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A Rare Case of Extensive Rhin0,Oculo Mucor in A Post Renal Transplant Patient,Treated With Aggressive Surgical Debriedments

KEYWORDS: mucormycosis, diabetic nephropathy, renal transplant, immunosuppression.

Dr Sandeep Inchanalkar
neurosurgeon, Department of Surgery, Dr. D.Y. Patil Hospital, Kadamwadi, Kolhapur

*** Dr Nikunj.r.shekhada**
Department of Surgery, Dr. D.Y. Patil Hospital, Kadamwadi, Kolhapur * corresponding author

Dr Abhijeet korane
nephrologist, Department of Surgery, Dr. D.Y. Patil Hospital, Kadamwadi, Kolhapur

Drshilpa Inchanalkar
ophthalmologist, Department of Surgery, Dr. D.Y. Patil Hospital, Kadamwadi, Kolhapur

ABSTRACT *Mucormycosis is a rare but devastating infection. we present a case of chronic kidney disease stage V D with diabetic nephropathy who underwent renal transplant, on significant immumnosuppresives which later developed to Rhino Oculo mucormycosis. Uncontrolled diabetes mellitus and immunosuppression are the major predisposing factors to infection with Mucorales. Mucorales are angioinvasive and can infect any organ system. Lungs are the predominant site of infection in solid organ transplant recipients. Despite advances in diagnosis and management, mortality rates are still high. Prompt diagnosis is challenging and influences outcome. Treatment involves a combination of surgical and medical therapies. In our case patient was investigated by MRI and CT SCAN, mucormycosis was suspected and Extensive surgical debridement was done which lead to completee recovery of patient.*

INTRODUCTION : Mucormycosis is an opportunistic, aggressive infection caused by organisms belonging to the class of Phycomycetes. [1] They occur almost exclusively in immunocompromised patients like uncontrolled diabetics, those on chemotherapy and steroids. [2] Invasive fungal infections (IFIs) occur in up to 20% of recipients of renal transplantation [3] and remain a diagnostic and therapeutic challenge. While Candida infections are the most common [4], invasive aspergillosis is the most fatal, with a mortality rate reaching 75% [5]. According to the TRANSNET report, a recent prospective and comprehensive study of invasive non-Aspergillus fungal infections, mucormycosis is much less common, occurring in 3 of 8494 renal transplants between 2001 and 2006 and accounting for 28 of 1208 cases of IFIs among all solid organ transplant (SOT) recipients [6]. Fungal infections in general occur in the intermediate (1–6 months) to late (more than 6 months) posttransplant period [7]; 37.8% of non-Aspergillus infections were reported to occur within the first 6 months and 33.3% two years after the transplant [6]. We report a case of a renal transplant recipient who developed rapidly progressive and disseminated mucormycosis one month post transplant

CASE REPORT

A 53year-old man presented in the department with chronic kidney disease stage v (D) with diabetic nephropathy on thrice weekly hemodialysis for the past three years,He underwent live donor transplant. Donor was his sister(4 antigen match) He had delayed graft function due to prolonged cold ischemia time of 6hours due to difficult vessel anastomosis. Post op, He required couple of hemodialysis. Inview of risk of rejection he received significant immunosuppression. He was on hemodialysis till15days Post transplant. at Discharge His immunosuppressants were Prednisolone 60mg, Tacrolimus 6mg/day, Mycophenolate, mofetil 2gm/day. over a month His blood sugars were uncontrolled requiring significant dose of insulin and OHA. at the end of 1 month His serum creatinine was 1.5mg/dl. T0 leaves at end of one month were 10.on Post Op day 45 he Noticed acute onset Proptosis and loss of Vision of the left eye along with watering of both eyes. He had worsening of renal functions with serum creat of 1.7mg/dl.In view of significant immunosuppression Rhino cerebral oculomucomycosis was suspected. patient was investigated by MRI and CT SCAN whichh cinfirmed to have mucormycosis of sinuses and orbit. He underwent medical treatment which included liposomal Amphoterisin B ,stopping anti-metabolites and reducing dose of Prednisolone and Tacrolimus. Endoscopic Debridement was done twice but failed to respond. clinicoradiological progression of disease was noted. he was then subjected to aggressive Surgical Debridement which included Extensive Explorationn of orbit and paranasal sinuses with removal of eyeball, extra ocular muscles and frontal ethmoid and left maxillary sinuses. the Specimen was sent for Histopathological Examination and revealed septette filamentous Hyphae of Mucormycosis. The patient responded well,his blood sugars came under control, and improved symptomatically.Following Extensive Surgical Debridement,liposomal Amphotericin,reduction of immunosuppression He showed considerablee clinical and radiological improvement. On discharge His serum creat was 1.3mg/dl and His current immunosuppressive drugs are Prednisolone of 5mg alternate day,Tacrolimus 2mg/day.

DISCUSSION

Mucorales are ubiquitous in nature and rarely cause disease in immunocompetent hosts, except in the settings of uncontrolled diabetes mellitus [8], heavy exposure as in natural disasters, [9,10] or rarely without apparent predisposing factors . Recipients of SOT are at higher risk given their multiple predisposing factors. Diabetes mellitus remains the leading risk factor among all studied patient populations, as 36% of Roden et al.'s 929 cases were diabetic, mostly type 2, and in the setting of ketoacidosis [8]. Even among the SOT and hematopoietic stem cell transplant (HSCT) recipients developing mucormycosis, the prevalence of diabetes mellitus was 43.8%. Thus it remains an independent risk factor even in the presence of other predisposing factors. Another major risk factor is the state

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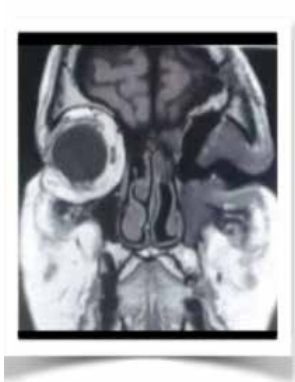
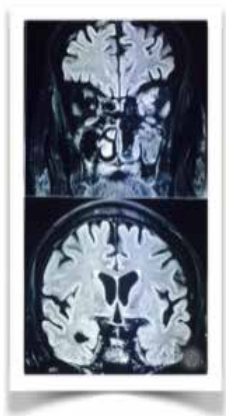
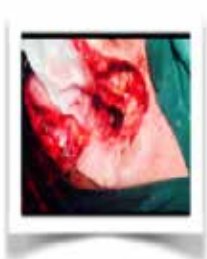
of immunosuppression, especially the use of potent T cell depleting agents [11,12] and the presence of neutropenia [3]. In the TRANSNET report, 50.6% of SOT and HSCT patients developing mucormycosis were neutropenic within 60 days prior to the onset of infection. Initial or subsequent graft rejection necessitating augmented IS, a condition commonly encountered in renal transplant recipients, was also associated with an increased risk of mucormycosis [5] Renal failure and prior exposure to caspofungin or voriconazole (antifungal agents with no activity against Mucorales) increase the risk of mucormycosis as well as the use of ureteral stents during renal transplant. Our patient had numerous risk factors associated with mucormycosis including new-onset poorly controlled diabetes after transplantation, significant immunosuppressive therapy, abnormal renal function, ICU stay.

In the reported literature, the species of Mucorales accounting for most of the cases is variable, likely reflecting regional and hospital variability. Rhizopus species is the most common, accounting for 35%–73% of cases, followed by Mucor (13%–37%) and Mycocladus (0%–13%) The infection is acquired through inhalation of spores or rarely through direct contact with the skin. The hyphae of pathogenic Mucorales are angioinvasive, which lead to hemorrhagic necrosis, vascular thrombosis, and tissue infarction [3, 10]. The primary site of infection varies according to the host's condition. Localized sinonasal or sino-orbital disease with involvement of the brain accounts for 66% of mucormycois in diabetic patients. However, pulmonary infection is the predominant site affected in recipients of SOT [6, 8], accounting for 39% of cases with involvement of other organ sites in 48% Mucormycosis can virtually involve every organ, such as the skin, gastrointestinal (GI), cardiovascular, genitourinary, and musculoskeletal systems as well as infections of surgical wounds and intravascular catheter exit sites [3, 6, 8, 13,14]. Of note, isolated renal infection without systemic involvement has been attributed to seeding during transient periods of fungemia [8, 15,16]. Donor-derived infection through







transmission with the allograft is also possible but it presents early after transplantatio .

Timely diagnosis and treatment are crucial due to the aggressive course of mucormycosis that may eventually lead to tissue necrosis and dissemination. Rhino-sino-orbital disease presents with facial or orbital pain and swelling, proptosis, visual loss, and ophthalmoplegias. Given the angioinvasive nature of Mucorales infection, rapidly progressive necrotic lesions caused by infarction of the tissue can be seen in the nasal and sinus mucosa. A high index of suspicion and suggestive signs and symptoms are needed, and the diagnosis is confirmed by a combination of radiological, histological, and microbiological studies. Plain or contrast-enhanced CT or magnetic resonance imaging (MRI) of the head, sinuses, brain, chest, and abdomen may show some suggestive radiological signs [3, 11]. CT features of pulmonary mucormycosis in SOT recipients commonly include consolidation or mass-like lesions, nodules, or cavities in about 25% of patients [13]. Opacification of the sinuses is seen in sinonasal disease with involvement of the maxillary sinuses being the most common, followed by the ethmoid and sphenoid sinuses [14]. Tissue biopsy is needed to confirm the etiological diagnosis, and direct identification of the organism by culture or histopathology is the gold standard. The hyphae of Mucorales are broad, irregularly branched, thin-walled, and sparsely septate (Figure). Molecular diagnostic tests for identification of Mucorales are increasingly used for early detection of infection and identification of genus even in cases when cultures are negative.

Timely initiation of treatment is crucial and associated with better survival . The optimal management of mucormycosis is based upon early recognition and initiation of treatment, surgical resection of necrotic tissue if possible, and reversal of predisposing factors, such as uncontrolled glycemia, IS, and neutropenia.Surgery is an essential part of the management of localized disease, such as rhino-orbito-cerebral disease, and surgical resection and debridement are associated with improved outcomes. .Amphotericin B is considered the drug of choice.[8]

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Volume : 6 | Issue : 5 | May 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

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