) and injection colistin with surgical debridement of the wound. Left Caldwell-Luc surgery with left inferior meatal antrostomy was performed for clearing fungal debris in left maxillary sinus. The purpose behind this paper is to highlight the need of early detection and aggressive management for successful management of mucormycosis.

Keywords: Mucormycosis, *Pseudomonas aeruginosa*, Early diagnosis, Immunocompromised, Chronic wound, Aggressive management

INTRODUCTION

Antibiotic drug resistance has become a worldwide health risk, as the development of antibiotics is now being outpaced by expeditious emergence of resistance.[1] Multidrug resistance in bacteria can broadly be either due to accumulation of multiple genes, each coding for resistance to a single drug or by increased expression of genes that code for multidrug efflux pumps.[2] In addition, a perplexing array of microorganisms in an immunocompromised patient creates a diagnostic and therapeutic dilemma for the clinician.[3] To effectively diagnose and manage these infections in such immunocompromised host, a prior knowledge of which host defect predispose to specific infections must be known.[4]

CASE REPORT

A 70 years old female was admitted under department of medicine with chief complaints of fever and shortness of breath for 1 week. Chest X-ray revealed bilateral pneumonia and was treated conservatively for the same. RTPCR test for COVID-19 was reported to be negative.

She was a known case of type 2 diabetes mellitus, hypothyroidism and dilated cardiomyopathy on medication with permanent pacemaker implant. Five days into treatment, patient was referred to ENT for left sided facial swelling along with a small wound on left cheek. Patient was advised for skin biopsy from the infected left cheek wound, which the patient and party were unwilling for. After resolution of the bilateral lung infiltrates, patient took discharge against medical advice.

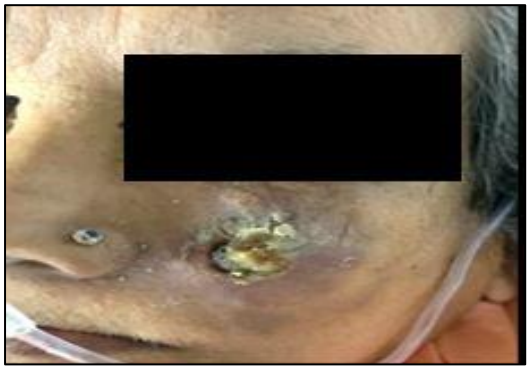

Figure 1: Chronic soft tissue wound with eschar formation.

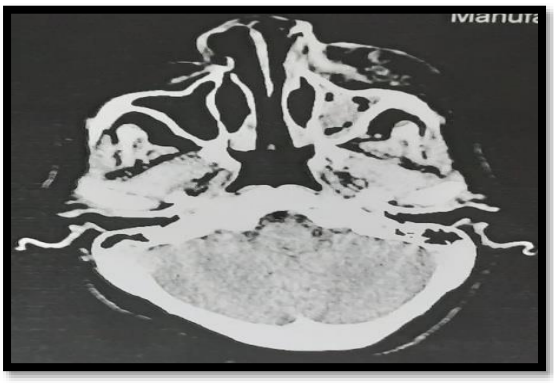

Figure 2: Left maxillary sinusitis.

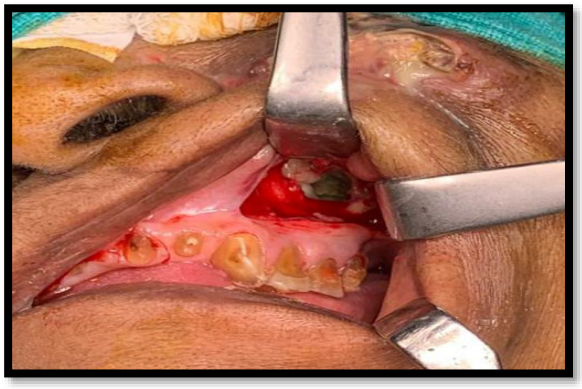

Figure 3: Left Caldwell-Luc approach.

She presented to ENT OPD after 1 month with complaints of pain and swelling over left half of the face and was admitted under us. On examination, left maxillary area showed an infected ulcer measuring (1×1) cm with eschar. Left periorbital edema with proptosis was present but vision was normal.

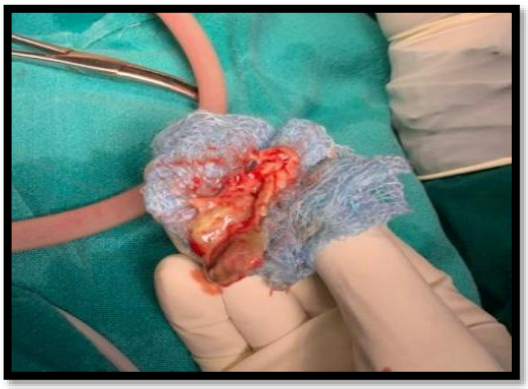

Figure 4: Fungal debris from left maxillary sinus.

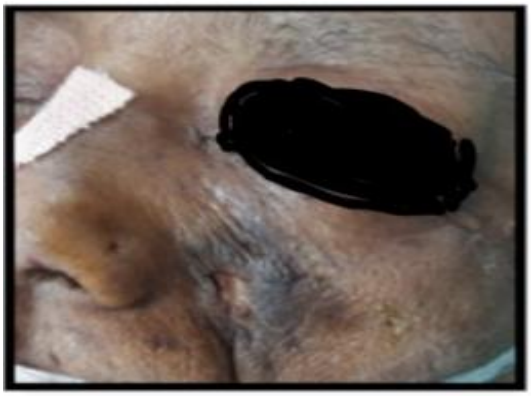

Figure 5: Left cheek wound post debridement and regular dressing.

CT PNS showed – an ill-defined soft tissue density with multiple air foci within the left pre-maxillary, upper lip and left preseptal region with surrounding fat stranding, suspiciously communicating to the left maxillary sinus through defect in the anterior wall. Soft tissue density seen in the bilateral maxillary sinus (left > right). Under local anesthesia, biopsy from the cheek wound was sent for histopathological examination, for fungal stain and bacterial culture. Histopathological examination reported large areas of necrosis with aseptate stout branching hyphae with dense neutrophilic aggregates surrounding it in a necrotic background. Findings suggestive of a fungal abscess- possibly mucormycosis. No evidence of malignancy noted. Tissue culture and sensitivity revealed gram-negative bacilli, *Pseudomonas aeruginosa* sensitive to colistin only. Injection Amphotericin B (liposomal) 50 mg IV/day started after nephrology review due to high serum creatinine level along with injection Colistin 2 MU/ IV/OD. Serum potassium and serum creatinine levels monitored every 3rd day.

On diagnostic nasal endoscopy, purulent discharge was seen in left middle meatus. Patient was posted for left Caldwell-Luc procedure and left inferior meatal antrostomy with debridement of cheek wound under high cardiac risk under intravenous sedation.

Tissue from left maxillary sinus was sent for histopathological examination and fungal culture. Histopathology report revealed several fungal hyphae with branching seen in necrotic areas, suggestive of fungal sinusitis- mucormycosis.

Regular wound dressing was done with topical application of diluted solution of 1% acetic acid. Postoperatively, douching was done using Colistin in left maxillary sinus under endoscopic guidance every alternate day for 1 week. Tissue sample from the maxillary wound was sent for both bacterial and fungal culture and sensitivity on every 7th day postoperatively. Injection Colistin was stopped on day 14 after bacterial culture showed no growth. Injection Amphotericin B (liposomal) was continued for persisting mucormycosis and dose was increased to 100 mg IV/day after nephrology review.

Three weeks post admission, patient had an episode of cardiac arrest secondary to her cardiac condition. Patient was intubated and shifted to HDU. Cardiologist, physician and nephrologist opinion was taken and treated accordingly. However, the patient expired despite of our best supportive care.

DISCUSSION

Mucormycosis is the third most common invasive fungal infection following candidiasis and aspergillosis, belonging to the class zygomycetes.[5] Infection usually affects immunocompromised individuals such as those undergoing or post chemotherapy, post organ transplantation, with hematological malignancies and patients with diabetes mellitus or any kind of acidosis.[6] Following are the six commonly affected systems: rhino-orbital-cerebral Mucormycosis (ROCM), pulmonary, cutaneous, gastrointestinal (GI), disseminated, and mucormycosis of uncommon sites.[7] A crucial factor in the pathogenesis of mucormycosis in diabetic ketoacidosis patients is altered iron metabolism.[8] It classically presents with involvement of nasal mucosa followed by invasion of the paranasal sinuses and orbit.[9] The pathognomonic feature being angioinvasion with thrombosis and tissue necrosis.[8] The incidence of mortality rate ranges from 62.5% in rhino-cerebral form to 100% in disseminated form.[10]

Pseudomonas aeruginosa is one of the renowned nosocomial pathogens worldwide.[11] It is an invasive, gram-negative bacterial pathogen capable of infecting virtually all tissues.[12] Several mechanisms such as adhesion, modulation, disruption of host cell pathways and altering the extracellular matrix are involved in pathogenesis of pseudomonas infection.[13] Pyoverdine, an iron binding molecule is secreted by *P. aeruginosa* acts as an antagonist to Mucorales group by decreasing the availability of iron molecules and hence inhibits its growth.[14] A wide range of clinical manifestations such as pneumonia, urinary tract infection and bacteremia have been found to be commonly associated with *Pseudomonas aeruginosa*.[15] Multidrug efflux pumps, β-lactamases and down regulation of outer membrane porins are the most common mechanisms involved in development of antimicrobial resistance.[16]

Medical management alone in Mucormycosis patients have shown poor drug delivery to the infective site.[17] It can become life threatening in immunocompromised patients due to extensive tissue loss secondary to vascular thrombosis.[18] Therefore we undertook thorough debridement on a regular basis to improve drug penetration. Two drugs approved for primary therapy are amphotericin B and isavuconazole while posaconazole can be used for salvage treatment in patients intolerant to Amphotericin B.[19] *S. aureus* and *P. aeruginosa* are two bacteria known to make a strong biofilm that maintains the chronic infection impairing the healing of the wound and increasing the development of antibiotic resistance.[20] Thus, invasive infections known or suspected to be due to *P. aeruginosa* should be empirically started with at least two antipseudomonal agents from different classes till culture sensitivity report is available.[21] In our case, the bacteria showed resistance to most other antibiotics. We used topical application of dilute acetic acid and colistin douching in our attempt to control infection and reduce further resistance.

CONCLUSION

Management of patients suffering from mucormycosis is individualised depending upon their time of presentation, clinical recovery, negative histopathology report, radiological improvement and recovery from any underlying comorbid conditions. Early diagnosis with aggressive treatment with antifungals, antibiotics and wide debridement remains the keystone of successful management.

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