EMERGING INFECTIONS DUE TO *RHIZOPUS MICROSPORUS* IN INDIA: SERIES OF EIGHT CASES FROM A SINGLE CENTRE

Immaculata Xess, Mragnayani Pandey, Gagandeep Singh, Reshu Agarwal,
Rakesh Kumar, Viveka P Jyotsna

Department of Microbiology, All India Institute of Medical Sciences (AIIMS), New Delhi

AIM OF THE STUDY

The study aimed to review epidemiology, clinical features, treatment modalities and outcome of mucormycosis by emerging *R. microsporus* in our tertiary care centre.

BACKGROUND

- *Mucormycosis* is being increasingly reported all over the world. The high incidence of mucormycosis in India is due to a large population with uncontrolled diabetes and other immunocompromised status.
- *Rhizopus oryzae* has been reported as a most common cause of mucormycosis followed by *Rhizopus microsporus*.
- Second most common cause in India is *Apophysomyces elegans*
- Present study highlights an increase in the number of cases of infection due to *R. microsporus* in India.

METHODOLOGY

- Culture-positive cases of invasive mucormycosis from January 2015 to December 2016 were included.
- The demographic details, findings of laboratory investigations, clinical course, and outcome were recorded.
- The outcome was considered improved when the patient was symptom free on discharge or when a marked reduction in lesions was seen either on radiological imaging or on clinical examination.
- Cultures were identified by phenotypic and genotypic methods.
- Identification of *R. microsporus* was confirmed by sequencing of the internal transcribed spacer (ITS) region of ribosomal DNA (rDNA).
- Phylogenetic relatedness was studied among Indian isolates and other reported cases from the world using the maximum likelihood method, with 500 bootstrap replicates implemented in MEGA v6.0.
- *In vitro* antifungal susceptibility testing was performed on these isolates as per Clinical and Laboratory Standards Institute (CLSI) document M38-A2.

- Diabetes mellitus was the most common (6/8) underlying predisposing condition.
- Five patients improved after treatment. However, morbidity in the form of loss of vision or orbital exenteration in three patients (3/5)
- The most common variety isolated was *R. microsporus* var. *rhizopodiformis* (7/8) and one was *Rhizopus microsporus* var. *oligosporus*
- Fatal outcome was recorded only in three cases (37.5%).
- Surgical debridement followed by liposomal amphotericin B was the mainstay of treatment in all the cases
- The MICs for the antifungals tested viz., amphotericin B, itraconazole, voriconazole and posaconazole, ranged from 0.06 to 0.5, 0.25 to 0.5, 2 to 8 and 0.125 to 0.5 µg/ml respectively.

	Amphotericin B	Itraconazole	Voriconazole	Posaconazole
S1	0.25	0.5	4	0.25
S2	0.25	0.5	2	0.25
S3	0.5	0.5	2	0.25
S4	0.5	0.5	8	0.5
S5	0.25	0.25	4	0.125
S6	0.06	0.5	ND	0.125
S7	0.125	0.5	8	0.25
S8	0.5	0.25	2	0.125
ND : Not Done				

Demographic and clinical details of all cases

S.No	Age /Sex	Residence in India/place of reporting case	Year	Predisposing factor (s)	Clinical diagnosis	Sample	Treatment	Outcome/ Morbidity	Identification	Reference
1.	20/F	Rajasthan	2015	Uncontrolled Diabetes Type I	ROCM	Nasal scraping	Surgical debridement, liposomal amphotericin B	Improved with loss of vision in left eye	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present study
2.	36/F	Haryana	2015	Uncontrolled Diabetes Type II with diabetic ketoacidosis	ROCM	Nasal Crust	Surgical debridement, liposomal amphotericin B	Expired after 1 day of therapy	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present study
3.	40/M	Delhi	2015	Uncontrolled Diabetes Type II	ROCM	Paranasal sinus biopsy	Surgical debridement, liposomal amphotericin B	Expired after 28 days of therapy	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present study
4.	55/M	Uttar Pradesh	2016	Uncontrolled diabetes, Diabetic nephropathy with Chronic kidney disease	ROCM	Orbital biopsy	Surgical debridement, liposomal amphotericin B, posaconazole	Improved with left orbital exenteration	<i>Rhizopus microsporus</i> var. <i>oligosporus</i>	Present study
5.	18/M	Uttar Pradesh	2016	Acute myeloid leukemia	ROCM	Nasal tissue	Surgical debridement, liposomal amphotericin B	Improved with right orbital exenteration	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present study
6.	42/M	Uttar Pradesh	2016	Uncontrolled Diabetes Type II	ROCM	Nasal tissue	Surgical debridement, liposomal amphotericin B	Expired after 20 days of therapy	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present Study
7.	50/M	Haryana	2016	Uncontrolled diabetes, Chronic kidney disease	PM	Sputum	Liposomal amphotericin B	Improved after 25 days of therapy	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present study
8.	45/M	Jharkhand	2016	Chronic myeloid leukemia	ROCM	Nasal tissue	Surgical debridement, liposomal amphotericin B	Improved after 17 days of therapy	<i>Rhizopus microsporus</i> var. <i>rhizopodiformis</i>	Present study

RESULTS

- During study period, *R. microsporus* was identified in eight cases among a total number of 45 culture positive mucorales (18%)
- Seven cases were diagnosed as rhino-orbital-cerebral (ROCM) mucormycosis and one with pulmonary mucormycosis (PM)

CONCLUSION

- This study reported for the first time such a large number of cases of invasive fungal infections by *R. microsporus* in immunocompromised individuals from a single institute of India.
- As incidence of mucormycosis is increasing and mortality remains high, awareness for this emerging fungal pathogen and timely and accurate management is warranted.

REFERENCES

1. Nawange SR, Singh SM, Naidu J, Jain S, Nagpal T, Behrani DS, Mellado E, Tudela JL. 2012. Zygomycosis caused by *Rhizopus microsporus* and *Rhizopus oryzae* in Madhya Pradesh (M.P.) Central India: a report of two cases. Mycopathologia 174:171–176. <https://doi.org/10.1007/s11046-012-9532-0>.
2. Verma R, Nair V, Vasudevan B, Vijendran P, Behera V, Neema S. 2014. Rare case of primary cutaneous mucormycosis of the hand caused by *Rhizopus microsporus* in an immunocompetent patient. Int J Dermatol 53:66–69. <https://doi.org/10.1111/ijd.12204>.
3. Chakrabarti A, Singh R. 2014. Mucormycosis in India: unique features. Mycoses 57(Suppl 3):S85–S90. <https://doi.org/10.1111/myc.12243>.