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MUCORMYCOSIS {BLACK FUNGUS}

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Abstract:
The fungus Mucorales causes a condition known as mucormycosis, which is an angio invasive infection. Although it is an uncommon condition, it is becoming more prevalent in those with immune impairment or poorly controlled diabetes mellitus. Even if vigorous therapy is administered, an overall higher death rate is recorded for the Rhino-orbito-cerebral, cutaneous, dissemination, intestinal, and pulmonary kinds. This review's primary goals and objectives were to provide a summary of mucormycotic disease, its etiopathogenesis, the mortality rate of rhino cerebral mucormycosis, and new developments in therapeutic and diagnostic approaches.

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INTRODUCTION*:*

The'mucor-mould' called mucormycetes, which is frequently found in plants, manure, soil, and rotting fruits and vegetables, is what causes the disease known as mucormycosis. Even healthy people's nose mucous and airborne particles include it. It is also present in air and dirt (dust particles). [9]

A variety of illnesses can be brought on by the opportunistic fungus Mucormycosis, which belongs to the Zygomycetes family. The majority of the time, the hosts have underlying problems that make them more susceptible to infection. Due to the fact that the causative fungus are common environmental microorganisms, immune - competent people often do not develop any symptoms. However, in immunocompromised individuals, these normally harmless organisms can cause a deadly and challenging-to-treat infection called. Clinical infections come in a variety of shapes and sizes, including pulmonary, intestinal, cutaneous, encephalic, and rhinos cerebral. The latter has to be distinguished from reactive fungal sinusitis, a localised overgrowth that doesn't spread and affects people who are immunocompetent. The infiltration of vascular system known as mucormycosis is characterised by tissue necrosis from thrombosis that often occurs after a fast development. High dosages of intravenous antifungal medication are essential components of the therapy, as well as early and rigorous surgical cleanup. [10]

The prevalence of Toxoplasmosis, sometimes known as black fungus, is rising, especially in COVID-19 recovered patients, and Karnataka is one of the places where this is happening. Two weeks after COVID healing, the disease is usually still present..[3]

History*:* -

A first instance of Mucormycosis was documented by German pathologist Paltauf in 1885, and he called it Candidiasis Mucorina. Mucormycosis was more frequently observed in immunocompromised people during the 1980s and 1990s. According to research done in France, the incidence rate indicated an annual amplified of 7.4%. It has been observed that Mucorales infections can occur everywhere in the world and may vary seasonally. [2]

COVID-19 Associated with mucormycosis

During in the COVID-19 "pandemic in I die in 2020 and 2021, many instances of Mucormycosis, tonsillitis, and candida associated to immunosuppressive therapy were documented. Early in 2021, a study on the connection between mucormycosis and COVID-19 listed eight instances of the disease, including one case each from Brazil, Italy, the UK, and Brazil, as well as 3 cases from the United States and two from India. The majority of patients who had COVID-19-related acute respiratory issues were hospitalised, improved, and then 10–14 days after receiving COVID-19 medication, they got mucormycosis. Mucormycosis was determined to be the cause of death in two of the seven cases. The absence of conventional risk factors in these three led the investigators to query the use of immunosuppression and steroid medications.

Mucormycosis that affects the eyes has been documented to develop up to many weeks after COVID-19 clearance, according to a study of COVID-19-related eye issues. Even However, other instances involved neither diabetic nor the use of immunosuppression medications. Even among children, there have been incidents documented. The BBC noted an uptick in instances in India in May 2021.

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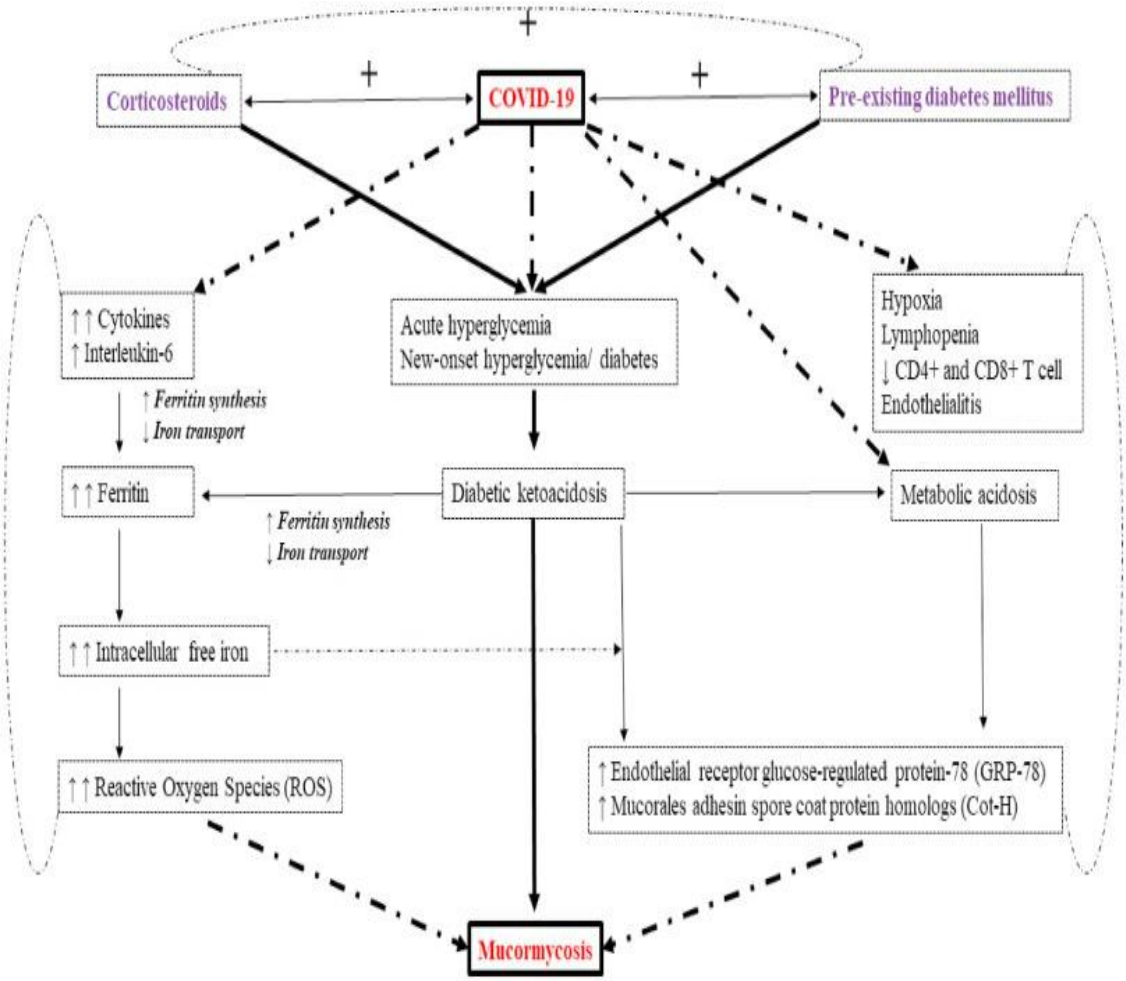

Etiology :-

An organism of the Zygomycetes category and Mucorales order of fungi causes the viral illness known as mucormycosis. The organisms most commonly found in patients are Apophysomyces (A. variables), Cunningham Ella (C. bertholletiae), Lichtheimia [Absidia] (L. corymbifera L. raosa), Mucor (M. circinelloides), Rhizopus (R. arrhizus (oryzae) R. microspores), Rhizomic (R. pusillus), and Saksenae The same goes for diabetic who are poorly managed, especially those who have a history of diabetic ketoacidosis.

By consuming or inhaling spores, as well as injecting spores subcutaneously, mucorales assault underlying tissue. The initial line of defence in the healthful host can eliminate the spores via oxidative compounds and cationic peptides as soon as they reach lung or epidermal tissue issues6. Uncontrolled diabetes mellitus, particularly ketoacidosis, steroid use, extreme ages, neutropenia, particularly with haematologic carcinoma, AIDS, renal insufficiency, organ or stem cell organ transplants, iron overload, epidermis trauma, a broad range of antibiotics, intravenous drug abuse, prophylactic fluconazole for candidiasis, and malnourishment are major risk factor.

Several possibilities exist, including:

1. Limited serum inhibition of Rhizopus species.

2. Increased iron available for the pathogen at a lower PH level

3. People with insulin resistance have respiratory macrophages that are less able to prevent the implantation of Basidiomycete species.

Rhizopus' ketone converter enables the growth of the organism in an acidic and higher glucose environment. Every kind of mucormycosis will manifest in DM, but especially in cases of ketoacidosis. Dialyzable inhibitory factor levels in diabetics are low, which creates favourable circumstances for fungal growth17. The acidic environment increases free iron by decreasing its binding to transferrin. Until amphotericin B and extensive surgery were administered, the mortality rate for Mucormycosis was known to be 90% or even higher. Mucormycosis is more likely to affect severely neutropenic individuals and people with impaired phagocytic activity. However, it differs for AIDS patients19.

It suggests that only neutrophil have a key role in preventing fungal growth rather than T cells. Patients who receive extended voriconazole treatment, particularly those with hematological transplants of stem cells and haematological malignancies, are more likely to develop mucormycosis. Additionally, Mucormycosis can occur in people who don't have any noticeable immunodeficiencies. Such disorders may have a connection to burns, trauma, or iatrogenic causes. [6]

Symptoms of Black Fungus or Mucormycosis Like COVID-19:-

The symptoms and consequences of this illness vary. It picks several parts of the body, including the brain, the lungs (pulmonary), the digestive system, and eventually the skin Mucormycosis, for possible harm. Cough, fever, chest discomfort, nasal or sinus congestion, excruciating headaches, and shortness of breath are some of the symptoms and signs of black fungus. In addition, it can migrate to any region of your body and create problems with your skin. You may have blisters, ulcers, redness, swelling, discomfort, and blackened skin tissue as a result of the black fungus. nasal congestion and hemorrhage eyes that are swollen and hurt eyeslid drooping Eventually, vision will get blurry. [9]

Risk factors for Black Fungus or Mucormycosis, especially for COVID-19 Patients:-

1. Diabetes or a weakened immune system

You can be in danger if you have COVID-19 and are either asymptomatic or symptomatic. Diabetes and a weakened immune system are among the most important risk factors (or high blood sugar).

2. During oxygen treatment, water contamination in humidifiers

3. The use of certain medications and steroids to treat COVID-19: According to medical professionals, individuals who received steroid and other medication treatments for COVID-19 to reduce inflammation are the patients who are more likely to develop mucormycosis. In some COVID 19 infection subtypes, steroids, however, are a life-saving drug. The immune response may be suppressed by some medications used to treat COVID-19. A blood sugar imbalance can also result from the use of steroids after COVID-19 therapy.Increased harm is done to people with high blood sugar (diabetes).Patients who have undergone transplants or stem cell procedures, cancer sufferers, or those with HIV/AIDS are all at risks. [9]

Case presentation:-

A 60-year-old male patient was hospitalised after exhibiting acute dyspnea for 3 days, as well as pyrexia, tachypnea, and general malaise. He had had diabetes for more than ten years and was using oral antihyperglycemic medications. His respiratory rate was 26/minute, blood pressure was 150/90 mmHg, he was afebrile at admission, and his heart rates was 80/minute. With oxygen supplement, his specific oxygen saturation increased to 86% at a rate of 10 litres per minute. A good cardiovascular and neurological examination was found along with bilateral swelling at the bases of the lungs during the pertinent physical examination. On his right foot, a non-healing lesion indicative of diabetic peripheral vascular disease was discovered. The SARS-CoV-2 viruses was detected in an oropharyngeal swab by a reverse-transcriptase polymerase chain reaction (RT-PCR).

A chest CT scan revealed several patchy ground-glass opacities in both lungs, affecting both upper lobes, the right middle lobe, and the lingula, mostly in a peripheral distribution, strongly indicative of COVID-19 illness. [9,10]

Over the following few days, acute respiratory distress syndrome rapidly worsened his condition. On day three, non-invasive ventilation was used to keep his oxygen saturation levels stable. On day 10, it was discovered that there was right eye prominence and bilateral lid edema, and topically moxifloxacin was recommended. The next day, a muscle tissue swelling in the right perceptive, malar, premaxillary, and retrobulbar areas was seen on an MRI of the brain, orbits, and paranasal sinuses. This swelling looked hyperintense on T2 and liquid inversion recoveries (FLAIR).

After receiving a preliminary diagnosis of right orbital cellulitis, he was sent to a canter for tertiary treatment. He was afebrile, short of breath and hypoxic when he was admitted. A thorough systematic and analytical assessment was performed on him. Relevant baseline tests showed a high serum creatinine level (1.57 mg/dl; normal 0.70-1.20), moderate lymphopenia (9.60%; normal 20-40%), and haemoglobin values of 10.40 gm/dl (normal 13–17 gm/dl). The level of CRP was 29.53 mg/l (normal). Conjunctival oedema, congestion, and indications of exposure keratitis were seen in the right eye. The infection that had spread to the other cavernous sinus or the COVID-19 coagulopathy were the two possible causes of the left eye's appearance of fixation and dilated non-reactive pupils (to lights). [10]

Pathophysiology : -

In immunocompetent individuals, Mucorales spore that enter the respiratory system stick to nasal mucus and are expelled by eating or sneeze. If there is a lesion in the mucous membranes, the polymorphonuclear neutrophils phagocytose and kill the fungal structures. Studies on the fungus Rhizopus arrhizus have shown that the ketone bodies in these individuals are digested by a ketone reductase, allowing them to thrive in an acidic environment. As a result, the fungi develop into hyphal forms in the host tissues and eventually infiltrate blood vessels. This widespread angioinvasion causes tissue inflammation and vascular thrombosis.Large patches of ischemia necrosis. Additionally, in a person whose immune system is already weakened due to one or more other disorders, metabolic acidosis hinders polymorphonuclear leukocyte chemotaxis, results in lower phagocytic activity, and diminishes locally inflammatory reaction. [7]

History and Physical:-

Various bodily systems can be affected by mould spores. The lung, central nervous system, paranasal sinuses, gastrointestinal system, and skin are among the organs that might get infected. Although its clinical signs and symptoms vary, they often show quick development. The way the fungus enters the body and the underlying condition both have a significant impact on the clinical symptoms. Brain of a rhino Spores entering the paranasal sinuses and invading tissue-bound capillaries are what cause mucormycosis to begin. Although it may proceed to facial numbness, blurred vision, nasal discharge, nasofrontal migraine, ocular discomfort, illness, diplopia, and chemosis, the illness usually begins with nasal congestion or release. Sublingual lesions often include fluid and necrotic tissue along with painless ulcerations and spread quickly over days. Maintaining a low threshold for obtaining a biopsy to rule out Mucormycosis in an immunocompromised patient with persistent nose symptoms is advised (often termed "invasive fungal sinusitis - IFS). Following the inhalation of infectious particles, pulmonary mucormycosis manifests as bilateral pneumonia that progresses quickly. Fever, hemoptysis, dyspnea, and coughing are the most typical clinical signs. Patients with hematologic illnesses experience this clinical manifestation more commonly.This respiratory disease might manifest as pulmonary embolism, bronchopneumonia, or even pneumonia. Although the illness can extend to other tissues, including the heart and pulmonary trunk, it can also cause cavitary lesions that resemble TB or a more benign allergic fungus illness. Both primary and secondary diseases can appear with cutaneous mycosis. The skin infection is caused by direct inoculation in primary illness and by spread from various sites in secondary disease. The main type, which frequently affects people who have had burns or even other traumatic skin issues, typically manifests as a single, indurated area of cellulitis that evolves into a necrotic lesion. Other manifestations include abscess, epidermal edema, and death.

Although the use of infected herbal remedies has been connected to the development of gastrointestinal sickness, the gastrointestinal form is caused by the consumption of contaminated food. There might be diarrhoea, hemoptysis, and melena, as well as nausea, vomiting, ulceration, and thrombosis of the gastric, oesophageal, and intestinal mucosa. Necrotic ulcers may result in perforation and peritonitis. Additionally, intestinal infarctions and hemorrhagic shock are associated with a bad prognosis. Except for the most

seriously immunocompromised individuals, gastrointestinal problems are uncommon. [15] (leukaemia sufferers, intestine transplant recipients, etc.), because the GI tract contains a lot of immunological tissue. A disseminated skin lesion is unquestionably an indication to suspect disseminated Mucormycosis and presages a poor prognosis. Dispersed Mucormycosis can develop from any main sites of infection, and its presentations are ambiguous, making diagnosis even more difficult.

Treatment: -

Anti - fungal medications are used to cure mucormycosis, however operation may eventually be needed. Doctors have stated that it is crucial to stop using immunomodulating medicines, minimise corticosteroid use, and manage diabetes. The right time, dose, and duration should be considered while using steroids. A multidisciplinary team including microbiologists, general surgery experts, intensivist neurologists, ENT professionals, ophthalmologists, dentists, maxillofacial/plastic surgeries, and others manages Covid patients with mucormycosis.

Life after surgery for Mucormycosis*:-*

The upper jaw and perhaps even the eye can be lost as a result of mycosis. "Patients would need to adjust to the loss of function caused by a lost jaw, which includes trouble biting, swallowing, facial aesthetics, and loss of self-esteem, according to experts. The upper jaw and the eye can both be replaced with the proper prosthetics or artificial replacements. While the replacement of the missing facial structures with prosthetics can begin once the patient is stable following surgery, doctors should reassure him about the availability of such initiatives rather than allowing him to feel fear over the unanticipated loss and exacerbate an already present case of post-traumatic stress disorder, according to maxillofacial prosthodontist Dr. B Srinivasan. "Prostheses repair can be done after surgery, but for better long-term results, interim solutions should be established even before surgical procedure of the jaws. Prosthetic reconstruction can make sure that the treatment is not worse than the illness, he added. [7]

Early identification, reversal of risk factors and underlying disease, surgical debridement, and quick treatment of intravenous antifungals—typically amphotericin B—are all necessary for the conventional care of mucormycosis. This calls for the rapid treatment of hyperglycemia, acidosis, and, where practical, the withdrawal of immunosuppressive medications. For Mucormycosis, Rifampicin is regarded as the primary treatment. However, even with the most vigorous treatments and dramatic invasive surgery, the results are indeed very poor unless immunological state can be restored.The improved neutrophil killing capacity and accelerated wound healing are both aided by the higher oxygen tension. [8]

DISCUSSION:

Secondary infectious diseases may be caused by a complicated interplay of variables, such as pre-existing illnesses like diabetes mellitus, prior respiratory pathology, use of immunosuppressive drugs, the risk of care facility infections, and systemic immune modifications of COVID-19 infection itself. These complications are becoming more widely recognised because of their impact on morbidity and mortality. In a recent analysis, 62/806 (8%) individuals experienced secondary bacterial or fungi illnesses while being admitted to the hospital. There was extensive usage of wide antibiotics, with as many as 1450/2010 (72%) of patients receiving these medications, frequently without any signs of infection for 10 days in patients who needed to be evacuated or additional oxygen, but not in instances with less severe symptoms. The recommendations make clear that receiving the proper treatment can significantly lower the chance of contracting a subsequent illness. [24]

He had diabetic foot sores, which indicated a lengthy history of diabetes. Only ten days after being hospitalised for COVID-19 illness and receiving both broad-spectrum antibiotics and steroids, the indications of orbital infections were discovered. Along with any potential pathophysiology reasons for COVID-19, all of these elements appear to favour fungal coinfection. In our situation, either a previously unknown Subsp virus was worsened or it later occurred.[1]

CONCLUSION:

Early detection of mucormycosis is lacking. It can be quite harmful to have a "black fungus infection." If a COVID patient experiences any Mucormycosis symptoms, including those related to badly managed diabetes mellitus or a depressed immune system, they should immediately contact their doctor. If a patient with a severe COVID-19 virus is suspected of having a Mucormycosis disease, this will enable clinicians to

take the essential medical steps. A serious Mucormycosis infection can be stopped in its tracks with prompt diagnosis and treatment. The most at risk for contracting this illness include others with diabetes, those who have been on steroids and humidified oxygen for a long period, and COVID sufferers with comorbid conditions.

Additionally, there are cancer sufferers and others who use long-term immunosuppression medications. It is crucial to comprehend and be aware of such medical issues and signs throughout the epidemic. It assists in prompt therapy initiation.

REFERENCE:

1. Mehta and Abha Pandey https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7599039/
2. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clinical Infectious Diseases, 2012.
3. Infections Published: 15th May 2021 03w05 AM by Indian express news https://www.newindianexpress.com/nation/2021/may/15/icmr-adviseson-how-to-fightmucormycosis-or-blackfungus-2302672.html
4. Wikipedia . https://en.wikipedia.org/wiki/Mucormycosis
5. Lewis RE, Kontoyiannis DP. Epidemiology and treatment of mucormycosis. Future Microbiol. Sep 2013. https://www.ncbi.nlm.nih.gov/books/NBK544364/
6. 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.
7. https://indianexpress.com/article/explained/mucormycosis-incovidpatients-fungal-infections-7308721/
8. Farmakiotis D, Kontoyiannis DP. Mucormycoses. Infect Dis Clin North Am. Mar 2016.
9. Apollo Pulmonologist May 11, 2021. https://healthlibrary.askapollo.com/all-about-black-fungus-ormucormycosis-incovid-19-patients/
10. Binder U, Maurer E, Lass-Flörl C. Mucormycosis--from the pathogens to the disease. Clin Microbiol Infect. 2014 Jun;20 , Article Author , Jorge L. Hernández1; Clifford J. Buckley 3.infections Published: 15th May 2021 03x05 AM by Indian express news https://www.newindianexpress.com/nation/2021/may/15/icmr-adviseson-how-to-fightmucormycosis-or-black- fungus-2302672.html
11. 11.Ribes JA, Vanover Sams CL, Baker DJ. Zygomycetes in human disease. Clin Microbiol Rev 2002;13:236–301. 2
12. Andrews DR, Allan A, Larbalestier RI. Tracheal mucormycosis. Ann Thorac Surg 1997;63:230–2.
13. Chamilos G, Lewis RE, Kontoyiannis DP. Lovastatin has significant activity against Zygomycetes and interacts synergistically with voriconazole. Antimicrobe Agents Chemother 2006;50:96–103.
14. Bauer H, Flanagan JF, Sheldon WH. The effects of metabolic alterations on experimental Rhizopus oryzae (mucormycosis) infections. Yale J Biol Med 1956;29:23–32.
15. Hibbett DS, Binder M, Bischoff JF. A higher-level phylogenetic classification of the fungi. Mycol Res 2007;111:509–47.
16. Song Y, Qiao J, Giovanni G, Liu G, Yang H, Wu J, et al. Mucormycosis in renal transplant recipients: a review of 174 reported cases external icon. BMC Infect Dis 2017;17:283.
17. Abdalla A, Adelmann D, Fahal A, Verbrugh H, Van Belkum A, De Hoog S. Environmental occurrence of Madurella mycetomatis, the major agent of human eumycetoma in sudan external icon.
18. Abramowitz I. Fatal perforations of the stomach due to mucormycosis of the gastrointestinal tract. S Afr Med J 1964;38:93–4.
19. Spellberg B, Edwards Jr J, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and external management icon. Clin Microbiol Rev 2005;18:556-69.
20. Voigt K, Cigelnik E, O'Donnell K. Phylogeny and PCR identification of clinically important zygomycetes based on nuclear ribosomal DNA sequence data. J Clin Microbiol 1999;37:3957–64
21. Voigt K, Wostemeyer J. Phylogeny and origin of 82 zygomycetes from all 54 genera of the mucorales and mortierellales based on combined analysis of actin and translation elongation factor EF-1alpha genes. Gene 2001;270:113–20
22. . Dannaoui E, Garcia Hermoso D. The zygomycetes. In: Kavanagh K. ed. New insights in medical mycology. Springer: New York; 2007. p. 159–83.

23. Sugar A. Agents of mucormycosis and related species. In: Mandell GL, Bennett JE, Dolin R. eds. Principles and practice of infectious diseases. 6th edn. New York: Elsevier; 2005. p. 2973– 84.
24. 24.Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosisexternal icon. Clin Infect Dis 2012;54:23-34.
25. James TY, Kauff F, Schoch CL. Reconstructing the early evolution of Fungi using a six-gene phylogeny. Nature 2006;443:818–22.
26. Marty FM, Cosimi LA, Baden LR. Breakthrough mucormycosis after voriconazole treatment in recipients of hematopoietic stem-cell transplants. N Engl J Med 2004;350:950–2.
27. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. Clin Microbiol Infect 2004;10:31–47.
28. Andrews PA, Abbs IA, Koffman CG, Ogg CS, Williams DG. Mucormycosis in transplant recipients: possible case transmission and potentiation by cytomegalovirus. Nephrol Dial Transplant 1994;9:1194–6.
29. Talmi YP, Goldschmied Reouven A, Bakon M. Rhino-orbital and rhino-orbito-cerebral mucormycosis. Otolaryngol Head Neck Surg 2002;127:22–31.
30. Anand VK, Alemar G, Griswold JA. Intracranial complications of mucormycosis: an experimental model and clinical review. Laryngoscope 1992;102:656–62.
31. Lass Florl C. Zygomycosis: conventional laboratory diagnosis. Clin Microbiol Infect 2009;15:60–5.