International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 167-173 www.ijprajournal.com ISSN: 2456-4494

Mucormycosis: A Review

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Date of Submission: 01-11-2024 Date of Acceptance: 10-11-2024

ABSTRACT
Mucormycosis is an angio invasive contamination that happens because of the fungi mucorales. It is an extraordinary sickness however more and more more identified in immunocompromised patients. It may be labeled into rhino-orbitocerebral, cutaneous, disseminated, gastrointestinal, and pulmonary types. Overall elevated mortality fee is reported, despite the fact that the competitive remedy is given. The predominant intention and cause of this evaluation associated with assessment and Etiopathogenesis of Mucormycosis, fatality of rhinocerebral Mucormycosis, latest advances in diagnostic and remedy methods.
Keywords: Diabetes mellitus (DM), Rhinocerebral Mucormycosis, Fungal invasion.

I. INTRODUCTION AND HISTORY

American pathologist R.D. Baker coined the time period Mucormycosis. It is likewise called Zygomycosis. It may be described as an insidious fungal contamination due to participants of Mucorales and zygomycotic species1. Mucormycotina are the not unusualplace saprobes originating from the rotten count number or soils. Infections with Mucorales are labeled with the aid of using fast progression1.

History In 1885, the German pathologist Paltauf, stated the primary case of Mucormycosis and defined it as Mycosis Mucorina2. During Nineteen Eighties and Nineties Mucormycosis become an increasing number of visible amongst immuno compromised individuals3. Based on the superiority rate, a observe done in France stated amplification with the aid of using 7.4% consistent with year4. Worldwide incidence alongside the opportunity of seasonal variant of mucorales contamination has been reported5

Background

The pandemic produced by the COVID-19 virus is still with us. Many secondary infections, particularly opportunistic fungal infections, have emerged as a result of this widespread illness. Mucormycoses are life-threatening fungi that most commonly affect haematological, solid organ transplant, and diabetes patients, although they can also harm immunocompetent patients after a trauma or burn . Mucormycosis is characterised by host tissue infarction and necrosis caused by hyphae invasion of the vasculature. Rhino-orbito-cerebral and pulmonary manifestations are the most common clinical presentations. According to multicentre research, the frequency of idiopathic pulmonary fibrosis is on the rise, owing to an idiopathic pulmonary.

Etiopathogenesis

Deep tissues maximum successfully get laid low with mucorales via way of means of the method of ingestion or inhalation of spores, and percutaneous injection of spores. But even though it enters the lung or cutaneous tissues the primary line of protection motion in a healthful frame gets rid of the spores with the assist of oxidative metabolites and cationic peptides however this will become a subject of difficulty withinside the presence of debilitating illnesses like diabetes, specially ketoacidosis,

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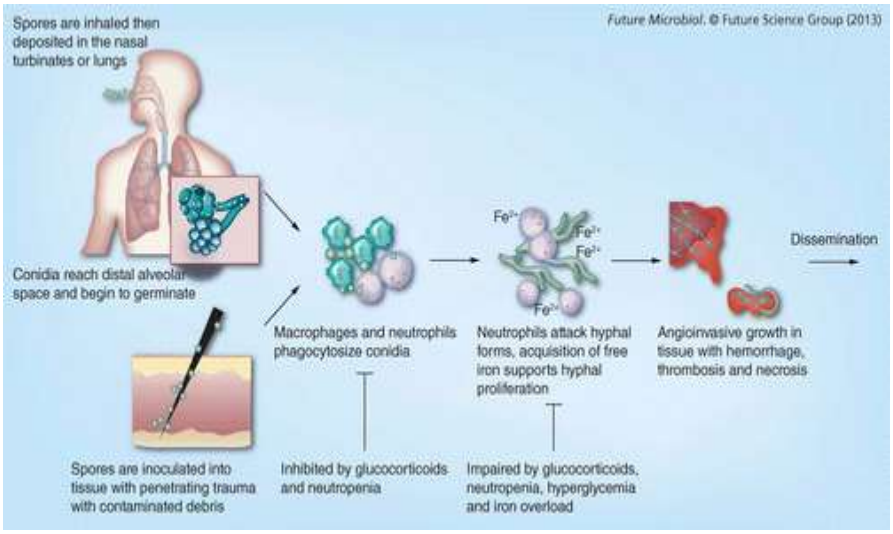

Fig1:Etiopathogenesis

whilst frame beneathneath steroids, vintage age, neutropenia or every other hematological malignancies, AIDS, situation like renal insufficiency, underwent any organ or stem mobileular transplantation iron overload, any varieties of trauma to skin, broad-spectrum antibiotics, intravenous drug abuse, prophylactic voriconazole particularly given for aspergillosis and malnutrition. Mucormycosis seems as a unfavourable and probably essential situation in diabetic sufferers because of elevated availability of micronutrients and decreased defence mechanism of the frame. Various hypotheses include- (i) Serum inhibitory hobby seems to be low towards Rhizopus species, (ii)With the discount in PH stage iron availability for pathogen enhance drastically. (iii)Capability of pulmonary macrophages of diabetes mellitus sufferers to inhibit germination of Rhizopus species look like decreased .The glucose and acidic surroundings is successfully raised in presence of Ketone reductase produced via way of means of Rhizopus species. There is a threat of prevalence of each varieties of mucormycosis in sufferers with DM specially with Ketoacidosis. An vital position in host defence mechanism is performed via way of means of Neutrophil towards mucorales so in case of host affected with DM feature of it receives impaired at every stage of DM. Moreover ketoacidosis in diabetes allows to similarly boost up the fungal invasion . The acidic heritage consequences in extra loose iron manufacturing via way of means of lowering its binding to transferrin and coffee stage of dialyzable inhibitory issue in diabetics offer appropriate situations for fungal duplication Mortality charge became stated to be as excessive as 90% or maybe extra with Mucormycosis contamination, previous to the management of amphotericin B and radical surgery. Severely neutropenic sufferers and people who lack phagocytic feature hence come beneathneath the notably danger class of growing mucormycosis. But it's now no longer equal with inside the case of AIDS sufferers hence implying that the T lymphocytes aren't that vital for hampering the fungal proliferation however handiest the neutrophils. Patients present process long time management of voriconazole specially people with haematological malignancies and hematopoietic stem mobileular transplants are taken into consideration to be extra inclined for mucormycosis. Apart from that mucormycosis contamination can also arise in sufferers without top notch immune deficiency situation. Most of the time such situations are associated with burns, trauma and or allied with iatrogenic factors.

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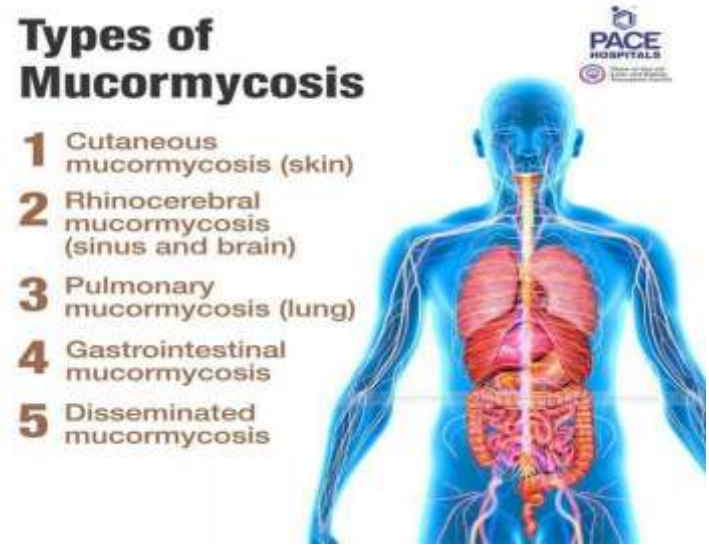

Fig 2: Types of Mucoromycosis

Clinical Symptoms and Presentations There are two forms of Mucormycosis infection in humans. 1 and 2 are superficial and visceral, and 2 and 3 are localised and disseminated. External ear, fingernails, and skin are examples of the superficial form. Pulmonary, gastric, and rhino cerebral kinds are examples of visceral forms. These spores might enter the body via the cutaneous or respiratory routes. (For example, spores can spread through contaminated food or poisoned needles.

1) Rhinocerebral Mucormycosis

Rhinocerebral Mucormycosis Incidence of Rhinocerebral Mucormycosis is 33 - 50%. Apophysomyces elegans is taken into consideration because the presumptive aetiological agent29. An contamination that starts offevolved from paranasal sinuses, next inhalation of spores, and likely extension to the mind and successively, sinuses, nostril and eyes are affected. Its scientific manifestation begins offevolved with palatal and sinuses necrosis, in addition enters to the orbit previous to getting intra-cranial structures. Symptoms encompass fever, blindness, exophthalmos, nostril-bleed, facial paralysis and symptoms and symptoms of invasion of the trigeminal nerve. Cavernous sinus thrombosis could be the impact of unsettled rhino-sinus mucormycosis. Appearance of reddish - black nasal turbinate and septum together with a nasal discharge is likewise seen. Progression of sickness into cranial vault results in blindness, lethargy and seizures accompanied with the aid of using death28. According to Lanternier et al., this contamination suggests various scientific look with multiplied prevalence of number one pores and skin contamination and a huge diagnosis predisposed with the aid of using localization30. In USA, the superiority of mucor contamination is round 500 people a year31. It is 10 to 50 instances fewer than candidiasis or aspergillosis32. Occurrence of mucormycosis can also additionally in all likelihood be round 2 - 3% amongst allogenic bone marrow transplant patients.

2) Mucormycosis of the lungs

Inhalation of sporangiospores by the mucormycetes can cause lung illness. Patients with hematologic malignancies such as leukaemia, lymphoma, extreme immunosuppression, or bone marrow transplantation are critically immunocompromised due to an entire lack of circulating neutrophils. In comparison to the rhinocerebral form, the lesions can be localised or widespread, and they are more common in patients with underlying diabetes mellitus. Chest discomfort, dyspnea, and hemoptysis are some of the nonspecific clinical symptoms. When patients exhibit a reverse halo sign on a chest CT scan and the proper clinical symptoms, this entity is suspected.

3) Cutaneous Mucormycosis

Iis a type of mucormycosis that affects the skin.The clinical symptoms of cutaneous mucormycosis are diverse, ranging from pustules or vesicles to wounds with necrotic zones in larger areas. Lesions mimic ecthyma gangrenosum in

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their early stages; cotton-like growth can be visible across the surface of tissues, a clinical symptom known as 'hairy pus.' Mucormycosis on the skin can be a primary infection or a sequel infection to the disseminated form.

4)Gastrointestinal mucormycosis Gastrointestinal mucormycosis is rare, accounting for about 7% of all cases of mucormycosis, most commonly gastric involvement. It is found primarily in patients suffering from extreme malnutrition and is believed to be acquired through ingestion of food contaminated with fungal spores. The causative agents of gastrointestinal mucormycosis are Lichtheimia corymbifera from Mucorales and Basidiobolus ranarum from Entomophthorales.

(5) Isolated renal mucormycosis Isolated renal mucormycosis is one of the emerging clinical entities that is a rare cause of renal infarction and can be fatal if not detected early. Any of the Mucorales species can infect the kidneys. Patients often present with flank pain, fever, and pyuria.

6) Disseminated mucormycosis Mucormycetes can be disseminated and affect the lungs, kidney, gastrointestinal tract, heart and brain, the lungs being the most affected. The most commonly reported clinical syndromes include pneumonia, stroke, subarachnoid hemorrhage, brain abscess, cellulitis, or gangrene of a skin structure. Complications Cavernous sinus thrombosis, multiple cranial nerve palsy, vision loss, frontal lobe abscess, carotid or jugular vein thrombosis

Histopathological Features

On histological examination, massive necrosis is manifested withinside the affected tissue at the side of sever a massive branching pale-staining, wide, flat non-septal hyphae with branching at proper or obtuse angles. The way of life regularly affords with usual spherical or ovoid fashioned sporangia. Hyphae that have skinny wall (occasionally septae) and non - parallel facets starting from three to 25µm in diameter, branching irregularly and regularly with bulbous hyphal swelling. Necrotic tissue containing hyphae is probably visible with symptoms and symptoms of angio – invasion and infarction are visible; in non granulocytopenic conditions, infiltration of the neutrophils and with persistent contamination granuloma formation may also be observed. Detection of host elements make a contribution drastically to the estimation of a patient's opportunity for invasive mucormycosis. PAS stains, direct examination,calcofluor, histopathological examination, Gomori methenamine silver stain, way of life, molecular strategies and fluorescent in situ hybridization are the diverse laboratory strategies for detecting mucor . Maxillary sinus neoplasia, maxillary sinus aspergillosis, gentle tissue infarction, gentle tissue radio necrosis, different deep fungal infections are the differential diagnosis.

Radiographic Characteristics

Sinus opacification can be seen in association with patchy effacement of the sinuses' bone walls. The "Black turbinate sign," which refers to a patch of non-enhancing mucosa on MRI35, can be used to interpret mucor infection in cavernous sinus thrombophlebitis. Thickened mucosa or murky sinuses, densely populated extraocular muscles, expanded compactness of the orbital apex, proptosis, and optic nerve inflammation36 can all be seen on a radiography or CT scan of the head. In the imaging of the lung in pulmonary Mucormycosis, tiny nodules as well as an extra 10 nodules were discovered, which is consistent with the findings of Chamilos et al.

Diagnostic Method

Diagnosis of mucormycosis consists of careful assessment of scientific manifestations, magnetic resonance imaging modalities, usage of computed tomography (CT) withinside the early stages, expert evaluation of cytological and histological provision, best software of scientific microbiological approach and execution of molecular detection40. Detection of host elements make contributions significantly to the estimation of a patient's opportunity for invasive mucormycosis. PAS stains, direct examination, calcofluor, histopathological examination, Gomori methenamine silver stain, culture, molecular strategies and fluorescent in situ hybridization are the diverse laboratory strategies for detecting mucor40. According to Kontoyiannis et al., a first-rate trouble withinside the identity of mucormycosis consists of its indefinable scientific look and recurrent occult distribution, and as a result a want for a touchy nonculture-primarily based totally investigative approach is required. Gold trendy analytic approach for affirmation is the tissue primarily based totally analysis20.

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Treatment

Successful remedy for mucormycosis consists of speedy correct diagnosis, surgical debridement, and management of drugs, adjunctive utility of hyperbaric oxygen, recombinant cytokines or transfusion of granulocyte and prosthetic obturator. According to Spellberg et al., presently to be had monotherapy suggests excessive mortality charge specifically with haematology sufferers and subsequently proposed the selection of "Combination therapy" for Mucormycosis42. Antifungal remedies consist of AmB Dexycholate, Liposomal AmB (5-10mg/kg), AmB lipid complex, AmB colloidal dispersion, Posaconazole (400mg bid) and manipulate of middle conditions. Second-line remedy consists of aggregate of caspofungin and lipid AmB, aggregate of lipid AmB and Posaconazole, now no longer grouping with Deferasirox is suggested. In case of gentle tissues, cerebral disseminated, localized pulmonary lesion and rhino-orbito- sorts surgical remedy need to be considered

Prognosis and Morbidity Rate

The diagnosis typically relies upon at the volume of manifestation of the ailment and powerful remedy initiated in reaction to the illnesses. The survival price for rhino-cerebral ailment in sufferers with out systemic illnesses is ready 75%; with different illnesses is ready 20%.; and in pulmonary ailment is taken into consideration to be fatal. Survival price varies with foci of the infection: rhino cerebral mucormycosis – 45%, focal cerebral mucormycosis – 33%, pulmonary forms – 36%, sinusitis with out cerebral involvement – 87%, cutaneous isolated – 90%, disseminated ailment – 16%, and involvement of gastro intestinal form –10D, 45. Better survival price may be completed in sufferers with low baseline serum awareness of iron / ferritin, neutropenia and malignant instances which isn't always related to infection.

II. CONCLUSION

To conclude, mucormycosis is a disorder which commonly indicates competitive and an alarming mortality rate. However the real etiopathogenesis stays numerous for the duration of the world, analysis of this disorder stays a undertaking for the clinicians. But nevertheless with inside the view of its excessive mortality rate, (i) early and activate analysis, (ii) restoration from the predisposing factors, (iii) early intervention with surgical debridement and healing capsules are the most effective hopes to enhance the circumstance from this devasting disorder.

REFERENCES

[1]. Mohammadi R, Nazeri M, Sayedayn SM, Ehteram H. A successful treatment of rhinocerebral mucormycosis due to Rhizopus oryzae. Journal of research in medical sciences: The Official Journal of Isfahan University of Medical Sciences, 2014; 19(1): 72.

[2]. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, Sein M, Sein T, Chiou CC, Chu JH, Kontoyiannis DP. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clinical Infectious Diseases, 2005; 41(5): 634-53.

[3]. Bitar D, Van Cauteren D, Lanternier F et al. Increasing incidence of zygomycosis (mucormycosis), France, 1997–2006. Emerg Infect Dis., 2009; 15: 1395–1401.

[4]. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clinical Infectious Diseases, 2012; 54(suppl_1): S23-34. 7. Waldorf AR. Pulmonary defense mechanisms against opportunistic fungal pathogens. Immunol Ser., 1989; 47: 243–271

[5]. Waldorf AR, Ruderman N, Diamond RD. Specific susceptibility to mucormycosis in murine diabetes and bronchoalveolar macrophage defense against Rhizopus. J. Clin. Invest., 1984; 74: 150 60.

[6]. Tedder M, Spratt JA, Anstadt MP, Hegde SS, Tedder SD, Lowe JE. Pulmonary mucormycosis: results of medical and surgical therapy. Ann. Thorac. Surg., 1994; 57(4): 1044- 50.

[7]. Joshi N, Caputo GM, Weitekamp MR, Karchmer AW. Infections in patients with diabetes mellitus. N. Engl. J Med., 1999; 341(25): 1906- 12.

[8]. Bhansali A, Sharma A, Kashyap A, Gupta A, Dash RJ. Mucor endophthalmitis. Acta Ophthalmol Scand., 2001; 79(1): 88-90.

[9]. Tsaousis G, Koutsouri A, Gatsiou C, Paniara O, Peppas C, Chalevelakis G.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 167-173 www.ijprajournal.com ISSN: 2456-4494

Liver and brain mucormycosis in a diabetic patient type II successfully treated with liposomal amphotericin B. Scand. J. Infect. Dis., 2000; 32(3): 335-7.

[10]. Waldorf AR, Levitz SM, Diamond RD. In vivo bronchoalveolar macrophage defense against Rhizopus oryzae and Aspergillus fumigatus. J. Infect. Dis., 1984; 150(5): 752-60.

[11]. Artis WM, Fountain JA, Delcher HK. A mechanism of susceptibility to mucormycosis in diabetic ketoacidosis: transferrin and iron availability. Diabetes, 1982; 31: 109–14.

[12]. Cohen SG, Greenberg MS. Rhinomaxillary mucormycosis in a kidney transplant patient. Oral Surg. Oral Med. Pathol., 1980; 50: 33–8. 18. Marchevskey AM, Bottone EJ, Geller SA. The changing spectrum of disease etiology and diagnosis of mucormycosis. Human Pathology, 1980; 11: 457.

[13]. Lanternier F, Poiree S, Elie C, Bakouboula P, Ribaud P, Wolff M, et al. Pilot ProspectiveStudy of High Dose (10 mg/kg/d) Liposomal Amphotericin B (L-AmB) for the Initial Treatment of Zygomycosis: AMBIZYGO Trial 50th ICAAC, American Society for Microbiology, Boston, 2010 (Abstract M-1046).

[14]. Rees JR, Pinner RW, Hajjeh RA, Brandt ME, Reingold AL. The epidemiological features of invasive mycotic infections in the San Francisco Bay area, 1992– 1993: results of population-based laboratory active surveillance. Clin. Infect. Dis., 1998; 27: 1138–1147.

[15]. Yamazaki T, Kume H, Murase S, Yamashita E, Arisawa M. Epidemiology of visceral mycoses: analysis of data in annual of the pathological autopsy cases in Japan. J. Clin. Microbiol., 1999; 37: 1732–1738

[16]. Maertens J, Demuynck H, Verbeken EK et al. Mucormycosis in allogeneic bone marrow transplant recipients:report of five cases and review of the role of iron overload in the pathogenesis. Bone Marrow Transplant, 1999; 24: 307–312.

[17]. Marty FM, Cosimi LA, Baden LR. Breakthrough zygomycosis after voriconazole treatment in recipients of hematopoietic stem-cell trans-plants. N. Engl. J. Med., 2004; 350: 950–952.

[18]. Safder S, Carpenter JS, Roberts TD, Bailey N. The “black turbinate” sign: an early MR imaging finding Of nasal mucormycosis. AJNR. Amer. J. Neuroradiol., 2010; 31: 771-774.

[19]. Rogers WD. Facial paralysis and epistaxis in a diabetic: a typical presentation for rhinocerebral mucormycosis. Ann. Emerg. Med., 1984; 13: 560 –1

[20]. Chamilos G, Marom EM, Lewis RE, Lionakis MS, Kontoyiannis DP. Predictors of pulmonary zygomycosis versus invasive pulmonary aspergillosis in patients with cancer. Clin. Infect. Dis., 2005; 41: 60-66.

[21]. Hamilos G, Samonis G, Kontoyiannis DP. Pulmonary mucormycosis. Semin. Respir. Crit. Care Med., 2011; 32: 693–702

[22]. Jensen HE, Salonen J, Ekfors TO. The use of immunohistochemistry to improve sensitivity and specificity in the diagnosis of systemic mycoses in patients with haematological malignancies. J. Pathol.,1997; 181(1): 100-5

[23]. Walsh TJ, Gamaletsou MN, McGinnis MR, Hayden RT, Kontoyiannis DP. Early clinical and laboratory diagnosis of invasive pulmonary, extrapulmonary, and disseminated mucormycosis (zygomycosis). Clinical Infectious Diseases, 2012; 54(suppl 1):S55-60.

[24]. Sciubba JJ, Regezi JA, Rogers RS. PDQ oral disease: diagnosis and treatment. PMPH-USA; 2002.

[25]. Spellberg B, Ibrahim A, Rolides E, Lewis RE, Lortholary O, Petrikkos G, Kontoyiannis DP, Walsh TJ. Combination therapy for mucormycosis: why, what, and how?. Clinical infectious diseases, 2012; 54(suppl 1): S73-8.

[26]. 26.Skiada A, Lanternier F, Groll AH, Pagano L, Zimmerli S, Herbrecht R, Lortholary O, Petrikkos GL. Diagnosis and treatment of mucormycosis in patients with haematological malignancies: guidelines from the 3rd European Conference on Infections in Leukemia (ECIL 3). Haematological, 2013; 98(4): 492-504.

[27]. Petrikkos G, Skiada A, Sambatakou H et al. Mucormycosis:ten-year experience at a tertiary-care center in Greece. Eur. J. Clin.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 167-173 www.ijprajournal.com ISSN: 2456-4494

Microbiol. Infect Dis., 2003; 22: 753–756.

[28]. Nithyanandam S, Jacob MS, Battu RR, Thomas RK, Correa MA, D'Souza O. Rhino-orbito-cerebral mucormycosis. A retrospective analysis of clinical features and treatment outcomes. Ind. J. Ophthalmol., 2003; 51: 231–236

[29]. Sipsas N, Gamaletsou M, Anastasopoulou A, Kontoyiannis D. Therapy of mucormycosis. Journal of Fungi, 2018; 4(3): 90.

[30]. Cheng VC, Chan JF, Ngan AH, et al. Outbreak of intestinal infection due to Rhizopus microsporus. J. Clin. Microbiol., 2009; 47: 2834–43