Case Report
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Disseminated Angioinvasive Aspergillosis

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Abstract

Disseminated angioinvasive aspergillosis is a rare fatal disease seen in immunocompromised hosts. Invasive pulmonary aspergillosis have been reported in immunocompetant patients with preexisting COPD having bulla, tuberculous cavity or bronchial cyst. A 22 years aged male patient was hospitalized after consumption of ratol, a rodenticide poison. Investigations revealed altered liver function,leukocytosis of 16,600cells/mm3, HIV and HbsAg negative status. Clinical diagnosis was fulminant hepatocellular failure.On fifth day, he suddenly developed massive haematemesis and dyspnea and succumbed to death. Autopsy revealed disseminated angio-invasive aspergillosis involving the lungs, heart and kidney. On histopathology, Invasive pulmonary aspergillosis, myocarditis, endocarditis, angioinvasion and renal aspergillosis showing septate hyphae branching at acute angle were seen. We report this case of invasive aspergillosis occurring in a non immunocompromised person, diagnosed on autopsy.Our case upholds the significance of autopsy.

Keywords: Aspergillosis; Autopsy; Disseminated; Hyphae.

Introduction

Aspergillus fumigatus is the most frequent cause of invasive aspergillosis. Occurrence of infection in immunocompromised hosts due to other aspergillus specieslike *A niger, A flavus, A terreus* is emerging. Patients with malignancy,chemotherapy, corticosteroid use, neutropenia are at risk [1,2]. Lung is the most commonly involved organ. Dissemination to brain, heart, kidney, eye and GIT can occur. In non neutropenic patients, colonization by aspergillus occurs, but invasive infection is rare. It is usually detected incidentally in immunocompetent patients with pre-existing lung disease such as advanced emphysema with bullae or previous cavity secondary to tuberculosis, neoplasm or bronchial cyst [1,3]. Ratol poison, a frequently used rodenticide, is a zinc phosphide compound. Phosphine is a protoplasmic toxin, inhibits cytochrome c oxidase, catalase and peroxidase and perturbs mitochondrial morphology. It can lead to cardiac, hepatic, renal and multiorgan failure [4,5]. We report a case of disseminated angioinvasive aspergillosis in an immunocompetant host with ratol poisoning.

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Case Summary

A 22 years aged male patient was admitted to hospital after attempted suicide for the reason of unemployment. He had consumed ratol, a rodenticide poison. Investigations showed hemoglobin 14.4gm/dl, leucocyte count 16,600cells/mm3, differential count of neutrophils65%, lymphocytes 30%, eosinophils 3%, monocytes 2%, ESR 15mm/hour. ELISA for HIV and Hepatitis B were negative. On second day, he developed jaundice, fever, cough with haemoptysis. Altered liver function tests were noted with severe thrombocytopenia.After three days, his liver function tests deteriorated, hemoglobin was 12gm% and platelet count 27,000/cumm. He had massive haemetemesis, dyspnea and succumbed to death on fifth day. Clinical diagnosis was Fulminant hepatocellular failure secondary to ratol compound

consumption. Autopsy was done.

Autopsy Findings

External surface of the organs showed petechiae. Both the lungs showed multiple grey white consolidated areas largest measuring 3x3cms. Multiple soft pale brown to gelatinous areas were seen in left ventricular wall and papillary muscles. A brown elevated friable endocardial nodule was seen at base of tricuspid valve along with multiple irregular vegetations adherent to mitral valve chordae (Figure 1). Kidneys showed multiple necrotic areas in the cortex largest measuring 1x1cm.

Microscopically, lungs showed invasive aspergillosis and bronchopneumonia with thin acute angle branching septate hyphae in the alveoli. Angioinvasion was seen. Sections from the heart showed fungal colony composed of uniform branching septate hyphae in endocardium, large areas of necrosis and acute inflammation in myocardium (Figure 2). Kidneys showed micro abscess with occasional aspergillus hyphae in interstitium. On PAS and GMS stains, dichotomously branching thin septate hyphae of aspergillus were seen. Liver showed centrilobular necrosis and fatty change.

Table 1: Differential diagnosis of fungi with hyaline septate branching hyphae[7,8,9]

	Aspergillus	**Fusarium**	**Pseudoallescheria&Scedosporium**	**Mucor**
Hyaline septate branching hyphae	+	+	+	Hyaline aseptate/ pauciseptate
Hyphae with yeast like structures	_	++	++	_
Hyphal diameter	Consistent diameter, 3.5 -4.5 µ	2-5 µ,often show variation in diameter	2-5µ	10-50 µ, broad hyphae, varied width
Hyphal Branching	Dichotomous acute angle, rarely 90º branching	both 45º and 90º branching, with constriction at branching	Predominantly branch at acute angles and irregular, haphazard branching	90º non dichotomous branching, folded or crinkled, sparse or fragmented
Constricted hyphae & varicosities	-	++	++	_
Skin involvement	+	+++	+++	+
Antibiotic sensitivity	Voriconazole, AmphotercinB	Voriconazole, Amphotercin B	Voriconazole	Amphotercin or Posoconazole

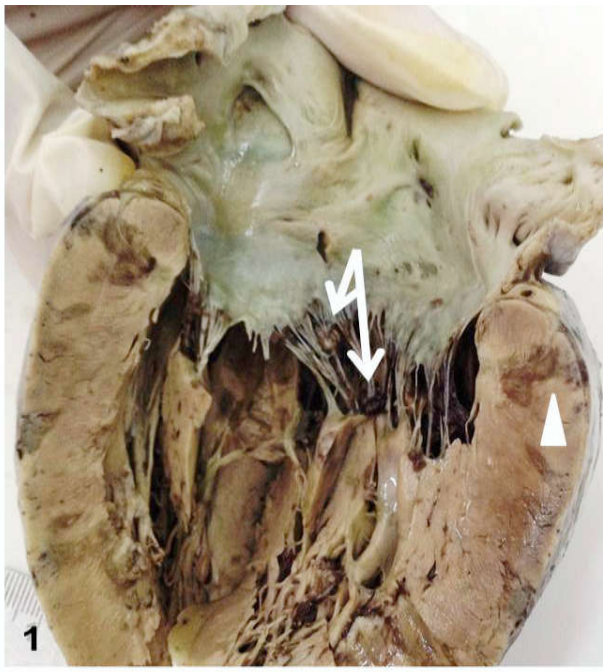

Fig. 1: Gelatinous areas in left ventricular wall(arrow head), mitral valve vegetations (arrows)

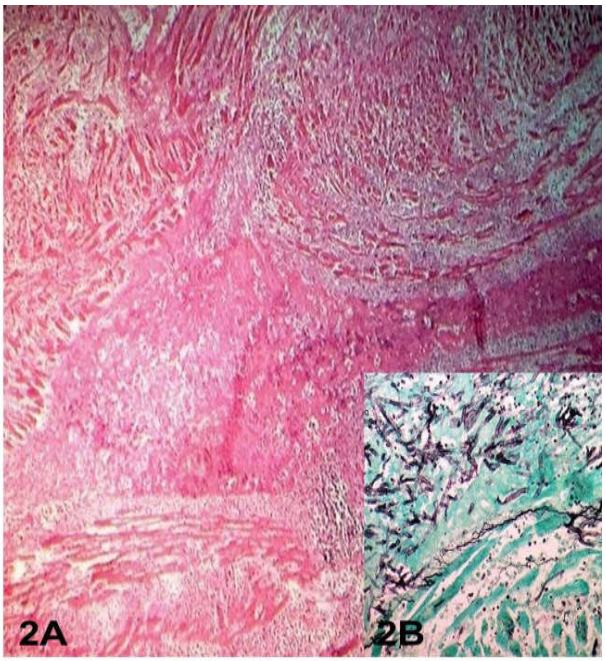

Fig. 2: Cardiac aspergillosis. 2A.Myocardial necrosis and inflammation(H&E,x40). 2B. Thin septate branching hyphae in necrotic myocardium(GMS,x400).

Discussion

Disseminated angioinvasive aspergillosis, a life threatening infection, occurs in immunosuppressed patients, causing abscesses in brain, heart, bone, eye and gastrointestinal tract. Incidence of aspergillosis has been reported to be 1.5-15% in liver transplant patients, 5-9% in bone marrow transplant patients, 3-24% in heart/heart-lung transplant patients and 14% in patients with hematologic malignancies [6]. But disseminated angio invasive aspergillosis in an immunocompetant host is rare.

Diagnosis of aspergillosis on histopathology alone may be difficult. Aspergillus shows dichotomous acute angled branching of hyaline septate hyphae. It forms fruiting bodies at high oxygen tension sites as pulmonary cavity and paranasal sinuses. Constricted and focal swollen hyphae can be seen in aspergillus and represent damaged hyphae, especially in patients with chronic granulomatous disease. Differentials include other hyaline septate branching hyphae like *Fusarium, scedosporium* and *pseudoallescheria*. Some authors state useful differentiating points on histopathology as stated in Table 1. Disseminated fusariosis, scedosporium and pseudoallescheria show skin involvement more commonly than in invasive aspergillosis. In our case no skin involvement was seen and the morphology was consistent with that of aspergillus. There are various laboratory modalities for diagnosis of aspergillosis which include blood culture, Galactomannan antigen test, ELISA, PCR, immunohistochemistry, In situ hybridization. However fungal culture remains the gold standard. Identifying and classifying the fungus is important. The treatment of aspergillus and fusarium infections is Voriconazole and Amphotercin B, whereas for mucor infection, treatment includes amphotericin B or posaconazole.*Scedosporium* shows Amphotercin resistance, but is susceptible to Voriconazole [7,8,9].

Ratol poison, a frequently used rodenticide, is a zinc phosphide compound. Phosphine is a protoplasmic toxin, inhibits cytoplasmic enzymes and can lead to cardiac, hepatic, renal necrosis. It is also known to induce neutropenia [4,5].

In our case, patient had neutrophilic leukocytosis and HIV negative status. Patient was non diabetic, nonalcoholic. Past respiratory infection and other immunodeficiency status were absent. Invasive aspergillosis in non immunocompromised hosts has been documented in literature and only few reports have been published. We report this case of disseminated angioinvasive aspergillosis with involvement of lungs, heart and kidneys in a patient with rodenticide poisoning.

Conclusion

Invasive aspergillosis can occur in an immunocompetent host and be fatal. Our case also upholds the significance of autopsy. The accurate diagnosis and early appropriate treatment are extremely important in the management of fungal infections in order to avoid unfavorable prognosis.

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