Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1843-1846 | ISSN:2251-6727

Comprehensive Review on Mucormycosis including Diagnosis and Treatment

Dr. Shikha Gupta[1], Dr. Amrita Upadhyay[2], Dr. Indu Yadav[3], Dr. Rehana Bano[4], Dr. Deepak Nair[5]

[1]MDS, Associate Professor, Department of Prosthodontics and Crown & Bridge, Babu Banarsi Das College of Dental Sciences, Lucknow, India

[2]MDS, Assistant Professor, Department of Prosthodontics and Crown & Bridge, Babu Banarsi Das College of Dental Sciences, Lucknow, India

[3]MDS, Assistant Professor, Department of Prosthodontics and Crown & Bridge, Babu Banarsi Das College of Dental Sciences, Lucknow, India

[4]MDS, Assistant Professor, Department of Prosthodontics and Crown & Bridge, Babu Banarsi Das College of Dental Sciences, Lucknow, India

[5]MDS, Assistant Professor, Department of Prosthodontics and Crown & Bridge, Babu Banarsi Das College of Dental Sciences, Lucknow, India

(Received: 27 October 2023 Revised: 22 November Accepted: 26 December)

KEYWORDS

Mucormycosis, Entomophthoramycosis, Zygomycetes, Mucorales, Entomophthorales, Mucor, Rhizopus, Apophysomyces, Conidiobolus, Basidiobolus

ABSTRACT:

The class Zygomycetes is divided into two orders, Mucorales and Entomophthorales. Genera from the order Mucorales (Rhizopus, Mucor, Rhizomucor, Absidia, Apophysomyces, Cunninghamella and Saksenaea) cause an angioinvasive infection called mucormycosis. The rhino-orbito-cerebral, pulmonary, disseminated, cutaneous, or gastrointestinal involvement is present with mucormycosis. Immunocompromising states such as haematological malignancy, bone marrow or peripheral blood stem cell transplantation, neutropenia, solid organ transplantation, diabetes mellitus with or without ketoacidosis, corticosteroids, and deferoxamine therapy for iron overload predispose patients to infection. Early diagnosis, along with treatment of the underlying medical condition, surgery, and an amphotericin B product are needed for a successful outcome. Genera from the order Entomophthorales produce a chronic subcutaneous infection called entomophthoramycosis in immunocompetent patients. The main aim and purpose of this review related to overview and Etiopathogenesis of Mucormycosis, fatality of rhinocerebral Mucormycosis, recent advances in diagnostic and treatment methods.

Introduction

American pathologist R.D. Baker coined the term Mucormycosis. It is also known as Zygomycosis. It can be defined as an insidious fungal infection caused by members of Mucorales and zygomycotic species. In 1885, the German pathologist Paltauf, reported the first case of Mucormycosis and described it as Mycosis Mucorina . During 1980s and 1990s Mucormycosis was increasingly seen among immuno compromised individuals.

Etiopathogenesis

It infiltrates the vascular lamina, causing infarction and necrosis as well as inflammation. It affects the head and neck, respiratory and central nervous systems, the gastrointestinal tract, and other areas. Rhino cerebral Mucor mycosis affects the head and neck, with the most common site being the nose, but the disease can spread to the paranasal sinuses, orbit, facial bones, and cranial cavity. Loose teeth, gingival abscess, and dental extraction are often the first symptoms that present to OMFS. Mucormycosis in the bone marrow may promote fungal growth by damaging the endothelial lining of vessels, resulting in vascular insufficiency and leading to bony necrosis and fungal osteomyelitis. Risk factors include uncontrolled diabetes mellitus, especially ketoacidosis, steroid use, extremes of age, neutropenia; especially with haematological malignancy, AIDS, renal insufficiency, organ or stem cell transplantation, iron overload, skin trauma, broad-spectrum antibiotics, intravenous drug abuse,

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1843-1846 | ISSN:2251-6727

prophylactic voriconazole for aspergillosis and malnutrition.[1-7] Neutrophils play a major role in host defence against mucorales. Ketoacidosis in diabetes accelerate the fungal invasion. In recent times, such as social distancing, wearing a face mask, sanitiser, and other protective kits as accelerated protective measures against COVID -19 infections has lessened conventional bacterial infections. At the same time, the administration of chemotherapy to target viral infection has influenced drug resistance for secondary bacterial infection. In parallel, "superinfections", i.e. the presence of co-infection in COVID 19 patients in hospitals, especially in ICU units, is seen to be increased. Clinical Presentations and Manifestations Infection of Mucormycosis in human beings occurs in two types.

1. Superficial and Visceral
2. Localized and Disseminated.

Superficial form occurs in external ear, fingernails, skin. Visceral forms are manifested as pulmonary, gastrointestinal and rhino cerebral types. Entry of these spores may takes place either through cutaneous or respiratory route. Overall, rhino-orbito-cerebral mucormycosis is the most common form (44–49%), followed by cutaneous (10–16%), pulmonary (10–11%), disseminated (6–11.6%) and gastrointestinal (2–11%) presentations. Diabetics usually develop rhino-orbito-cerebral or pulmonary mucormycosis. Patients can develop a slowly progressive form of rhino-orbito-cerebral mucormycosis with signs and symptoms of more than 4 weeks duration. Intravenous drug use places patients at risk for isolated cerebral mucormycosis. The angioinvasive nature of mucormycosis, characterised by thrombosing vasculitis, and its role in host invasion have been attributed to increased expression of platelet-derived growth factor (PDGFRB) signalling.

Risk Factors

Haematological malignancy is a major risk factor for mucormycosis, with leukaemia or lymphoma being the underlying diagnosis in the majority of patients. When mucormycosis is suspected, adequate imaging to document the extent of the disease is strongly advised, followed by surgical debridement. The use of high dose liposomal amphotericin B as a first-line treatment is strongly suggested, whereas intravenous isavuconazole and intravenous or delayed-release-tablet posaconazole have also been advocated.[8-10]

Radiographic Features

Opacification of the sinuses may be observed in conjunction with patchy effacement of bony walls of sinuses. In cavernous sinus thrombophlebitis mucor infection can interpret with "Black turbinate sign" which refers to an area of non-enhancing mucosa on MRI. A radiographic or CT scan of the head may show thickened mucosa or cloudy sinuses, densely crowded extra ocular muscles, enlarged compactness of the orbital apex, proptosis and inflammation of the optic nerve.

Histopathological Features

On examination, the affected tissue with lesions show extensive necrosis with numerous large branching pale-staining, wide, flat non-septal hyphae with branching at right or obtuse angles. Round or ovoid sporangia are also frequently seen in culture. Thin - walled hyphae (infrequently septae) with non - parallel sides ranging from 3 to 25µm in diameter, branching irregularly and often with bulbous hyphal swelling. Necrotic tissue containing hyphae might be seen with signs of angio–invasion and infarction is seen; in non granulocytopenic conditions, infiltration of the neutrophils and with chronic infection granuloma formation will also be observed. Gomori Methamine Silver (Grocott) or Periodic-acid Schiff are the staining of choice.

Diagnostic Method

Diagnosis of mucormycosis includes cautious evaluation of clinical manifestations, magnetic resonance imaging modalities, utilization of computed tomography (CT) in the early stages, specialist assessment of cytological and histological provision, and finest application of clinical microbiological technique and execution of molecular detection. Detection of host factors contributes extensively to the estimation of a patient's possibility for invasive mucormycosis. PAS stains, direct examination, calcofluor, histopathological examination, Gomori methenamine silver stain, culture, molecular methods and fluorescent in situ hybridization are the various laboratory techniques for detecting mucor. The 1950 Smith and Krichner criteria for the clinical diagnosis of mucormycosis are still considered to be gold standard and include:

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1843-1846 | ISSN:2251-6727

- Black, necrotic turbinate's easily mistaken for dried, crusted blood,
- Blood-tinged nasal discharge and facial pain, both on the same side,
- Soft peri-orbital or peri-nasal swelling with discoloration and induration,
- Ptosis of the eyelid, proptosis of the eyeball and complete ophthalmoplegia and,
- Multiple cranial nerve palsies unrelated to documented lesion.

Differential Diagnosis

Differential finding of mucormycosis include maxillary sinus neoplasia, maxillary sinus aspergillosis, soft tissue infarction, soft tissue radio necrosis, other deep fungal infections.

Treatment

Successful treatment for mucormycosis includes rapid accurate diagnosis, surgical debridement, and administration of drugs, adjunctive application of hyperbaric oxygen, recombinant cytokines or transfusion of granulocyte and prosthetic obturator. According to Spellberg et al., currently available monotherapy shows high mortality rate especially with haematology patients and hence proposed the choice of "Combination therapy" for Mucormycosis42. Antifungal therapies include AmB Dexycholate, Liposomal AmB (5-10mg/kg), AmB lipid complex, AmB colloidal dispersion, Posaconazole (400mg bid) and manage of core conditions. Second-line treatment includes combination of caspofungin and lipid AmB, mixture of lipid AmB and Posaconazole, not grouping with Deferasirox is suggested43

Prognosis and Morbidity Rate

The prognosis generally depends on the extent of manifestation of the disease and effective treatment initiated in response to the diseases. The survival rate for rhino-cerebral disease in patients without systemic diseases are about 75%; with other diseases is about 20%.; and in pulmonary disease is considered to be fatal. Better survival rate can be achieved in patients with low baseline serum concentration of iron/ferritin, neutropenia and malignant cases which is not associated with infection.[41]

Conclusion

To conclude, mucormycosis is a disease which usually shows aggressive and an alarming mortality rate. However the actual etiopathogenesis remains varied throughout the world, diagnosis of this disease remains a challenge for the clinicians. But still in the view of its high mortality rate, (i) early and prompt diagnosis, (ii) recovery from the predisposing factors, (iii) early intervention with surgical debridement and therapeutic drugs are the only hopes to improve the condition from this devasting disease

References

1. RM Prabhu and R Patel. Mucormycosis and Entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. Clin Microbiol Infect 2004;10(Suppl.1):31–47.
2. Ramalingam Suganya, Narasimhan Malathi, Vinithra Karthikeyan and Vyshnavi Mucormycosis: A Brief Review. J Pure Appl Microbiol, 2019;13(1):161-165.
3. Kundakarla Bhanuprasada, Abi Manesha, Emily Devasagayama, Lalee Varghese b, Lisa Mary Cherianb, Regi Kurienb, Rajiv Karthika, Divya Deodhar A, Harshad Vanjarec, Jayanthi Peter D, Joy S. Michael E, Meera Thomas F, Prasanna Samuel G, George M. Varghesea. Risk factors associated with the mucormycosis epidemic during the COVID 19 pandemic . International Journal of Infectious Diseases 2021;111:267–27.
4. Awadhesh Kumar Singh, Ritu Singh, Shashank R Joshi, Anoop Misra. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2021;15:102-146.
5. Vishal US Rao, Gururaj Arakeri, Gaurav Madikeri, Ashwin Shah, Rachel S Oeppen, Peter A Brennan . COVID-19 associated mucormycosis (CAM) in India: a formidable challenge. British Journal of Oral and Maxillofacial Surgery2021;9:1095–1098.
6. Asim Azhara, Wajihul Hasan Khanb, Parvez Anwar Khand, Khaled Alhosainie, Mohammad Owaisa, Aijaz Ahmad . Mucormycosis and COVID-19 pandemic: Clinical and diagnostic approach. Journal of Infection and Public Health 2022;15:466–479.
7. George Petrikkos, Anna Skiada, Olivier Lortholary, Emmanuel Roilides, Thomas J. Walsh and Dimitrios P Kontoyiannis. Epidemiology and Clinical

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1843-1846 | ISSN:2251-6727

Manifestations of Mucormycosis. Clinical Infectious Diseases 2012;54(S1):S23–34 .

8. Karthika Pushparaj, Haripriya Kuchi Bhotla, Vijaya Anand Arumugam, Manikantan Pappusamy, Murugesh Easwaran, Wen-Chao Liu, Utthapon Issara, Kannan R, Rengasamy Arun Meyyazhagan , Balamuralikrishnan Balasubramanian . Mucormycosis (black fungus) ensuing COVID-19 and comorbidity meets-Magnifying global pandemic grieve and catastrophe begins. Science of the Total Environment 2022;805:1503-55.
9. Shreya Singh, Nupur Pal, Jagdish Chander, Raman Sardana, Bella Mahajan, Noyal Joseph, Arunaloke Chakrabarti, Shivaprakash M Rudramurthy, P Hariprasath, Saikat Paul, Harsimran Kaur, Anup Ghosh. Mucormycosis caused by Syncephalastrum spp.: Clinical profile, molecular characterization, antifungal susceptibility and review of literature. Clinical Infection in Practice 2021;11:1000-74.