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Invasive Cerebral and Pulmonary Mucormycosis in An Immunocompromised Patient

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Abstract

Mucormycosis is a rare opportunistic infection caused by saprophytic commensal fungi. Disseminated infection can be lethal in diabetic and immunocompromised patients. This case of disseminated cerebral and pulmonary mucormycosis in a diabetic patient with a fatal outcome reflects the insidious multisystem dissemination in a culture negative case wherein the diagnosis was made at autopsy.

Key Words: Mucormycosis, opportunistic infection, diagnosis, autopsy

Introduction

Mucormycosis is a rare opportunistic infection caused by saprophytic commensal fungi of family Mucoraceae. Multiple clinical syndromes including rhinocerebral (most common), pulmonary, gastrointestinal, cutaneous and disseminated forms have been described worldwide (1, 2). Disseminated infection can cause fulminant and lethal complication in diabetic and immunocompromised patients. A case of disseminated cerebral and pulmonary mucormycosis in a diabetic patient with a fatal outcome is being discussed.

Case Report

A diabetic and hypertensive patient of 48 years of age, having admitted in a state of altered sensorium and abnormal limb movements, developed sudden repeated cardiac arrests with a fatal outcome. The patient had a prior 3-day history of fever and was found to be conscious, but disoriented with sluggishly reacting pupils, papilloedema, neck rigidity, decreased plantars and bilateral chest crepitations. Contrast enhanced computed tomography (CECT) of brain showed hypodense areas suggestive of space occupying lesion in basifrontal and frontal region. Magnetic resonance imaging (MRI) of brain showed hyperintensities extending to temporal lobes. He was treated on the lines of pneumonia with febrile encephalopathy. Laboratory findings revealed a leucocyte count of 11550/mm^3 with 68% neutrophils, hemoglobin 11.7 g/dL and platelet count of 306,000/mm^3. Blood urea was 25 mg/dL, creatinine 1.3 mg/dL, sodium 173 mEq/L, potassium 2.9 mEq/L, calcium 9.7 mg/dL, blood sugar 305 mg/dL, bilirubin 0.5 mg/dL, total protein 4.1 g/dL, albumin 1.6 g/dL, transaminases 46 and 58 IU/L, alkaline phosphatase 96 IU/L, amylase 95 IU/L, prothrombin time 13/15, and INR 1.22. Widal, HIV and Dengue tests were negative. Urine showed proteins and sugar in traces, 2-3 erythrocytes and 5-7 pus cells per high-power field. All cultures were negative. Lumbar puncture yielded turbid fluid with 20 RBC/mm^3, 200 WBCs/mm^3, predominant lymphocytes, protein value 127 g/dL, glucose 132 mg/dL and chloride 159 mEq. Gram, Zeihl Neelson and India ink stains showed no organisms.

Whole body autopsy revealed meningeal congestion and loss of sheen, widened gyri and narrowed sulci. Extensive liquefactive necrosis of frontal, basifrontal, temporal lobes and thalamus was seen. Spinal canal hematoma compressed the spinal cord. Cerebellar hemorrhage dissecting parenchyma was seen. Pleura was thickened and adherent, and lungs were heavy, boggy and congested with multiple septate cavities with necrotic debris. Spleen was soft and congested, liver was enlarged, and gall bladder showed multiple pigmented stones. Both kidneys were contracted, had multiple serosanguinous fluid filled surface cysts, and mild attenuation of corticomedullary junction was seen. Left ventricular hypertrophy and left coronary artery obstruction were seen. Pleural and pericardial cavities had 20 ml and 15 ml fluid, respectively. Microscopically, meningitis with neutrophilic and lymphocytic infiltration of meninges and parenchyma, extensive parenchymal necrosis and extravasation of erythrocytes in cerebellum and midbrain was seen. Frontal, temporal, occipital lobes and thalamus showed broad ribbon shaped nonseptate hyphae with random right angled branching. Vessels were invaded by fungal hyphae and thrombosed. Extensive lobar pneumonitis, neutrophilic and histiocytotic alveolar infiltration, edema and hemorrhage were seen. Fungal hyphae similar to that in brain were seen in right

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middle and left upper lobes forming a fungal ball, the morphology of which was confirmed by PAS and Grocott's methenamine silver stains to belong to Mucoraceae (Figure 1). Left coronary was atherosclerotic and had a calcified plaque. Portal tracts showed inflammatory infiltrate and hepatocytes showed macrosteatosis. Gall bladder showed neutrophilic infiltration and prominent Rokitansky Aschoff sinuses. Red pulp was congested and vessels thickened in spleen. Few sclerosed glomeruli, onion skinning of vessels, acute tubular necrosis and lymphomononuclear interstitial infiltrate were seen. Mild autolytic changes in stomach, intestines and pancreas were seen. No evidence of malignancy or metastasis was seen. Autopsy cultures were negative from heart blood and cerebrospinal fluid. No viruses were identified.

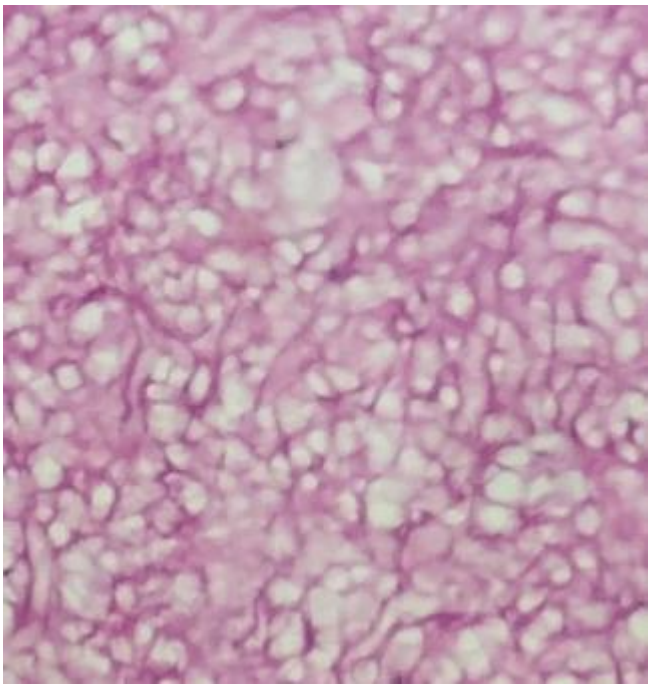

Fig. 1. High-power microscopy (400X) shows broad aseptate hyphae with liquefactive necrosis suggestive of mucormycosis.

Discussion

Mucormycosis is a rare disease with approximately 1.7 cases per million people in United States (1). A review of mucormycosis cases at a U.S. cancer center found that 0.7% of patients had mucormycosis at autopsy and 20 patients per 100,000 admissions had the disease (3). Breakthrough mucormycosis in the setting of antifungal prophylaxis or therapy to which mucormycosis is resistant is emerging, especially in immunocompromised (4, 5). Risk factors contributing to mucormycosis are diabetes mellitus, metabolic acidosis, lymphoma, leukaemia, tuberculosis, chronic renal and hepatic disease, extensive burns, organ or haematopoietic cell transplantation, neutropenia, chronic immunosuppression, energy malnutrition, administration of steroids, antibacterial drugs, antimitotic drugs, immunosuppressants, desferrioxamine, radiation therapy and intravenous drug abuse (1, 2). Mucormycosis has also been reported without any of these predisposing factors (6, 7). Poorly controlled acidotic diabetes mellitus becomes a high risk factor for development of mucormycosis as granulocyte phagocytic ability and polymorphonuclear phagocytic response are reduced. Rhizopus species are the most common followed by Mucor, Cunninghamella, Apophysomyces, Absidia, Saksenaea, Rhizomucor amongst others (1). Organisms enter through the respiratory or digestive tract and invade blood vessels followed by dissemination through blood, lymphatics or nerve trunks (8). Arteries are mainly involved where the fungus proliferates within the internal elastic lamina dissecting it away from the media. As the hyphae penetrate the endothelium, thrombotic arteritis, infarction, hemorrhage, and extensive necrosis follow (9). Direct soft tissue invasion frequently leads to abscess formation. Pulmonary mucormycosis may exist as a chronic indolent disease (10). Diagnosis requires culture of a biopsy specimen as swabs and discharge may be unreliable (2). Clinical features are nonspecific and cultures may fail to grow despite the presence of widespread and aggressive disease making the diagnosis difficult. MRI and CT scans may show destruction of soft tissue or bone in advanced disease and chest X-rays may show a lung cavity.

Multisystem invasive mucormycosis was seen in this diabetic patient who had nonspecific clinical presentation and sterile cultures. Autopsy revealed meningitis, cerebellar and midbrain haemorrhage and cerebral oedema along with conclusive features of cerebral mucormycosis. Widespread liquefactive necrosis and meningeal congestion are also unusual findings. Pulmonary consolidation and bilateral cavitation implies chronic indolent infection. No nasal sinus, orbital or other primary locus of fungus infection was discovered. The fungus probably entered the respiratory system either from the environment *via* inhalation of conidia or aspiration of infectious material from upper respiratory tract followed by hematogenous spread to the brain. The patient also had fatty liver, and cystic and hypertensive changes in the kidney which may have contributed to predisposition. There was also evidence of cardiovascular disease in the form of left ventricular hypertrophy and complicated atherosclerosis of left coronary artery, cholecystitis with cholelithiasis, the role of which in the disease process remains to be determined.

Conflict of Interest: None

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