



Original Article

Clinical Outcomes of Invasive Fungal Infections in Hospitalized Patients

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Abstract

Introduction: Fungal infections are becoming a public health issue and is setting a challenge to healthcare professionals. The present study was undertaken to study the risk factor, clinical and radiological profile of the patients of invasive /systemic fungal infections.

Methodology: Patients hospitalised with suspected fungal infection were screened for fungal aetiology. Patient diagnosed with invasive fungal disease after microbiological assessment were included in the study. Past medical history, presenting complaints and clinical course of the patients was analysed.

Results: Most common age group was 41 to 60 years. Diabetes mellitus and HIV/AIDS were the most common risk factor. Aspergillus and Mucor occurred most frequently in patients of diabetes mellitus while Cryptococcus in HIV patients. Candida was found in patients with neutropenia. Headache was the common presenting symptom in patients diagnosed with Cryptococcus and Mucor while convulsions were seen in 87.5% of the patients with Cryptococcal infection. Mucor and Aspergillus were isolated mainly from rhino-cerebral and naso-orbital site, while Candida from blood and esophagus. CSF samples of all eight cases of Cryptococcus tested positive for the organism. Imaging found that all cases of Aspergillus and Mucor had tissue invasion and bony erosions. Of the patients studied, 18 (53%) survived and 16 (47%) expired. Final outcome of the patients was not significantly associated with the type of fungal organism isolated.

Conclusions: Invasive fungal infections result in high mortality, which warrants a high degree of suspicion for early diagnosis so that effective treatment can be initiated in a timely fashion.

Keywords: Invasive fungal pathogens; diabetes; diagnosis; immunodeficiency.

Introduction

Fungal infections, both systematic as well as invasive, have demonstrated an increased burden. Slowly it is becoming a public health issue and is setting a challenge to healthcare professionals. Fungal infections occurring in patients admitted in

hospitals and health care facilities are other reasons behind the rising trend. Changes in medical practices such as extensive use of immunosuppressive drugs and intensive chemotherapy have raised the population of immunocompromised individuals that are prone to

fungal infections.¹ While some of the fungal infections may be fatal, others that are subcutaneous and superficial infections affecting the skin, mucous membranes, and keratinous tissues, which can still lower patients' quality of life considerably.² *Candida albicans*, the most prominent pathogenic species are observed in 17% of the patients treated in the intensive care unit (ICU), and these infections are greatly associated with mortality and morbidity.³ Diagnostic delays, low sensitivity, difficulty in the discrimination of colonization from invasive candidiasis, limitations in current diagnostic techniques are the present challenges in the treatment programs of fungal infections.⁴ The clinical outcome of patients with invasive fungal infections depend significantly on host related factors rather than the virulence of fungal organism. In addition, understanding the role of various co morbid conditions in the causation of fungal infections can help achieve improve early treatment goals and improve the overall outcome of the patient. The present study was undertaken to study the risk factor, clinical and radiological profile of the patients of invasive /systemic fungal infections.

Methodology

Study Design and Sampling

Our prospective study was conducted in the Department of Medicine of a tertiary care hospital in Mumbai over a period of 12 months. Patients hospitalised with suspected fungal infection or the patients hospitalised for any illness and suspected to have fungal illness during course of stay were screened and worked up in detail for fungal aetiology. Only adult patients admitted in any ward or intensive care units were included. The patients whose samples were sent to microbiology department for fungal growth were traced and evaluated. Also radiological suspected fungal infections cases were worked up. Patient who were diagnosed to have definitive invasive fungal disease were finally included in the study. A total of 70 such patients were screened for the study. Aims, procedures and investigative course of the

present study were explained to every patient and request for written informed consent was made to every individual. Patients were included in the study only after obtaining valid written consent.

Data Collection and Data Analysis

Demographic details of the patients were recorded in the case record form. Age was taken as informed by patient or previous medical records. Details of the present and past illnesses were elucidated in each patient. History of the risk factors like diabetes mellitus, HIV status or use of systemic steroids were specifically enquired and assessed. Past history of Tuberculosis, any form malignancy or any major illness was noted. Details of all medications was recorded and all patients were subjected to routine haematological and biochemical investigations. Imaging studies were ordered by the treating physician as deemed necessary. All the samples were sent for fungal organism demonstration to microbiology laboratory. Fungal agents were demonstrated under microscope or cultured using selective media. Fungal organisms were identified according to their morphology.

Once diagnosis of invasive fungal infection was established antifungal medications were started. All the patients managed routinely and monitored regularly and followed till death or discharge (up to a period of 6 months). Diabetic patients were managed aggressively for sugar control and other associated co-morbid conditions. All patients with HIV seropositive positive patients were started on the antiretroviral therapy and antifungal drugs. Amphotericin B was the drug of choice for invasive/systemic fungal infection. It was initially started at smaller doses and then gradually increased to reach therapeutic level.

Data were compiled and analysed using SPSS (version 23, IBM). Quantitative data were described as means and standard deviation and qualitative data as frequency distribution. Qualitative data were compared using chi-square or Fisher's exact test, p value < 0.05 as statistically significant.

Results

Out of the 70 patients, 62 were suspected as cases of invasive fungal infection on the basis of risk factor and clinical criteria, while 8 were on radiological criteria. Of these 70 patients, 4 patients expired before adequate samples were collected for final diagnosis. Of the remaining 66 patients, 34 were proved by mycological culture method as cases of invasive fungal infection and were included for final analysis. Mean age of the patients included in the study was 47.15 ± 5.29 years and the most common age group was 41 to 60 years (Table 1). There were 56% males in the study and the mean age of patients of either gender was similar as well. There were 13 cases of Mucor, 6 of Aspergillus, 7 of Candida and 8 cases were of Cryptococcus, which were confirmed by the mycological cultures. In our patient population Diabetes mellitus was the most common risk factor and was noted in 44% patients. AIDS was the next most common risk factor in 30% patients, followed by neutropenia secondary to chemotherapy in 9% of the patients (Table 2). The association of various risk factors with the type of fungal organism isolated was statistically significant. Aspergillus and Mucor occurred most frequently in patients of diabetes mellitus while Cryptococcus in HIV patients. Candida was found in patients with neutropenia. Headache was the

common presenting symptom in patients diagnosed with Cryptococcus and Mucor (100% each), and convulsions were seen in 87.5% of the patients with Cryptococcal meningitis. Mucor and Aspergillus were isolated mainly from rhino-cerebral and naso-orbital site, while Candida from blood and esophagus. CSF samples of all eight cases of Cryptococcus tested positive for the organism. Imaging found that all cases of Aspergillus and Mucor had tissue invasion and bony erosions. Of the patients studied, 18 (53%) survived and 16 (47%) expired. Final outcome of the patients was not significantly associated with the type of fungal organism isolated.

Table 1 Baseline characteristics of the patients included in the study

Variables	N	%
Age distribution (in years)		
Less than 20	1	3%
21 to 40	8	24%
41 to 60	20	59%
More than 60	5	15%
Gender distribution		
Females	15	44%
Males	19	56%
Organisms isolated		
Aspergillus	6	18%
Candida	7	21%
Cryptococcus	8	24%
Mucor	13	38%

Table 2 Association of various patient related variables with the fungal organisms isolated

Variables	Fungal organisms				p value*
	Aspergillus (n=6)	Candida (n=7)	Cryptococcus (n=8)	Mucor (n=13)	
Risk factors					
Diabetes mellitus	4	2	0	9	<0.001
HIV/AIDS	0	2	8	0	
Chemotherapy	0	3	0	0	
Post TB lung cavity	1	0	0	0	
Postpartum sepsis	0	0	0	1	
Prolonged ICU stay	0	0	0	2	
Repeated VP shunt	1	0	0	1	
Presenting symptoms					
Headache	4	4	8	13	NA**
Altered sensorium	1	1	8	0	
Convulsions	0	1	7	0	
Abdominal symptoms	0	3	0	0	
Cough	1	0	0	0	
Dysurea	0	0	0	0	
Site of infection					

Blood	0	3	0	0	<0.001
Meningeal	0	1	8	0	
Ear	2	0	0	0	
Esophagus	0	2	0	0	
Naso-orbital	2	0	0	7	
Renal abscess	0	1	0	0	
Rhino-cerebral	2	0	0	6	
Imaging findings					
Tissue invasion	6	1	0	13	NA
Bony erosions	6	0	0	13	
Final outcome					
Survived	4	2	4	8	0.46
Expired	2	5	4	5	

*p value analyzed using Chi-square or Fisher's exact test;

**Not applicable: p value could not be calculated from the available data

Discussion

Invasive fungal infections in otherwise healthy individuals is extremely rare. In the present study we evaluated 34 patients who were diagnosed with invasive fungal infections. In our patient population, Diabetes mellitus was the most common risk factor, AIDS was the next most common, followed by neutropenia. Aspergillus and Mucor occurred most frequently in patients of diabetes mellitus while Cryptococcus in HIV patients and candida was found in patients with neutropenia.

Uncontrolled diabetes mellitus can alter the normal immunologic response of patients to infections as they have decreased granulocyte phagocytic ability with altered polymorphonuclear leucocyte response.⁵ Invasive aspergillosis is most frequent when there is a high amount of airway exposure, for instance, in the setting of construction, or when the host has a condition in which conidia are not effectively cleared. Historically, the highest risks for invasive infections have been seen in severely immunosuppressed patients, particularly allogeneic hematopoietic cell transplant or solid organ transplant recipients, and patients who experience prolonged durations of neutropenia.⁶ In the paranasal sinuses, aspergillosis can present in an identical fashion to mucormycosis. However, rhinocerebral aspergillosis is usually seen in neutropenic patients, whereas mucormycosis more often occurs in those with diabetes mellitus. Of the 13 cases of mucormycosis in our study, 7

presented with naso-orbital disease and 6 with rhino-cerebral presentation. Imaging findings may be subtle and can include focal soft tissue lesions, subtle focal bony erosions, focal enhancement of the sinus lining on magnetic resonance imaging or focal hypodense areas on computed tomography scan.⁷ In our patients as well, all cases with Aspergillosis and Mucormycosis had tissue invasion and bony erosions, as demonstrated by imaging studies.

Headache was the common presenting symptom in our study population and was most commonly seen among patients diagnosed with Cryptococcus and Mucor. Rhino-orbital-cerebral mucormycosis presents as acute sinusitis with fever, nasal congestion, purulent nasal discharge, headache, and sinus pain.⁸ Isolated infection of the central nervous system with mucormycosis typically arises from an adjacent paranasal sinus infection. We also observed convulsions to be present in 87.5% of the patients with Cryptococcal infections. Seizures are important neurologic complications that may occur early or late in both HIV-negative and HIV-infected cryptococcal meningitis.⁹ The reported incidence varies from 7.6% to 28.6% in different series.¹⁰

Conclusion

Diabetes mellitus and HIV/AIDS were the most common risk factors. Aspergillus and Mucor occurred most frequently in patients of diabetes mellitus while Cryptococcus in HIV patients and candida was found in patients with neutropenia.

All cases with Aspergillosis and Mucormycosis had tissue invasion and bony erosions. Outcome was worst in those with neutropenia and HIV/AIDS with an overall mortality being 47%. Such high mortality warrants a high degree of suspicion for early diagnosis so that effective treatment can be initiated in a timely fashion.

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