A Rare Case of Pulmonary Mucormycosis Caused By Rhizopus Homothallicus in Post Heart Transplant Patient

Abstract

We report a case of pneumonia due to Rhizopus homothallicus in a post cardiac transplant and diabetic patient. This is the rare case of R. homothallicus infection described in India and first case described in post cardiac transplant patient worldwide. The organism was isolated from bronchoalveolar lavage fluid and identified after culture followed by amplification and sequencing of the internal transcribed spacer region.

Keywords: Rhizopus homothallicus, Mucorales, Pneumonia

Introduction

Mucorales are ubiquitous fungi causing infection in immunocompromized hosts like carcinomas, immunosuppressive therapy, uncontrolled diabetes, neutropenia, or patients on desferroxamine therapy amongst which pulmonary mucormycosis is the second common [1]. Mucormycosis is characterized by host tissue infarction and necrosis resulting from vasculature invasion by hyphae starting with a specific interaction with endothelial cells [2]. However, infections due to Rhizopus homothallicus appear to be rare compared with those caused by other species of zygomycetes [3]. Low incidence may be attributed to reduced pathogenicity or its lower prevalence in the soil compared with other Mucor species.

Case Report

A 57-year-old male, known case of post cardiac transplant 5 years back (on triple-drug immunosuppression - cyclosporine, azathioprine, and prednisolone) along with type II diabetes mellitus for more than 13 years with diabetic triopathy, hypertension, non-oliguriac end stage renal disease (stage IV) presented to us with high grade fever with cough, generalized weakness and loss of appetite of one week duration. He had history of hospitalization around two months back for acute gastroenteritis. He was on antihypertensive drugs (β-blockers, calcium channel blocker and alpha blocker) and insulin for diabetes mellitus. His chest X-ray revealed focal patch of opacity in right mid-lower zone suggestive of consolidation. He had history of hospitalization around two months back for acute gastroenteritis. He was on antihypertensive drugs (β-blockers, calcium channel blocker and alpha blocker) and insulin for diabetes mellitus. His chest X-ray revealed focal patch of opacity in right mid-lower zone suggestive of consolidation. At our institute, contrast-enhanced computed tomography of the thorax revealed patchy sub-lobar consolidation in right middle and lower lobes with surrounding ground glass attenuation with large inhomogeneous area of ground glass attenuation in right perihilar region with small mediastinal and right hilar lymphadenopathy suggesting possibility of mycotic pathology (Figure 1). No pleural effusion was noticed. Echocardiography ruled out endocarditis. His blood sugar levels ranged from 153 to 226 mg/dl, total leucocyte counts 14600 per cumm with polymorphs 84%, B. urea 103, S. Creatinine 4.1. His serum procalcitonin levels were raised along with HbA1c of 12.82, indicating uncontrolled diabetic status.

Diagnostic bronchoscopy was performed and direct microscopic examination with 10% KOH of the bronchoalveolar lavage specimen revealed ribbon-like broad aseptate hyphae with branching at right angles. The samples were cultured on Sabouraud’s dextrose agar (SDA) (HiMedia, Mumbai, India) and...
incubated at 25° and 37°C. After 4 days of incubation, fast growing, identified as ³°C. Based on these characteristics, the isolates was presumptively thermotolerant and were able to grow when incubated up to 48
Figure 2

The isolates were to the larger, globose suspensor cell (Figure 2). The isolates were showing golden brown, globose zygospores with stellate spines. Lactophenol cotton blue mount of R. homothallicus.

and was managed with hemodialysis at regular intervals. After showing initial improvement on amphotericin B, deteriorated subsequently and developed sepsis leading to multi-organ failure and death.

Discussion

Among the agents of zygomycosis, Rhizopus spp. are the most commonly implicated agents causing human infection. This is followed by genera such as Lichtheimia and Mucor. Among Rhizopus spp., R. oryzae is the predominant species, being implicated in 90% of the reported cases of invasive zygomycosis [3] R. homothallicus which was earlier considered an environmental isolate, has been increasingly reported to cause invasive infections. It has been reported to cause invasive pulmonary mucormycosis, rhino-orbitocerebral and cutaneous mucormycosisis six patients in India [4-6]. One case of fatal invasive pulmonary mucormycosis has also been reported from France [7].

Mucorales gain entry to a susceptible host through inhalation, ingestion of contaminated food, or through abraded skin. One of the characteristic features of mucormycosis is its angioinvasive property, resulting in vascular thromboses and ultimately tissue necrosis. Angioinvasion was reported to be related to the interaction between a spore-coating protein family (CotH) on Rhizopus spp. surface and endothelium glucose regulator protein 78 (GRP78) expressed at the surface of endothelial cells. This interaction triggers host cell injury and subsequent fungus hematogenous dissemination [8]. Elevated levels of serum glucose, iron, and ketone bodies increase fungal growth and induce the expression of GRP78 and CotH, resulting in increased ability of Rhizopus to invade host tissues and explaining the susceptibility of diabetic and deferoxamine treated patients to mucormycosis [8].

In India, Chakrabarti et al. have described an overall prevalence of rhino-orbito-cerebral mucormycosis (48%), followed by pulmonary mucormycosis (17%), gastrointestinal mucormycosis (13%), cutaneous mucormycosis (11%), renal and disseminated mucormycosis (5% each) [4]. The MIC patterns observed with the isolates of R. homothallicus were consistent with those reported for other Rhizopus species with amphotericin B MIC of 0.5 µg/ml [4]. This suggests that the first-line recommended antifungal agent is liposomal Amb (L-Amb) or Amb lipid complex (ABLC). ECM/M/ESCMID and ECIL-6 guidelines recommend the use of L-Amb with a daily dosage of at least 5 mg/kg/day for mucormycosis [9,10]. Recently, isavuconazole has been added to the armamentarium of antifungal agents, however, its use has not yet been specified in the most recent guidelines [9]. Management of invasive mucormycosis includes comprehensive approach like antifungal therapy, surgery and control of underlying conditions like reduction of immunosuppressive therapy in this case.

Conclusion

The purpose of this case report is to emphasise that R. homothallicus, although a rare fungus, its differentiation is important as it has major therapeutic implications. Mucormycosis
is a life-threatening fungal infection causing angioinvasion that occurs mostly in immune-compromised patients and is associated with an increasing incidence and mortality despite the availability of therapeutic tools. Earlier diagnosis and optimal medico-surgical treatment can improve survival and reduce morbidity. Comparative studies are needed to better optimize induction and consolidation treatment.

Acknowledgement

Authors thank Dr. Arunaloke Chakrabarti, Professor and In Charge, Centre of Advance Research in Medical Mycology, WHO collaborating Centre for Reference and Research of Fungi of Medical Importance, National Culture Collection of pathogenic Fungi and Head, Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research, Chandigarh, for their kind help in the genomic sequencing of the organism.

References