DOI 10.47176/alkhass.3.4.6

Review Article

SRPH

ALKHAS, 2021; 3(4): 6-10

Another Perspective on Black Fungus Disease in Veterinary

Donya Nikaien[1], Neshat Resalepour[2] and Seyyed Alireza Rezaie[2*]

[1]Department of Microbiology and Immunology, Faculty of Veterinary Medicine, University of Tehran, Iran
[2]General PhD Student, Faculty of Veterinary Medicine, University of Tehran, Iran.

***Corresponding Author:**
rezaeia@gmail.com

Received: 15 October, 2021
Accepted: 30 November, 2021
Published: 30 December , 2021

ABSTRACT

Mucormycosis, also known as black fungus is an opportunistic and serious fungal infection which is created by the order Mucorales. These fungi have a wide geographical distribution. The most important predisposing factors for this disease are hyperglycemia, metabolic acidosis, overuse of corticosteroids, neutropenia and blood malignancies. The disease occurs in several different forms; The most common of which is gastrointestinal and respiratory disorders in animals. Proper and timely diagnosis of the disease can play a key role in the prognosis, control and treatment of the disease. Since the disease can occur as a secondary infection in patients with COVID-19 who are being treated with corticosteroids to reduce inflammation, this study examines the status of black fungus disease in case reports of coronavirus in susceptible animals. Up to now, some cases of coronavirus and pneumoarthritis have been reported in animals.

Keywords: Black fungus, Corticosteroids, Coronavirus, Pneumoanthritis, Opportunistic, Serious

Introduction

Mucormycosis, previously called zygomycosis, is a serious fungal infection caused by fungus of the order Mucorales. Mucorales can affect different parts of body, including the sinuses, brain, lungs, and so on. Therefore, it can be prevalent in people who have recovered from COVID-19 or have it. Common symptoms associated with mucormycosis include swelling on one side of the face, fever, headache, nasal and sinus involvement, and black lesions on the bridge nasal or upper and inner mouth. Fungus that most often cause mucormycosis include Rhizopus species, Mucor species, Rhizomucor species, Syncephalastrum species, Cunnighamella Bertholletia species, Apophysomyces species, and Lichthemia species. Mucormycosis can come in many forms including gastrointestinal mucomycosis (most common in veterinary medicine), pulmonary mucomycosis (relative prevalence in veterinary medicine, and more common in people with cancer and people who have had organ transplants or stem cell transplants). Disseminated mucormycosis, rhinocerebral mucormycosis (higher prevalence in medicine and people with uncontrolled diabetes or kidney transplantation) and cutaneous mucormycosis. Chemotherapy long with corticosteroid therapy results in a neutropenia phase and provides the conditions for opportunistic pathogens, including the order Mucorales [3]. Coronavirus, which was reported in Wuhan, China in late December 2019 following a series of unexplained cases, is a serious public health concern. Immune system disorders and medical conditions such as diabetes mellitus and the widespread use of immunosuppressive agents and broad-spectrum antibiotics create the conditions conducive to secondary and potential infections, including mycosis [4].

Pathogenesis: The Mucorales enters the body through the release of small fungal spores, traumatic insemination and swallow [5]. When fungal spores invade the lungs or subcutaneous tissues, they are exposed to the body's first line of defense, mononuclear and multinuclear phagocytes. Healthy host phagocytes are able to kill Mucorales spores by producing oxidative metabolites and defense peptides [6]. Neutropenic patients with severe immunodeficiency or those with hyperglycemia and phagocytes disorders, are more at risk of mucormycosis [7].

[DOI: 10.47176/alkhass.3.4.6]

Publisher: Scientific Research Publishing House (SRPH), Shirvan, Iran
http://srpub.org
Email: alkhas@srpub.org

Another risk factor for mucormycosis is the high concentration of iron in the blood serum. Patients treated with deferoxamine show a high incidence of mucormycosis disease. This is because Mucorales uses this chelate as siderophore to get more iron [8]. Studies have shown that iron or deferoxamine prescription for infected animals with mycosis infections reduces their chances of survival [9]. The increased risk of mucormycosis in patients with ketoacidosis may also be due to the release of iron bound to plasma proteins [10]. If spores can escape from the host immune system and phagocytes, they can invade blood vessels and attach to endothelial cells to some extent. Rhizopus oryzae is even able to survive in conditions that the fungus is not viable [11].

Types of Mucormycosis in Veterinary

In ruminants, the disease occurs in the form of gastrointestinal lesions and inflammation of rumen, as well as lymphadenitis [12]. Types of mucormycosis have been studied as the case reports and include the following: Following antibiotic therapies, natural rumen microbial flora is destroyed and conditions for mucormycosis disease are provided in livestock [13]. Exposure to Mucorale fungus through contaminated food causes swelling of the intestinal lymph nodes, which is macroscopically indistinguishable from bovine tuberculosis granulomas [14]. In ruminants, gastrointestinal mucormycosis can occur in the other parts of gastrointestinal tract. Respiratory and systemic types are often reported due to invasion of fungus to the blood vessels and spread of hematogen to various organs [15]. In horses, lesions caused by mucormycosis have been reported in various organs, especially in the respiratory and gastrointestinal tract, and the disease may progress and become systemic [16]. Cases of cutaneous mucormycosis have also been reported in horses [18]. Few scattered reports of the occurrence of mucormycosis in poultry species are available; Respiratory and gastrointestinal disorders, in particular, have been reported frequently [19].

Treatment of Mucormycosis

Treatment of the disease requires rapid diagnosis and correction of predisposing factors, surgery and appropriate antifungal therapies. Unfortunately, diagnostic tools are so limited so that in some studies, 50% of cases are diagnosed only after death [20, 21, 22]. Delay in diagnosis indicates a poorer prognosis for the disease. In many cases of the disease, especially pulmonary and diffuse types, the surgery has been considered impossible in patients with neutropenia, however in some cases that surgery is possible, surgery with antifungal drugs is better than using antifungal drugs alone [24-29]. One of the reasons for the difficulty of treatment in the studies done, is the lack of large-scale clinical trials. The choice of the best antifungal drug depends on the results of studies on animal models and human experience. According to current data, the selective treatment of mucormycosis is liposomal amphotericin B, which also is less toxic [30-32].

Itraconazole is an unsuitable medicine according to the evidence of lack of appropriate treatment in patients with mycosis [33]. According to recent data, the use of Posaconazole is recommended in clinical cases that treatment with amphotericin has not been successful [34-36]. Cytokines such as gamma interferon, granulocytes, and macrophages have also been used to treat mucormycosis [37-38].

What Causes Black Fungus and Covid 19?

Coronavirus disease causes a state of immunosuppression and increases the risk of secondary infections such as mucormycosis. Coronavirus attributed to acute respiratory syndrome was declared as a global epidemic by WHO in March 2020 [39-42]. This pandemic with more than 162 million registered cases and more than 30 million deaths worldwide is still a public health concern [43]. As the incidence of the disease worsens around the world, many potential side effects of covid-19 including the susceptibility to secondary bacterial and fungal infections, increase [44-47]. Impaired immune response in covid-19 is associated with underlying diseases and concomitant medical conditions such as diabetes mellitus and the widespread use of immunosuppressive agents and broad-spectrum antibiotics [44]. The fungal infection most commonly studied in this study is mucormycosis and more likely to develop in the more advanced stages of covid-19 infection [48]. There is also a higher risk of mortality in the concurrency of covid-19 infection and mucormycosis [44].

Mucormycosis as previously mentioned in the pathogenesis of the disease, affect the patients with immunodeficiency, especially those with diabetes mellitus, long-term corticosteroid therapy, neutropenia transplant recipients and hematologic malignancies [44, 49, 50, 51]. On the other hand, it provides suitable conditions for mucormycosis due to the suppression of the immune system of people with covid-19 and also the prescription of corticosteroids to reduce pulmonary inflammation. Therefore, it is needed to increase awareness about mucormycosis among patients with covid-19 (since both conditions can lead to significant mortality).

Coronavirus in Veterinary

There are reports of coronavirus disease in the cat population worldwide named Feline coronavirus (FCoV). The only exceptions based on the absence of this disease in cats are the Falkland and the Galapagos Islands [52, 53].

[DOI: 10.47176/alkhass.3.4.6]

The virus causes Feline coronavirus enteric (FECV) disease in cats, which causes intestinal epithelial cells to become infected. In coronavirus enteritis, shortening of the intestinal villi, fusion or adhesion of the villi, and rounding of the villi and hyperplasia of the surrounding crypts can be seen on a microscopic level. Lieberkühn glands become necrotic, inflammation and swelling of the mesenteric lymph nodes next to the intestine are other symptoms of the disease [54]. The disease mainly occurs in the small intestine and can even be fatal in cats [54].

This intestinal infection can show few clinical symptoms and is usually chronic. In asymptomatic carriers, the virus is excreted in the feces and PCR tests of fecal samples are used to diagnose the disease.

Conclusion

Regarding to the research studies done by the others, it can be concluded that it can be expected the secondary infection of black fungus in cats with coronavirus enteritis as an emerging disease in medical science in the coming years due to the close relationship between human life and animals such as cats, also considering the formation of mucormycosis infection following infection with covid-19, which belongs to the family of coronaviruses.

References

1. What is Mucormycosis? Severe fungal infection cases linked to COVID-19? https://timesofindia.indiatimes.com/life-style/healthfitness/health-news/coronavirus-severe-fungalinfection-cases-linked-to-covid-19-heres-what-weknow/photostory/79836584.cms?picid=79836589

2. Shikha G, Mucormycosis. A rare fungal infection linked to COVID-19: causes, symptoms, types, prevention, and treatment, 2020; https://www.jagranjosh.com/generalknowledge/mucormycosis-a-rare-fungal- infection1608646233-1

3. Zurl C, Hoenigl M, Schulz E. et al. Autopsy proven pulmonary mucormycosis due to Rhizopus microspores in a critically ill COVID-19 patient with underlying hematological malignancy. *J Fungi.* 2021; 7(2): 88. https://doi.org/10.3390/jof7020088

4. Gorbalenya AE. Severe acute respiratory syndrome-related coronavirus–The species and its viruses, a statement of the Coronavirus Study Group. BioRxiv. 2020.

5. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. *Clin Microbiol Infect.* 2004; 10(suppl 1): 31-47.

6. Waldorf AR. Pulmonary defense mechanisms against opportunistic fungal pathogens. *Immunol Ser.* 1989; 47: 271-342.

7. Chinn RY, Diamond RD. Generation of chemotactic factors by Rhizopus oryzae in the presence and absence of serum: relationship to hyphal damage mediated by human neutrophils and effects of hyperglycemia and ketoacidosis. *Infect Immun.* 1982; 38: 1123-1129.

8. Boelaert JR, de Locht M, Van Cutsem J. et al. Mucormycosis during deferoxamine therapy is a siderophoremediated infection. In vitro and in vivo animal studies. *J Clin Invest.* 1993; 91: 1979-1986.

9. Abe F, Inaba H, Katoh T, Hotchi M. Effects of iron and desferrioxamine on Rhizopus infection. *Mycopathol.* 1990; 110: 87-91.

10. Artis WM, Fountain JA, Delcher HK, Jones HE. A mechanism of susceptibility to mucormycosis in diabetic ketoacidosis: transferrin and iron availability. *Diabetes.* 1982; 31: 1109-1114.

11. Ibrahim AS, Spellberg B, Avanessian V, Fu Y, Edwards JE Jr. Rhizopus oryzae adheres to, is phagocytosed by, and damages endothelial cells in vitro. *Infect Immun.* 2005; 73: 778-783.

12. Jensen HE. Systemic bovine aspergillosis and zygomycosis in Denmark with reference to pathogenesis, pathology, and diagnosis. *APMIS Suppl.* 1994; 42: 1-48.

13. Jensen HE, Basse A, Aalbaek B. Mycosis in the stomach compartments of cattle. *Acta Vet Scand.* 1989; 30: 409-423. [PMC free article] [PubMed] [Google Scholar]

14. Ortega J, Uzal FA, Walker R. et al. Zygomycotic lymphadenitis in slaughtered feedlot cattle. *Vet Pathol.* 2010; 47: 108-115.

15. Jensen HE, Krogh HV, Schonheyder H. Bovine mycotic abortion - a comparative study of diagnostic methods. *Zentralbl Veterinarmed B.* 1991; 38: 33-40.

16. Thirion-Delalande C, Guillot J, Jensen HE. et al. Disseminated acute concomitant aspergillosis and mucormycosis in a pony. *J Vet Med A.* 2005; 52: 121-124.

17. Guillot J, Collobert C, Jensen HE. et al. Two cases of equine mucormycosis caused by Absidia corymbifera. *Equine Vet J.* 2000; 32: 453-456.

18. Awadin W, Mosbah E, Youssef ES. et al. A case of subcutaneous destructive facial swelling in a dog caused by Mucor species. *J Vet Sci Med Diag.* 2015; 4; doi:10.4172/2325-9590.1000163

19. Suzuta F, Kimura K, Urakawa R et al. Variations in the morphology of Rhizomucor pusillus in granulomatous lesions of a Magellanic penguin (Spheniscus magellanicus). *J Vet Med Sci.* 2015; 77: 1029-1031.

20. Kontoyianis DP, Vartivarian S, Anaissie EJ, Samonis G, Bodey GP, Rinaldi M. Infections due to Cunninghamella bertholletiae in patients with cancer: report of three cases and review. *Clin Infect Dis.* 1994; 18: 925-928.

21. Tietz HJ, Brehmer D, Janisch W, Martin H. Incidence of endomycoses in the autopsy material of

[DOI: 10.47176/alkhass.3.4.6]

the Berlin Charite Hospital. *Mycoses.* 1998; 41(suppl 2): 81-85.
22. Mori T, Egashira M, Kawamata N. et al. Zygomycosis: two case reports and review of reported cases in the literature in Japan. *Nippon Ishinkin Gakkai Zasshi.* 2003; 44: 163-179.
23. Petrikkos G, Skiada A, Sambatakou H. et al. Mucormycosis: ten-year experience at a tertiary-care center in Greece. *Eur J Clin Microbiol Infect Dis.* 2003; 22: 753-756.
24. Kontoyiannis DP, Wessel VC, Bodey GP, Rolston KV. Zygomycosis in the 1990s in a tertiary-care cancer center. *Clin Infect Dis.* 2000; 30: 851-856.
25. 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: 1044-1150.
26. Welk B, House AA, Ralph E, Tweedy E, Luke PP. Successful treatment of primary bilateral renal mucormycosis with bilateral nephrectomy. *Urology.* 2004; 64: 590.
27. Reid VJ, Solnik DL, Daskalakis T, Sheka KP. Management of bronchovascular mucormycosis in a diabetic: a surgical success. *Ann Thorac Surg.* 2004; 78: 1449-1451.
28. Pavie J, Lafaurie M, Lacroix C. et al. Successful treatment of pulmonary mucormycosis in an allogenic bone-marrow transplant recipient with combined medical and surgical therapy. *Scand J Infect Dis.* 2004; 36: 767-769.
29. Asai K, Suzuki K, Takahashi T, Ito Y, Kazui T, Kita Y. Pulmonary resection with chest wall removal and reconstruction for invasive pulmonary mucormycosis during antileukemia chemotherapy. *Jpn J Thorac Cardiovasc Surg.* 2003; 51: 163-16
30. Walsh TJ, Hiemenz JW, Seibel NL. et al. Amphotericin B lipid complex for invasive fungal infections: analysis of safety and efficacy in 556 cases. *Clin Infect Dis.* 1998; 26: 1383-1396.
31. Spellberg B, Fu Y, Edwards JE Jr, Ibrahim AS. Combination therapy with amphotericin B lipid complex and caspofungin acetate of disseminated zygomycosis in diabetic ketoacidotic mice. *Antimicrob Agents Chemother.* 2005; 49: 830-832.
32. Barron MA, Lay M, Madinger NE. Surgery and treatment with high-dose liposomal amphotericin B for eradication of craniofacial zygomycosis in a patient with Hodgkin's disease who had undergone allogeneic hematopoietic stem cell transplantation. *J Clin Microbiol.* 2005; 43: 2012-2014.
33. Eisen DP, Robson J. Complete resolution of pulmonary Rhizopus oryzae infection with itraconazole treatment: more evidence of the utility of azoles for zygomycosis. *Mycoses.* 2004; 47: 159-162.
34. Sun QN, Fothergill AW, McCarthy DI, Rinaldi MG, Graybill JR. In vitro activities of posaconazole, itraconazole, voriconazole, amphotericin B, and fluconazole against 37 clinical isolates of zygomycetes. *Antimicrob Agents Chemother.* 2002; 46: 1581-1582.
35. Dannaoui E, Meletiadis J, Mouton JW, Meis JF, Verweij PE. In vitro susceptibilities of zygomycetes to conventional and new antifungals. *J Antimicrob Chemother.* 2003; 51: 45-52.
36. Pfaller MA, Messer SA, Hollis RJ, Jones RN. Antifungal activities of posaconazole, ravuconazole, and voriconazole compared to those of itraconazole and amphotericin B against 239 clinical isolates of Aspergillus spp. and other filamentous fungi: report from SENTRY Antimicrobial Surveillance Program, 2000. *Antimicrob Agents Chemother.* 2002; 46: 1032-1037.
37. Abzug MJ, Walsh TJ. Interferon-gamma and colony-stimulating factors as adjuvant therapy for refractory fungal infections in children. *Pediatr Infect Dis J.* 2004; 23: 769-773.
38. Gil-Lamaignere C, Simitsopoulou M, Roilides E, Maloukou A, Winn RM, Walsh TJ. Interferon-gamma and granulocyte–macrophage colony-stimulating factor augment the activity of polymorphonuclear leukocytes against medically important Zygomycetes. *J Infect Dis.* 2005; 191: 1180-1187.
39. Huang C, Wang Y, Li X. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020; 395(10223): 497-506.
40. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA.* 2020; 323(13): 1239-1242.
41. Zhu NA, Zhang D, Wang W. et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020; 382(8): 727-733.
42. WHO. Listings of WHO's response to COVID-19. 2021; https://www. who.int/news/item/29-06-2020-covidtimeline
43. CCfSSa. Coronovirus COVID-19 global cases. 2021; https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740 fd40299423467b48e9ecf6
44. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus.* 2020; 12(9): e10726.
45. Hughes S, Troise O, Donaldson H, Mughal N, Moore LSP. Bacterial and fungal coinfection among hospitalized patients with COVID-19: a retrospective cohort study in a UK secondary-care setting. *Clin Microbiol Infect.* 2020; 26(10): 1395-1399.
46. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. *J Laryngol Otol.* 2021; 1-6.
47. Garg D, Muthu V, Sehgal IS. et al. Coronavirus disease (Covid-19) associated mucormycosis (CAM):

[DOI: 10.47176/alkhass.3.4.6]

case report and systematic review of literature. *Mycopathol.* 2021; 186(2): 289-298.
48. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. *Mycopathol.* 2020; 185(4): 599-606.
49. Mekonnen ZK, Ashraf DC, Jankowski T. et al. Acute invasive rhinoorbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome. *Ophthalmic Plast Reconstr Surg.* 2021; 37(2): e40-e80.
50. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. *Am J Emerg Med.* 2021; 42(264): e265-e264.e268.
51. Sen M, Lahane S, Lahane TP, Parekh R, Honavar SG. Mucor in a viral land: a tale of two pathogens. *Indian J Ophthalmol.* 2021; 69(2): 244-252.
52. Addie Diane D, McDonald Mike, Audhuy Stéphane, Burr Paul, Hollins Jonathan, Kovacic Rémi, Lutz Hans, Luxton Zoe, Mazar Shlomit, Meli Marina L. Quarantine protects Falkland Islands (Malvinas) cats from feline coronavirus infection. *J Feline Med Surg.* 2012; 14(2): 171-176. doi:10.1177/1098612X11429644. PMID 22314098. S2CID 4989860
53. Levy JK, Crawford PC, Lappin MR, Dubovi EJ, Levy MG, Alleman R, Tucker SJ, Clifford EL. Infectious diseases of dogs and cats on Isabela Island, Galapagos. *J Vet Intern Med.* 2008; 22(1): 60-65. doi:10.1111/j.1939-1676.2007.0034.x. PMC 7166416. PMID 18289290. S2CID 23423426.
54. Rottier PJM, Nakamura Kazuya, Schellen Pepijn, Volders Haukeline, Haijema Bert Jan. Acquisition of Macrophage Tropism during the Pathogenesis of Feline Infectious Peritonitis is Determined by Mutations in the Feline Coronavirus Spike Protein. *J Virol.* 2005; 79(22): 14122-14130. doi: 10.1128/JVI.79.22.14122-14130.2005 PMC 1280227. PMID 16254347

ALKHAS

Citation: Nikaien D, Resalepour N, Rezaie SA. Another Perspective on Black Fungus Disease in Veterinary. ALKHAS. 2021; 3(4): 54-58.

https://doi.org/10.47176/alkhass.3.4.6

[DOI: 10.47176/alkhass.3.4.6]