

Case Reports

Deep Fungal Infection- An Emerging Problem in Bangladesh

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Abstract

Objective: Invasive deep fungal infections have become a major cause of morbidity and mortality over the past three decades. Organ transplantation, the use of aggressive chemotherapy and the availability and widespread use of immunosuppressive treatments for many medical ailments have resulted in large populations of patients who are at risk of fungal infections. We report our experience to increase awareness of the clinical spectrum of disseminated fungal infection and its similarity to other infections and malignancy.

Materials and Methods: Case reports from different medical institution for last 6 months were searched through case registry and recent scientific presentation and publications.

Results: Recently a case of Histoplasmosis was reported in Dhaka Medical College Hospital (DMCH) where a 57 years old male presented with low grade fever for 3 months, backache followed by progressive weakness of both lower limbs, there was spastic paraplegia with sensory loss upto the level of D₁₀. An open biopsy from paravertebral soft tissue showed histopathological features consistent with histoplasmosis. Other deep fungal infections e.g. pulmonary blastomycosis, mucormycosis and pulmonary aspergilloma were also reported in DMCH and Bangabandhu Sheikh Mujib Medical University (BSMMU) and RMCH.

Conclusion: As these fungal infections are not commonly encountered in our country and most of the dissemination has similar clinical features of chronic inflammatory process and malignancy, we need a high index of suspicion to diagnose with different diagnostic approach. Bangladesh may be experiencing increase load of disseminated fungal infections and awareness is now very important to explore its underlying aetiology.

Keyword: Endemic mycoses, histoplasmosis, blastomycosis, mucormycosis, aspergilloma, Bangladesh

Introduction

Fungus is one of the cause of wide variety of disease conditions, from the embarrassing athlete's foot and ringworm to the potentially life threatening systemic diseases. Endemic mycoses is often asymptomatic, but in appropriate hosts it can cause severe and even fatal infections. Deep fungal infections comprise two distinct group of conditions, the subcutaneous and systemic mycoses. In recent years, the systemic mycoses have become important opportunistic infectious complications in immunocompromised patients, including those with AIDS and the patients with malignancies.¹ Systemic fungal infections cause 25% of infection related deaths in leukemics.² Serious fungal infections may cause 5-10% of deaths in those undergoing lung, pancreas or liver

transplantation.² Frequent use of antibiotics, oncostatics, immunosuppressants and indwelling catheters lead to the causation of deep fungal infections.³ Histoplasmosis is the most common endemic mycosis in human. *Histoplasma capsulatum* is a dimorphic fungus distributed worldwide, but endemic in the Americas, Africa, and Asia.⁴ Approximately, 10% cases of histoplasmosis develop into progressive disseminated histoplasmosis (PDH).⁵ Disseminated histoplasmosis may present as acute PDH with fever, malaise, cough mimicking pulmonary tuberculosis. Chronic PDH manifests as fever, sweats, weight loss, organomegaly, lymphadenopathy. Pulmonary aspergilloma is a rare disease, usually presenting as secondary saprophytic infection of preexisting cavities in the lung.^{6,7} Patients who have blastomycosis exhibit a spectrum of pulmonary

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manifestation ranging from mild self limited pneumonia to diffuse pneumonia accompanied by acute respiratory distress syndrome (ARDS).^{8,9,10} Rhinocerebral zygomycosis is usually caused by *Rhizopus oryzae* or *Rhizopus arrhizus*. The disease typically commences in the nasal cavity or paranasal sinuses and causes pain, nasal discharge, and fever; the organisms may then invade the palate to produce black, necrotic oral ulcers. Orbital invasion may reduce orbital cellulitis, impaired ocular movements, proptosis, and ptosis. Intracranial invasion follows penetration of ophthalmic vessels or the cribriform plate.¹¹

Materials and Methods

Case reports from different medical institution for last 6 months were searched through case registry and recent scientific presentation or publication. Original article and case series were searched for disseminated fungal infection in Bangladesh from all available national and international journal. Search engine was Google and Pubmed. Search item was Fungal infection, Deep Mycosis, Histoplasmosis, Aspergillosis, Mucormycosis, Blastomycosis, Bangladesh etc. Selective search of case series and reports were mainly focused on searching and special consideration was given in Bangladesh. Review articles on deep mycosis was also searched for last 6 yrs for collating and correlating with the case reports.

Case Series

Case number 1: A 57 years old male, non diabetic, normotensive, smoker and farmer presented with low grade fever for 3 months, backache for 2 and a half

months followed by progressive weakness of both lower limbs along with constipation and urinary incontinence. On examination, he was ill looking, anaemic, there was generalized lymphadenopathy. On neurological examination, there was spastic paraplegia with sensory loss upto the level of D₁₀. Examination of abdomen revealed mild hepatomegaly. Investigations showed Hb 8.9 gm/dl, ESR 90 mm in first hour, peripheral blood film showed normochromic normocytic anaemia with increased rouleaux formation. Bone marrow showed hyper-reactive marrow. Radiological evidence of x-ray and MRI spine were reduction of the intervertebral disc spaces and destruction of vertebral body (Fig 1a) with paravertebral soft tissue mass mimicking features of tuberculosis or malignancy. An open biopsy from paravertebral soft tissue showed histopathological features consistent with histoplasmosis (Fig 1b).¹²

Case number 2: Another case was reported in BSMMU where a 45 years old male diagnosed and treated as a case of abdominal tuberculosis presented with fever for 15 days, abdominal pain, jaundice and hiccup for same duration and a painful growth in oral cavity for same time. On examination, there was generalized lymphadenopathy and there was a growth on the tongue which was raised, fungating, ulcerated and covered with necrotic material (Fig 2). There was another growth on the hard palate which was rounded and ulcerated. Histopathology from ulcer showed features consistent with histoplasmosis.



Fig.-1(a): Sagittal MRI of dorsal spine showing involvement of vertebral body & disc © HAM Nazmul Ahasan

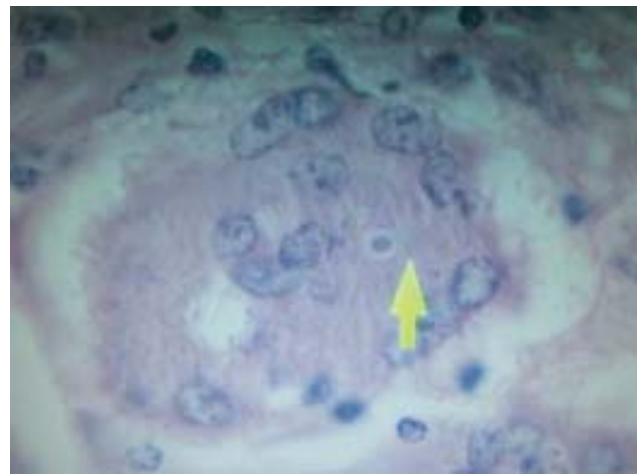


Fig.-1(b): Biopsy specimen showing *Histoplasma Capsulatum* (leishman stain) © HAM Nazmul Ahasan



Fig.-2: Fungating ulcer at tongue and palate © MA Jalil Chowdhury



Fig.-3(a): CXR showing opacity © HAM Nazmul Ahasan

Case Number 3: In 1995 in RMCH, a 50 year old male, smoker presented with fever and dry cough for 3 months. Chest x-ray showed homogenous opacity in left upper zone (Fig 3a), sputum showed inflammatory cells with some fungal yeasts and hyphae. Percutaneous lung aspiration showed double walled budding cysts suggestive of blastomycosis (Fig 3b).¹³

Case number 4: In 2004 in BSMMU a 42 year old male who was on long term steroid therapy for bone marrow failure developed left orbital swelling and blindness along with prolonged fever. Neurological examination revealed proptosis of the left eyeball with complete ptosis and periorbital oedema. There was total ophthalmoplegia with dilated pupil on the left side and impairment of sensation over the distribution of the trigeminal nerve. There was ulceration of both lips with crust formation. Histopathology from nasal mucosa showed features consistent with mucormycosis (Fig 4).¹⁴

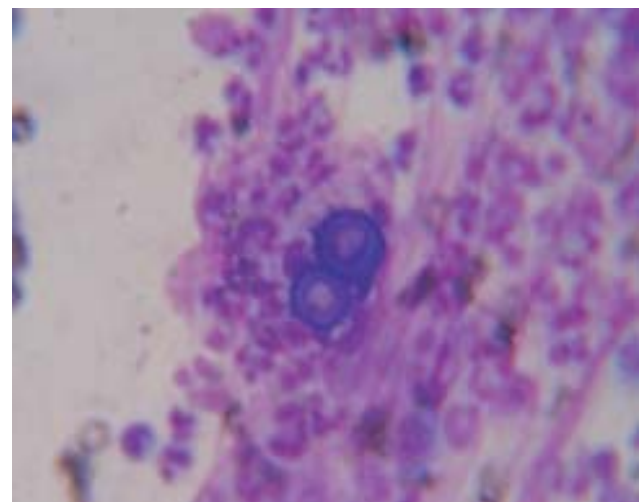


Fig.-3(b): FNAC with histopathology © Joe Mills

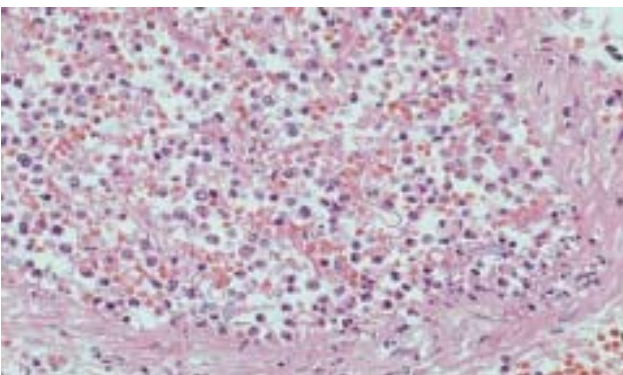


Fig.-4: Histopathology of nasal mucosa showing mucormycosis © MA Jalil Chowdhury

Case number 5: In 1994, a similar case was reported in RMCH where a 22 years old housewife, a known case of ITP, treated with steroid, presented with low grade fever and swelling of the left side of the face for 5 days. She had history of irregular intake of steroid and found to be diabetic. On examination, there was a large ulcer with sharp margin and greyish white slough was present on the hard palate (Fig-5) and there was complete ptosis, proptosis and III, IV, VI and 1st division of Vth nerve palsy on left. Histopathology from palatal ulcer showed features consistent with mucormycosis.

Case number 6: A 70 year old male, normotensive, smoker presented in DMCH in 2009 with the complains of cough ,respiratory distress and low grade fever for 2 years and left sided chest pain for 2 months. He had past history of tuberculosis 12 years back. On examination, features of cavitary lung lesion was present. Investigations showed ESR 86 mm in 1st hr, OGTT 12.60 mmol after 1 hrl, 11.56 mmol after 2 hrs, Chest X ray and CT scan showed cavitary lesion in the upper lobe of left lung with a mass within it and a crescentic rim surrounding the mass (Fig-6). CT guided FNAC showed polymorphs, macrophage and fungal hyphae which led to the diagnosis of aspergilloma.¹⁵



Fig.-6(a): Chest X ray showing cavitary lesion © Ahmed Hossain

Discussion:

Deep fungal infection is not a very common disease that is encountered in health care facilities. Although in a developing country like Bangladesh there are many reasons for immunosuppressive states and diseases persists, lack of systemic observation and diagnostic facilities makes the diagnosis of these deep fungal infections very difficult.

Histoplasmosis:

It is the most frequently diagnosed systemic mycoses and reported in 30 countries of the world. It is commonly found in bird and bat faeces. In endemic areas the organism is a soil saprophyte, and more than 70% adults appear to be infected, typically with subclinical manifestations as a result of inhaling spores. There could



Fig.-5: A ulcer at hard palate

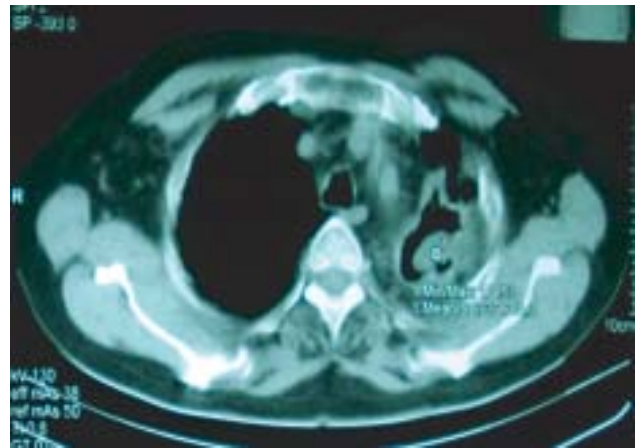


Fig.-6(b): CT scan of chest showing a crescentic rim surrounding the mass suggestive of mycetema © Ahmed Hossain

be three major manifestation of histoplasmosis: pulmonary, primary cutaneous, progressive disseminated histoplasmosis (PDH).¹⁶ Symptomatic acute disseminated infection occurs almost entirely in those who are immunosuppressed.^{8,16} The most common manifestations are chills, fever, malaise, anorexia, and weight loss. Central nervous system histoplasmosis is uncommon. The most common presentation is that of chronic lymphocytic meningitis, but focal lesions also can occur in the brain and the spinal cord and are best seen with MRI techniques. In our 1st case of histoplasmosis the patient had involvement of lymph nodes and spinal cord of CNS. The dissemination could be initially from lymph node and later involving the

spinal cord. Both sites are not very common involvement and so indicating the bizarre form of presentation. It may also be that the pattern of deep histoplasmosis varies from different area of the world. Gastrointestinal involvement is reflected in diffuse ulcerations of the mucosa and sometimes malabsorption¹⁷. In second case of our case series it has been identified to have oral mucosal ulceration of prolonged period and consist with other observation in different countries.

Blastomycoses: Blastomycoses is one of the great mimickers in medicine; verrucous cutaneous blastomycoses resembles malignancy and mass like opacities due to *B. dermatitidis* often confused with cancer.^{9,18} Chronic illness may occur and simulate tuberculosis or lung cancer, with symptoms of low-grade fever, a productive cough, night sweats, and weight loss. Sputum is mucopurulent or purulent, and hemoptysis may be present. In our 3rd case of case series the lesion was highly suggestive for malignancy or pulmonary tuberculosis. Because of the brief and self-limited nature of these symptoms, blastomycosis may go undiagnosed except in the setting of a known outbreak. So in an immunosuppressed the blastomycosis should be a clinical query for physician.

Mucormycosis:

Mucor and *rhizopus* species are the most common agents to cause Zygomycoses. Fungi of the order mucorales is responsible for most mucormycosis. These fungi are ubiquitous worldwide in soil, manure and decaying organic matter. Mucoraceae are commonly cultured from the nose, throat, mouth and feces of many healthy individuals. The most common clinical presentation is induration of the skin with surrounding erythema with rapidly progressing to necrosis.^{11,19} The two cases in our series, there were involvement of eyes and nasal mucosa in one case and oral mucosa in other one. The destroying capability and morbidity and mortality are very high in the mucormycosis. The quicker invasion close to central nervous system makes the disease more aggressive and with poor prognosis. The chronic steroid use was responsible for immunosuppression in both the cases indicating that patient on steroid should be regularly followed up for any changes of symptomatology with special attention to oronasal mucosa that could lead to suspicion of disseminated fungal infection specially mucormycosis.

Aspergilloma:

Pulmonary aspergilloma is a saprophytic form of aspergillosis and the diagnosis is usually based on radiological findings of thickened cavitory wall and

fungal ball and positive serum antibody.⁶ It has been proven that aspergilloma is locally invasive in patient having post tuberculosis cavity.²⁰ In case number 6, it has also been observed that he had received a course of antituberculosis drug prior to development of symptoms with persistent cavitory status. The dissemination or aggressiveness is less common in aspergillosis. High index of suspicion is crucial to make the diagnosis possible.

Conclusion

Deep mycoses are caused by primary pathogenic and opportunistic fungal pathogens. The primary pathogenic fungi are able to establish infections in a normal host, whereas opportunistic pathogens require a compromised host in order to establish infection. The primary deep pathogens usually gain access to the host via the respiratory tract. Opportunistic fungi causing deep mycosis invade via the respiratory tract, alimentary tract or intravascular devices. Most cases will have underlying immunosuppressed states due to underlying disease or iatrogenic therapy with immunosuppressed agents. So clinical clue for these groups or agents are crucial to make deep fungal infection diagnosis appropriately. Most of the disseminated infections have similar clinical features of chronic inflammatory process and malignancy, so high index of suspicion is needed to diagnose these cases. Bangladesh may be experiencing increased load of disseminated fungal infections and so awareness is important to explore the aetiology.

Conflict of interest: None

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