

Original Article



Mucormycosis in Patients without Cancer: A Case Series from A Tertiary Care Hospital in South India

A Ghafur¹, PS Shareek¹, Nambi P Senthur¹, PR Vidyalakshmi¹, V Ramasubramanian¹, Ashok Parameswaran², MA Thirunarayan³, R Gopalakrishnan¹

Abstract

Background: Mucormycosis (Zygomycosis) is a life-threatening infection. We attempted to analyse clinical features and risk factors of Mucormycosis cases in a tertiary care referral institution in India, in patients without underlying malignancy.

Methods: We retrospectively analyzed data of patients diagnosed as having Mucormycosis over a 10 year period of 2000-2010. Patients with a histopathology report and/or a Microbiology report of Zygomycetes or Mucor from a biopsy specimen were included in the study.

Results: Out of the 27 cases, rhino-orbital/rhino-cerebral involvement occurred in 12 (44.4%) patients, pulmonary involvement in 3 (11.1%) cases, soft tissue involvement in 11 (40.7%) cases and gastrointestinal involvement in one patient (3.7%). Diabetes mellitus is the main risk factor, followed by renal failure and trauma. Mean ESR value of these patients was 118 mm/1hour. Mean WBC count was $20 \times 10^9/L$, and neutrophil count 82%. The mean absolute neutrophil count (ANC) was $16.8 \times 10^9/L$.

Conclusion: The interesting finding in our study was the presence of neutrophilic leucocytosis and high ESR in most of the patients. In a predisposed individual, especially in a diabetic, in countries with high environmental fungal burden; presence of high ESR and neutrophilic leucocytosis with a compatible clinical presentation should raise suspicion of Mucormycosis.

Introduction

Mucormycosis is a life-threatening fungal infection predominantly affecting immuno compromised individuals, though it can affect immuno competent patients as well.¹ In tropical countries like India, the disease may be under-reported.² Diabetes mellitus is increasingly common in the Indian population and is an important predisposing factor.² We attempted to analyse clinical features and risk factors in a tertiary care referral institution, in patients without underlying malignancy.

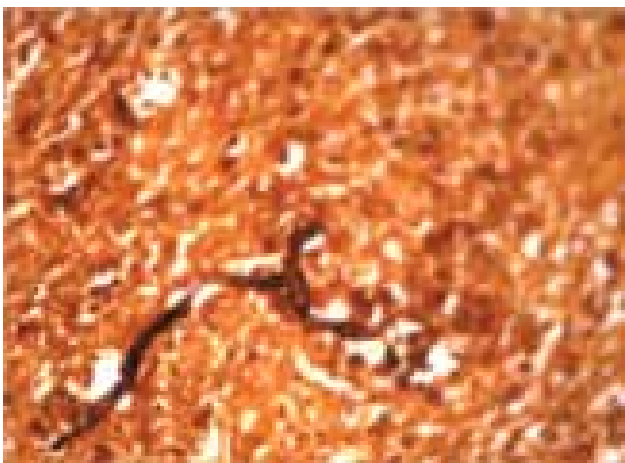


Fig. 1 : Mucor in tissue; broad, ribbon shaped, aseptate hyphae

¹Department of Infectious Diseases,²Department of Pathology,
³Department of Microbiology, Apollo Hospitals, Chennai, India
Received: 24.05.2012; Accepted: 23.11.2012

Materials and Methods

Our hospital is a tertiary care referral institution with all subspecialties except oncology. We retrospectively analyzed data of patients diagnosed as having Mucormycosis over a 10 year period of 2000-2010. Histopathology and Microbiology registers and random rare case documentation by Infectious diseases department were searched. Case records of patients who were diagnosed as Mucormycosis/Zygomycosis were reviewed. The diagnosis in all cases was confirmed by histopathological confirmation and/or culture from sterile sites. Full identification of isolates was not done and the term Mucormycosis in the article is used synonymously with Zygomycosis. Patients with a histopathology report of broad, predominantly aseptate and occasional pauciseptate, thin-walled fungal hyphae (Figure 1) and/or a Microbiology report of Zygomycetes or Mucor from a biopsy specimen were included in the study. Records of all patients were reviewed regarding the following parameters: demographic data, underlying risk factors, clinical features, laboratory parameters, radiologic features, culture results, histopathology reports, treatment received and cause of death.

Results

All the necessary details of only 27 cases of proven Zygomycosis cases could be tracked out of more than 200 reported cases by Microbiology and Histopathology departments. The mean age of the patients was 42 (Table 1). Males and females were equally affected. Diabetes was the main risk factor in nineteen (70.3%) out of the 27 patients. Six patients had ketosis at the time of presentation. In nine cases (33.3%) trauma was the risk factor (Table 2). one of these cases was surgical site infection following circumcision. Eight patients had renal failure of which 3 were on maintenance hemodialysis.

Table 1 : Demographic and clinical characteristic of patients

Characteristic	All patients	Proportion(%) of patients expired
Age(mean)	42	
Male	14	
Female	13	
Underlying condition at the time of infection		
Diabetes	19	7/19 (36.8%)
Renal failure	8	4/8 (50%)
Solid organ transplantation	2	0/2
Deferoxamine therapy	0	0
Bone marrow transplantation	0	0
HIV infection	0	0
Systemic lupus erythematosus	0	0
Trauma/surgery	9	5/9(55.5%)

Table 2 : Risk factor analysis

Risk factor	No. of patients
Diabetes	19(70.3%)
Renal failure	8(29.6%)
Trauma	9(33.3%)
Malignancy	0
Solid organ transplantation	2(7%)
Bone marrow transplantation	0
Desferioxamine therapy	0
HIV infection	0
Low birth weight infants	0
SLE	0
No risk factors	0

Two cases were in renal transplant recipients receiving steroids. Rhino orbital/rhino cerebral involvement (Figure 2) occurred in 12 (44.4%) patients, pulmonary involvement (Figure 3) in 3 (11.1%) cases, soft tissue involvement (Figure 4) in 11 (40.7%) cases and Gastrointestinal involvement in one patient (3.7%) (Chart 1). Out of the 19 patients in the diabetic group, 9 had rhino orbital involvement, 3 had rhino cerebral involvement, three had lung involvement, 3 had soft tissue infection and one had gastro intestinal presentation (Table 3). In patients having renal failure, two had lung involvement, 5 had soft tissue and muscle involvement and one had gastrointestinal involvement. Out of the 12 patients who had rhino-orbital/rhino cerebral involvement, all were diabetics (100%),out of which 5 had ketosis. None of the patients in this group had renal failure though one had trauma as the risk factor. All the three patients with pulmonary involvement were diabetics (100%), none had ketosis and 2 out of these three had renal failure (66%). Out of 11 patients with skin and soft tissue involvement, 5 had diabetes (45%), one had ketosis, 4 had renal failure (36%) and 7 had breach of skin including trauma or surgery (63%). The only patient who had gastrointestinal Mucormycosis was a diabetic with renal failure (Table 4).

Mean ESR value of these patients was 118 mm/1hour. Mean WBC count was $20 \times 10^9/L$, and neutrophil count 82%. The mean absolute neutrophil count (ANC) was $16.8 \times 10^9/L$. Surgical debridement was done in 22 (81.4%) cases. Twenty one patients received Amphotericin B treatment. Twelve patients received only conventional amphotericin at a dose of 1mg/kg, five patients received liposomal amphotericin at a dose of

**Fig. 2 : Rhinocerebral Mucormycosis**

3mg/kg and three patients initially received conventional then changed to liposomal amphotericin. Out of the twenty one patients who received amphotericin, eight patients expired. All the eight expired patients received conventional amphotericin B. Six patients received only surgical debridement (all of them had soft tissue involvement, had either amputation or curative excision). Of the 10 patients expired, rhino-cerebral involvement was seen in three patients, lung involvement in one case and one had gastrointestinal Mucor. Two patients had only sinus involvement and four had soft tissue involvement, of which one had Fournier's gangrene. Of the six patients with ketosis, three expired. Of the ten patients who expired 6 received both surgical and medical treatment. Out of the three patients with pulmonary Mucor two received surgery and Amphotericin B treatment and both survived; one had only Amphotericin B treatment without surgery and died. The average duration of antifungal treatment in survived patients was 25 days. Seventeen patients (62.9%) were considered cured and discharged and 10 (37.1%) patients died.

Out of the 27 patients with Mucormycosis, 21 had leucocytosis. The mean WBC count of the 27 patients was $20 \times 10^9/L$ and the mean Neutrophil percentage was 82. Only 6 of the 21 patients with leucocytosis were having diabetic ketosis at admission, a condition well known to be associated with leucocytosis. Among patients with leucocytosis, eight had sino-orbito-cerebral involvement; ten had skin and soft tissue involvement, two with lung and one with gastric involvement. The mean ESR value of the 27 patients was 118 mm/1 hr.

Discussion

The first Indian case report of Mucormycosis was in 1963.³ Since then there have been several reports from India, which contributes almost 40 % of the global burden of this disease.² Most of the Indian cases, in fact more than 300, are reported from one centre only. The commonest risk factor for the development of Mucormycosis in our study was diabetes, being the predominant risk factor in 70.3% of patients. In a meta-analysis, 36% of the patients had diabetes as the risk factor for Mucor. Another Indian study has reported diabetes as the main risk factor in 70% of the patients.⁴ In our study, 66% of the patient with pulmonary Mucormycosis had renal failure. But all these patients were diabetics as well. Although there have been reports of isolated renal Mucormycosis from different parts of India, we could not identify a single case in our series. Interestingly, none of our Mucormycosis patients had HIV as a risk factor. All the patients in the rhino-orbital/rhino-cerebral group were

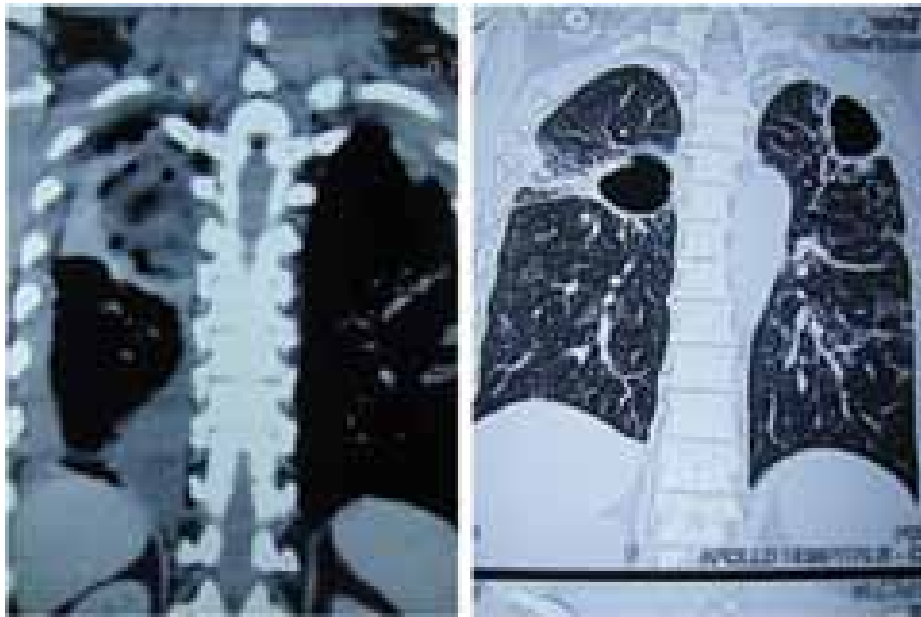


Fig. 3 : Pulmonary Mucormycosis before and after treatment



Fig. 4 : Injection site mucormycosis

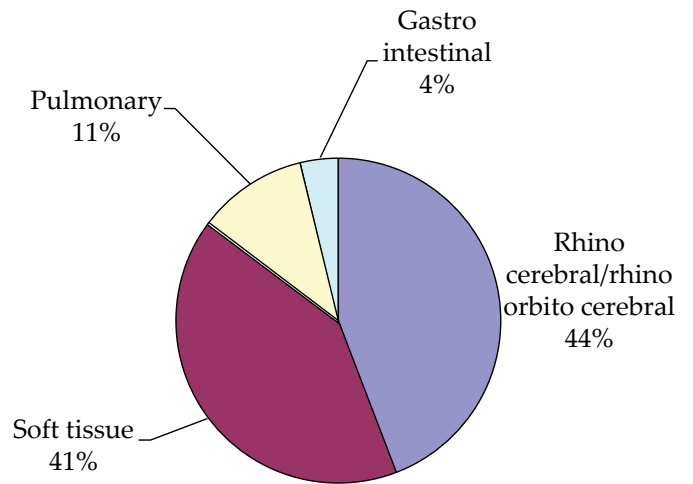


Chart 1 : Site of infection

Table 3 : Clinical presentation in major risk factor subgroups

Clinical presentation	Diabetes N=19	Renal failure N=8
Rhino-orbital	9 (47.3%)	0
Rhinocerebral	3 (15.7%)	0
Pulmonary	3(15.7%)	2 (25%)
Soft tissue	5 (26.3%)	5 (62.5%)
Gastro-intestinal	1 (5.2%)	1(12.5%)

Table 4 : Risk factor analysis of clinical subgroups

Risk factor	Rhino orbital / Rhino- cerebral N=12	Pulmonary N=3	Skin and soft tissue N=11	Gastrointestinal N=1
Diabetes	12 (100%)	3 (100%)	5 (45.4%)	1 (100%)
Renal failure	0 (0%)	2 (66%)	4 (36.6%)	1 (100%)
Trauma/surgery	1 (8.3%)	0 (0%)	7 (63.6%)	0 (0%)

diabetics. Overall mortality in our study is 37%, lower than the rates reported by others.¹⁵ A possible selection bias could explain the lower mortality; the study being retrospective in nature, it

was easier to track the files of patients who were alive at the time of analysis.

The interesting finding in our study was the presence of neutrophilic leucocytosis and high ESR in most of the patients.

In a predisposed individual, especially in a diabetic, in countries like India with high environmental fungal burden; presence of high ESR and neutrophilic leucocytosis with a compatible clinical presentation should raise suspicion of Mucormycosis.

Acknowledgements

We thank Prof. Christopher Kibbler for his suggestions prior to submission.

Conflict of Interest

AG has received lecture fees or advisory fees from multiple pharmaceutical companies producing antifungals. VRS has received lecture fees or advisory fees from multiple pharmaceutical companies producing antifungals. RGK has received lecture fees or advisory fees from multiple pharmaceutical companies producing antifungals. SPS, SNP, VPR, AP, TMA nothing to declare.

References

1. Maureen M Roden, Theoklis E Zaoutis. Epidemiology and Outcome of Zygomycosis: A Review of 929 Reported Cases. *Clinical Infectious Diseases* 2005;41:634–53.
2. A.Chakrabarti et al .Overview of opportunistic fungal infections in India. *Jpn J microbiology* 2008;49:165-172.
3. Balasubramaniam, Chaudari S.A case of pulmonary Mucormycosis. *Indian J of Path Bacteriol* 1963;6:60 -62.
4. A.Chakrabarti et al.The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. *Med Mycol* 2006;44:335-42.
5. A.Chakrabarti et al. Invasive zygomycosis in India: experience in a tertiary care hospital. *Postgrad Med J* 2009;85:573-581.