

## Central nervous system fungal infections: Observations from a large tertiary hospital in northern India

Prahlad K. Sethi<sup>a</sup>, Laxmi Khanna<sup>a</sup>, Anuradha Batra<sup>a</sup>, Ish Anand<sup>a</sup>, Nitin K. Sethi<sup>b,\*</sup>, Josh Torgovnick<sup>c</sup>, Edward Arsura<sup>d</sup>

<sup>a</sup> Department of Neurology, Sir Gangaram Hospital, New Delhi, India

<sup>b</sup> Department of Neurology, New York-Presbyterian Hospital, Weill Cornell Medical Center, New York, USA

<sup>c</sup> Department of Neurology, Saint Vincent's Hospital and Medical Centers, New York, USA

<sup>d</sup> Department of Medicine, Saint Vincent's Hospital and Medical Centers, New York, USA

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### ABSTRACT

**Objective:** To report our observations regarding fungal infections of the brain over two years from a large tertiary hospital in northern India. To identify fungal infections in immunocompetent and immunocompromised patients and to compare the two groups with respect to their age of occurrence, demographic data, clinical profile, radiological findings, response to treatment and outcome.

**Methods:** All consecutive cases of central nervous system (CNS) fungal infections admitted to the hospital over two years were included in this study. The patients were categorized as immunocompetent and immunocompromised, the predisposing factors, symptoms and clinical presentation were studied in detail and the outcomes of the two groups were compared.

**Results:** Of the 50 cases, 25(50%) were that of mucormycosis, 17(34%) were cryptococcosis and 8(16%) cases were that of aspergillosis. 14(28%) cases were immunocompetent and 36(72%) were immunocompromised. The outcome studied was as follows: 28% died of which 4% were HIV positive, 12% were diabetics with severe rhinorbital involvement, 2% had idiopathic thrombocytopenic purpura (ITP), 6% had advanced cancer and 4% had no predisposing illness.

**Conclusions:** We observed fungal infections of the brain in both immunocompetent and immunocompromised patients. In immunocompetent patients, early diagnosis and appropriate treatment frequently leads to recovery from the illness. The mortality and morbidity of fungal infections are less in the immunocompetent group of patients.

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Primary central nervous system fungal infections are being detected more often with the widespread availability of neuroimaging and laboratory facilities. The presenting clinical syndrome depends upon a complex interplay between the virulence of the infecting organism and the immune status of its human host. Certain fungal infections such as aspergillosis are more common in neutropenic hosts while others such as rhizopus thrive in the acidic carbohydrate rich environment of a diabetic host. *Cryptococcus neoformans* and aspergillosis can affect the immunocompetent. The frequently cited risk factors for fungal brain infections are human immunodeficiency virus infection, hematopoietic stem cell transplant, lymphoid malignancies, neutropenia, hereditary immune defects, immunosuppressive medications, diabetes mellitus,

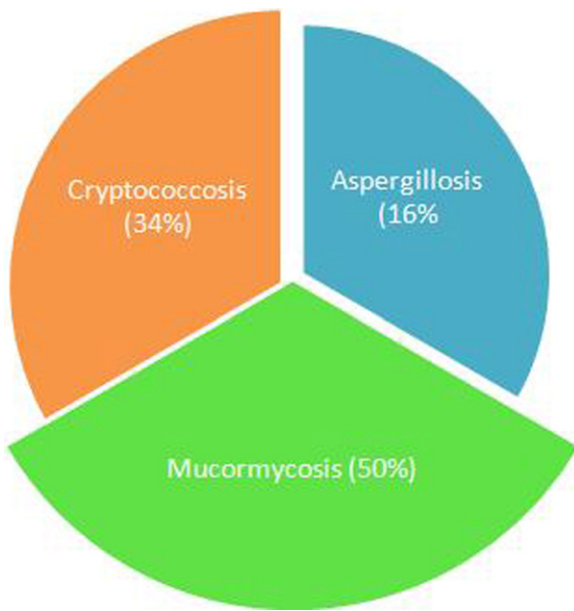
intravenous drug abuse and mechanical breakdown of the blood–brain barrier by surgery or trauma.

### 1. Methods

All consecutive cases of CNS fungal infections admitted to the hospital over two years from March 2008 to March 2010 were included in this study. Sir Ganga Ram Hospital is a 650 bed modern multi-speciality private teaching hospital in New Delhi. It provides comprehensive health care services to patients in Delhi and the satellite towns and villages. Patients were categorized as immunocompromised based on the presence of any of the following factors: HIV seropositivity, chronic renal failure, diabetes mellitus, chronic steroid use, malignancy, hematological diseases and tuberculosis. All other patients were categorized as immunocompetent. All groups of patients were investigated with HbA1C, HIV, CD4 count, serum complement levels, serum immunoglobulin levels, angiotensin converting enzyme levels and lumbar puncture studies. Imaging modalities like CT scans and MRI brain were done

\* Corresponding author at: New York-Presbyterian Hospital, Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10065, USA. Tel.: +1 212 746 2346; fax: +1 212 746 8845.

E-mail address: [sethinitinmd@hotmail.com](mailto:sethinitinmd@hotmail.com) (N.K. Sethi).



**Pie diagram 1.** Showing distribution of cases.

in both patient groups. The final diagnosis was based on a combination of clinical presentation, laboratory results, neuroimaging studies and pathology when available. The predisposing factors for the illness, symptoms, clinical presentation, radiological, microbiological investigations and treatment were studied in detail. The outcomes of the two groups were compared. A written informed consent was obtained from all patients who participated in this study.

**2. Statistics**

The data was analyzed using SPSS version 17.0 software and proportions were tested with chi-square or Fischer’s test. Odds ratio (OR) with 95% confidence interval (CI) were calculated to identify the associated factors. A *p* value of <0.05 was considered statistically significant.

**3. Results**

14(28%) cases were immunocompetent and 36(72%) were immunocompromised. The invasive fungal infections were mucormycosis in 50%, cryptococcosis in 34% and aspergillosis in 16% cases (Pie diagram 1). 28% patients were young males with no predisposing illnesses. 30% of these patients were farmers exposed to compost and manure. There were 70% males as compared to 30% females. The predisposing factors in the immunocompromised group of patients were diabetes in 44%, HIV infection in 14%, chronic renal failure in 20%, steroids in 10%, malignancies in 10%, sarcoidosis in 4%, ITP in 4% and tuberculosis in 2% (Pie diagram 2).

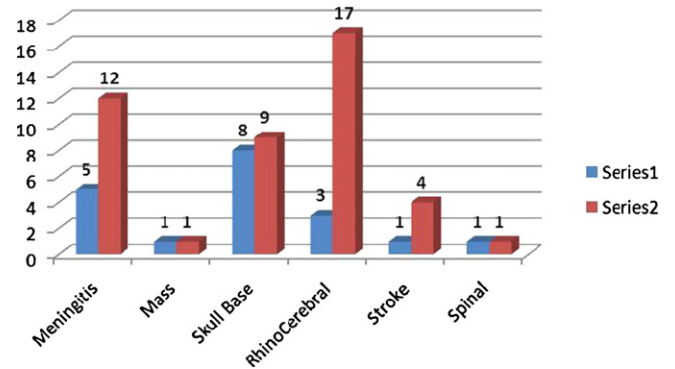
The symptoms and clinical features were as follows: headache occurred in 74% cases and fever in 54%. Stroke like presentation was seen 12% patients and cranial nerve palsies in 24% cases. 4% had seizures and 2% had backache (Table 1).

The patients were further categorized according to their clinical presentations. The immunocompetent group (series 1) of patients had 8 cases of skull base lesions (57%), 5 cases of chronic meningitis (35.8%) and 3 cases of rhino cerebral involvement (21.4%) and the immunocompromised group (series 2) had 9 cases of skull base lesions (25%), 12 cases of chronic meningitis (33.33%) and 17 cases of rhino cerebral syndromes (47%). There was 1 patient with spinal cord involvement (7%) and 1 case of stroke in the

**Table 1**  
Symptoms and clinical features.

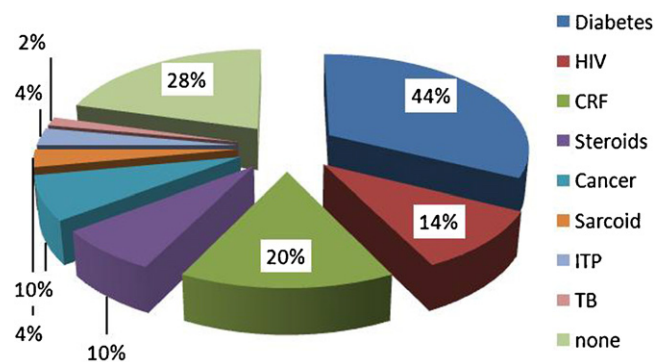
Fever	54%
Headache	74%
Decreased vision	50%
Hemiparesis	18%
Altered sensorium	30%
Epistaxis	10%
Swelling round eyes	36%
Seizures	4%
Backache	2%

**Table 2**  
Showing clinical presentation: immunocompetent vs immunosuppressed group.



immunocompetent group (7%) as compared 1 case of spinal cord involvement (2.7%) and 4 cases of stroke like presentation (11%) in the immunocompromised group (Table 2).

All patients were treated with antifungal drugs (azole class of antifungals and amphotericin B) and extensive surgical debridement where indicated. The mortality was higher in the immunocompromised group as compared to the immunocompetent group. The outcome studied was as follows: 28% of patients died of whom 4% were HIV positive, 12% were diabetics with severe rhinoorbital involvement, 2% had ITP, 6% had advanced cancer and 4% had no predisposing illness. Of these 2 patients were immunocompetent and 12 patients were immunocompromised. 2/14(14.28%) patients who died in the immunocompetent group had overwhelming fungal infection leading to meningitis, mass lesions and evidence of intracranial infection. While 12/36(33.33%) patients in the immunocompromised group who died had overwhelming sepsis, severe diabetes mellitus or HIV infection which contributed to the mortality.



**Pie diagram 2.** Showing predisposing factors in the immunosuppressed group of patients.

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