

Mediastinal Zygomycosis (Mucormycosis): an Unusual Manifestation of Invasive Zygomycosis (Mucormycosis), Presenting as a Mediastinal Mass in an Immunocompetent Adult Male

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Abstract

The common causes of mediastinal mass are neoplasms including Hodgkin's disease, neuroblastoma and non-Hodgkin's lymphoma. About one third of the cases are benign such as teratomas, neurofibromas and lipomas. Histological findings are essential to distinguish between benign and malignant conditions. Zygomycosis is a rare fungal infection usually presenting as a subcutaneous infection. Visceral involvement is reported usually with pulmonary and gastrointestinal tract involvement. Here the authors report a case of zygomycosis in an immunocompetent adult male who presented with mediastinal mass.

Introduction

Mucormycosis is an angioinvasive infection caused by the ubiquitous filamentous fungi of the Mucorales order of the class Zygomycetes. It is third most common invasive mycosis after candidiasis and aspergillosis in patients with hematological and allogeneic stem cell transplantation. Mucormycosis also remains a threat in patients with diabetes mellitus, also recognized recently in developing countries such as India, in patients with diabetes or trauma. A considerable proportion of patients with mucormycosis have no apparent immune deficiency [1,2]. These patients typically have primary cutaneous mucormycosis associated with trauma or burns. Mucormycosis is a very rare fungal infection in humans. It generally affects the immunocompromised host and manifests in six distinct forms based on anatomical localization: (1) Rhinocerebral (2) Pulmonary (3) Cutaneous (4) Gastrointestinal (5) Disseminated and (6) Uncommon presentation.

Mucormycosis has emerged as an important fungal infection with high mortality rate, it is caused by fungi of the class Zygomycetes (consisting of the orders Mucorales and Entomophthorales). The majority of human cases are caused by mucorales, therefore the term mucormycosis and zygomycosis are interchangeable, (the term phycomycosis is also used) [3,4]. The mucorales species most often recovered from clinical specimens are those of the *Rhizopus* (most common genus associated with mucormycosis), *Lichtheimia* (formerly known as *Absidia* and *Mycocladius*) and *Mucor*. Species of other Zygomycetes genera such as *Rhizo*, *mucor*, *Saksena*, *Cunninghamella*, and *Apophysomyces* are less common [4,5]. Fungi of the order Entomophthorales are uncommon pathogens, with infection typically restricted to tropical areas and produce chronic cutaneous and subcutaneous infections result from direct inoculation of fungal spores in the skin. In general these infections occur in immunocompetent hosts and progress locally via direct extension into adjacent tissues but occasionally are angioinvasive or become disseminated [4,6]. The reverse (dissemination from internal organs to

the skin) is very rare [3,7] Roden et al noted such reverse dissemination in only 6 cases (3%). Depending on the extent of the infection, cutaneous mucormycosis is classified as localized when it affects only skin or subcutaneous tissue, deep extension when it invades muscles, tendons, or bones, and disseminated when involves other noncontiguous organs. In contrast Mucorales species are vasotropic causing tissue infections and the mucormycosis spectrum ranges from cutaneous, rhinocerebral, and sinopulmonary to disseminated and frequently fatal infections especially in immunocompromised hosts [3]. Very rarely zygomycosis can present as a mediastinal mass [1,2]. The common causes of mediastinal mass in an immunocompetent patient are neoplasms that include the Hodgkin's disease, non-Hodgkin's lymphoma and neuroblastoma. One third of cases are benign including the germ cell tumor, teratoma, thymomas and very rarely chronic fibrosing mediastinitis may present as mediastinal mass. Hence histopathology is a very important and essential tool for the confirmation of diagnosis. Here we report a case of zygomycosis presenting as mediastinal mass with superior vena cava obstruction syndrome in an immunocompetent adult male.

Case Report

A 30 year-old male presented with bilateral neck swelling, non-productive cough, and exertional dyspnoea, hoarseness of voice and weight loss of four months duration. He had no co-morbidities and was a non-smoker. There was no history of alcohol intake or tobacco chewing. Examination revealed bilateral neck fullness with multiple, matted and palpable lymph nodes. The left side of the chest and upper abdomen showed engorged veins with upward flow from the umbilicus. Respiratory system examination revealed diminished breath sounds over the right infraclavicular region with crackles. Other systemic examinations were unremarkable. His investigations revealed normal hemogram with normal white cell and platelet count. Renal and liver function tests were normal HIV tests (1 and 2), HCV and HBSAg were non-reactive. X-ray chest showed an abnormal opacity in the right superior mediastinum with mediastinal widening

(Figure 1). CT scan chest revealed a large infiltrative soft tissue mass in anterior, middle, posterior and superior mediastinal compartment with displacement and compression of superior vena cava and great vessels of the arch. Bilateral hilar lymphadenopathy was noted; few nodular lesions were seen in the right upper and middle lobe with involvement of adjacent pericardium (Figure 2). Sputum for Gram's stain, fungal stain and Z. N. stain were negative.

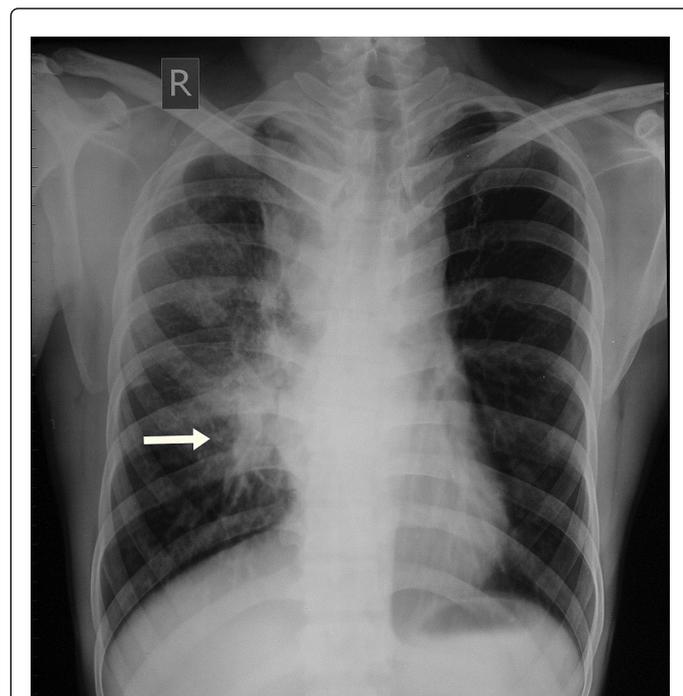


Figure 1: X-Ray chest showing opacity in right superior mediastinum with right superior mediastinal widening.

Sputum for bacterial, AFB and fungal and culture were also negative. Supraclavicular lymph node biopsy showed a granulomatous lymphadenitis with plenty of septate branching hyphae suggestive of zygomycete species (Figure 3a). There was no evidence of Hodgkin's disease, lymphoma or Langerhan's giant cell granulomatosis. Tissue culture for fungus was not done. Antibiotic (Meropenem) and antifungal (Amphotericin-B) were started.

A surgical reference was made for the excision of the mass but the cardiothoracic surgeon deferred surgical intervention in view of inoperability. Bronchoscopy was performed to rule out endobronchial obstruction. Bronchoscopy showed extensive compression along the right lateral and anterior wall of lower trachea with areas of yellowish cheesy material at the indentation site. The lower end of trachea could not be negotiated and carina could not be seen due to a large extrinsic compression on the anterior wall (Figure 3b). Bronchial wash examination did not reveal any specific infection or malignant cells.

Oesophago-gastroduodenoscopy showed an extrinsic compression due to a large mass anterior to the oesophagus at 30 cm (subcarinal, infiltrating the oesophageal adventitia, with no central necrosis). Endoscopic ultrasound guided FNAC was done and histopathology revealed a granulomatous lesion consistent with fungus (Zygomycete). Patient's clinical condition further deteriorated despite treatment therefore he was shifted to ICU, intubated and ventilated. Antibiotics

and antifungal treatment were continued but no improvement was noted and eventually the patient succumbed to the infection.



Figure 2: CT Scan chest revealed a soft tissue infiltrative mass in anterior and posterior mediastinal compartment with compression and displacement of superior vena cava and arch of aorta. Bilateral Hilar Lymph adenopathy with few nodular lesion in upper and middle lobe of right lung with involvement of pericardium.

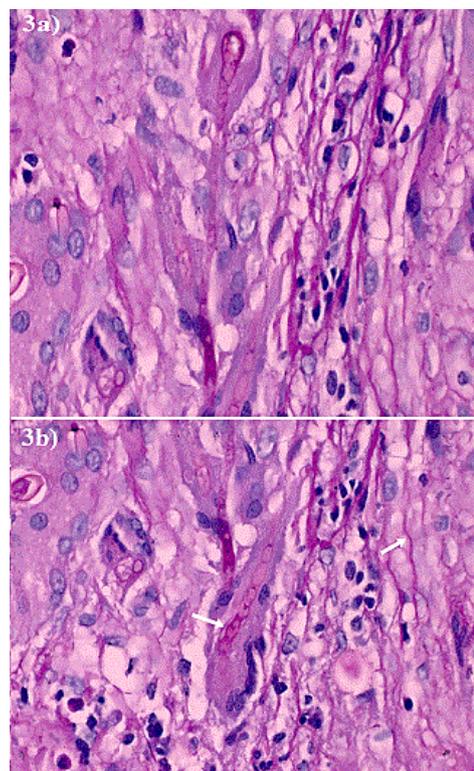


Figure 3(a, b): Histopathology specimens from the case showing granulomatous lymphadenitis with plenty of septate branching hyphae consistent with Zygomycete species.

Discussion

Mucormycosis is a serious life threatening invasive fungal infection caused by fungi of the class zygomycetes, order mucorales. Zygomycetes are saprophytic fungi present in soil and decaying organic matter. Mucorales species that are pathogenic in humans grow rapidly on carbohydrate substrate and produce abundant sporangiospores. Spores are airborne and inhalation of zygomycetes conidia into the respiratory tract occurs daily although hematogenous and lymphatic spread to lungs may occur from other sites also. Disease may be localized in lungs or it may disseminate. The diagnosis is based on the histological demonstration of broad, infrequently septated hyphae, which have irregular branching [8]. Culture of the organism from body fluids is successful in fewer than 20% of cases [9]. A positive culture helps in further differentiating the various species. The Entomophthorales can cause cutaneous and mucocutaneous infections largely in immunocompetent host in tropical and subtropical regions. In contrast, the mucorales, histologically distinct order are commonly associated with the invasive, disseminated and fatal forms of zygomycosis. The most common species causing human disease are *Rhizopus arrhizus* accounting for more than 70% cases. Zygomycosis characteristically afflicts immunologically compromised host, with a rhino cerebral form occurring most often in patients with poorly controlled diabetes mellitus and pulmonary zygomycosis in leukaemia, lymphoma and neutropenic patients. It has also been reported in chronic renal failure, transplant recipient and patients receiving immunosuppressive therapy. However, pulmonary and cutaneous involvement has also been reported in apparently healthy individuals. Besides this patients with iron overload status undergoing chelation therapy with deferoxamine are at increased risk for zygomycosis. Deferoxamine abolishes the fungicidal effects of serum and increase the in vitro fungal growth by acting as siderophore to bind iron. This allows the fungus to uptake the mineral which is essential for the pathogenicity of this mold. Antifungal agents with no activities against zygomycetes, such as voriconazole and caspofungin have also been implicated in breakthrough zygomycosis. Hospital environment, Nosocomial mucormycosis, health care associated procedures and devices, contaminated wound dressings, transdermal nitrate patches were also reported for this infection. The reported incidence of mucormycosis ranges from 0.4% to 16% depending on the SOT type. The clinical hallmark of invasive mucormycosis is tissue necrosis resulting an subsequent thrombosis, in most cases the infection is progressive and results in death unless underlying risk factors (ie. metabolic acidosis) are corrected and aggressive treatment with antifungal and surgical excision is instituted. The most common reported sites of invasive mucormycosis have been the sinuses (39%), lungs (24%), and skin (19%). Dissemination developed in 23% of these cases. The overall mortality for the disease is 44% in diabetes, 35% in patients with no underlying conditions, and 66% in patients with malignancies. Pulmonary mucormycosis occurs most often in neutropenic patients with cancer undergoing induction chemotherapy and those who have undergone HSCT and have graft versus host disease [13]. The overall mortality in patients with pulmonary is high (76%), it is even higher in severely immunocompromised patients. The clinical features of pulmonary mucormycosis are nonspecific and cannot be easily distinguished from those of pulmonary aspergillosis. Patients usually presents with prolonged high grade fever (>38°C), unresponsive to antibiotics, non-productive cough is a common symptom, whereas hemoptysis, pleuritic chest pain and dyspnea are less common. In rare circumstances pulmonary mucormycosis can present as an endobronchial or tracheal lesion especially in diabetics,

endobronchial mucormycosis can cause airway obstruction, resulting in lung collapse, which can lead to invasion of hilar blood vessels with subsequent massive hemoptysis [10,11]. Pulmonary mucormycosis may invade lung adjacent organs, such as the mediastinum, pericardium, and chest wall [8]. The signs of pulmonary mucormycosis on chest images are also nonspecific and undistinguishable from those of pulmonary aspergillosis. The most frequent findings include infiltration, consolidation, nodules, cavitation, atelectasis, effusion, posterior tracheal band thickening, hilar or mediastinal lymphadenopathy and even normal findings [12-14]. The air crescent sign may be observed [15,16]. In a study of Computed Tomography (C. T.) scan feature in 45 patients with HMs who had pulmonary mucormycosis or aspergillosis, Chamilos et al. [17], found that the presence of multiple lung nodules >10 and pleural effusion on initial C. T. scan was an independent predictor of pulmonary zygomycosis. The case under discussion had no identifiable predisposing factor and had disease involving the lungs and mediastinum. Mediastinal zygomycosis is rare and forms the subject matter of some case reports. To the best of our knowledge superior mediastinal involvement with compression of SVC due to Zygomycosis has been reported in very few cases [1,2]. Treatment with amphotericin-B used alone or in combination with surgical debridement of diseased tissue has helped in affecting cures and reducing mortality rates in zygomycosis in 20% patients [9]. In summary Zygomycosis can lead to symptoms and radiological signs similar to lymphoma, it is vital not to miss the diagnosis of neoplasm but possibilities of a mass mimicking zygomycosis should always be kept in mind and confirmed histologically.

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