pISSN 2349-3283 | eISSN 2349-3291

Review Article

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20212500

COVID-19 associated mucormycosis in head and neck region of pediatric patients: a life-threatening disease in current pandemic

Santosh Kumar Swain*

Department of Otorhinolaryngology and Head and Neck Surgery, IMS and SUM hospital, Siksha "O" Anusandhan University, K8, Kalinga nagar, Bhubaneswar, Odisha, India

Received: 20 May 2021 Accepted: 16 May 2021

*Correspondence:

Dr. Santosh Kumar Swain,

E-mail: santoshvoltaire@yahoo.co.in

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Mucormycosis is a severe form of fungal infection and often affect immunocompromised patients. It is associated with high morbidity and mortality and characterized by extensive angioinvasion and necrosis of the affected tissue. It is potentially fatal invasive fungal infection in the pediatric age group. It results in rapid spread of the disease with tissue destruction and its nature of angioinvasion can cause wide-spread dissemination. Currently this dreaded mucormycosis is rising among COVID-19 pediatric patients during their treatment period or after their discharge from hospital. It is also called COVID-19 associated mucormycosis (CAM) or black fungus. Classically, uncontrolled diabetes mellitus (DM) and other immunosuppressive conditions or corticosteroid therapy during COVID-19 treatment are known risk factors for causing mucormycosis in pediatric patients. Early identification and prompt treatment in pediatric patients with CAM are required. In the head and neck area, rhino-orbital-cerebral mucormycosis is a fatal clinical entity associated with COVID-19 infections result in higher morbidity and mortality of the pediatric patients. Aggressive endoscopic surgical debridement for local control and appropriate systemic antifungal treatment will help to improve the prognosis and survival of the patients. The aim of this review article is to discuss the detail of epidemiology, etiopathology, clinical profile, diagnosis and current treatment options of the CAM in children.

Keywords: COVID-19 associate mucormycosis, Pediatric patient, Head and neck region, Rhino-orbital-cerebral mucormycosis, Amphotericin B

INTRODUCTION

COVID-19 infection is a contagious and rapidly spreading disease of respiratory tract caused by the novel virus, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is highly infectious disease which spreads all over the world in short span of the time. On March 11th, 2020, the World Health Organization (WHO) declared COVID-19 as a global pandemic. Currently fungal infection like mucormycosis is rising in COVID-19 patient, resulting into a fatal consequence. It is affecting to all age groups including pediatric patients with COVID-19 infections. Mucormycosis is a life-threatening infection and can manifest as a local or systemic invasion. After candidiasis and aspergillosis, mucormycosis is considered

as third most common fungal infections.² In the head and neck region, the most common forms of mucormycosis are rhino-orbital-cerebral infection.³ The critical ill COVID-19 pediatric patients those were admitted to the intensive care unit (ICU) and required mechanical ventilation or had prolonged duration hospital stays and those are taking systemic steroid for prolonged period or suffering from uncontrolled diabetes are likely to get co-fungal infections such as mucormycosis, called COVID-19 associated mucormycosis (CAM).^{4,5} Patients of mucormycosis in the head and neck region may present with headache, chemosis, multiple cranial nerve paralysis, unilateral periorbital facial pain, proptosis, blepharoptosis, changes of ocular motility, ophthalmoplegia and vision loss by acute onset are most common symptoms and signs 2 The

diagnosis of the CAM is confirmed by histopathology, culture and KOH mount.⁶ Early diagnosis and treatment approach are helpful to cure this disease.⁷ Clinical suspicion, diagnosis and early treatment with surgical debridement and broad-spectrum antifungal agents are key for preventing this fatal clinical entity. The CAM in children is less frequently documented in the literature. The objective of this review article is to discuss the detail of epidemiology, etiopathology, clinical profile, diagnosis and current treatment options of the CAM in children.

METHODS OF LITERATURE SEARCH

Current research articles regarding mucormycosis in head and neck area of the COVID-19 pediatric patient were searched through a multiple systematic approach. First, we conducted an online search of the Scopus, Pub Med, Medline and Google Scholar databases with the word COVID-19 associated mucormycosis, pediatric patients, head and neck region and rhino-orbital-cerebral mucormycosis. The abstract of the published articles was identified by this search method and other articles identified manually from the citations. This manuscript reviews the details of the COVID-19 associated mucormycosis specifically in head and neck region of the COVID-19 patients in pediatric age group. This review article presents a baseline for further prospective trials towards this fatal fungal infection in pediatric age group such as mucormycosis of the head and neck region or rhino-orbital-cerebral part with COVID-19 infection in current pandemic. It will also help as a spur for further research in this dreaded fungal infection such as mucormycosis of COVID-19 patients in pediatric age group and so will be helpful to protect from such fatal fungal infection, also called as black fungus.

EPIDEMIOLOGY

Mucormycosis represent the third most common etiology for invasive fungal infection after Candida and Aspergillus species.⁸ Currently the mucormycosis infections is increasing in current COVID-19 pandemic and affecting both adult and children. There are several factors associated with increase in number of cases of mucormycosis in COVID-19 infection. This infection is more in diabetes mellitus patient, malignancy patient and those are taking immunosuppressive medication. immunomodulators like tocilizumab. 9 Use of voriconazole in immunocompromised patients has been singled out as risk factor for mucormycosis.9 important Mucormycosis accounts for 10% of all fungal infections. 10 Despite intensive antifungal treatment and surgical debridement, the mortality rate of these patients is more than 40% for many decades.11

ETIOPATHOLOGY

Mucormycosis is caused by fungi which belongs to order Mucorales of the class Zygomycetes. These fungi are ubiquitous saprophytes and seen in soil, decomposed

vegetables and in healthy human respiratory tract and digestive system.8 Mucormycosis is usually found in individuals with lower body immunity. COVID-19 patients usually show higher levels of inflammatory cytokines (interleukin (IL)-2R, IL-6, IL-10 and tumor necrosis factor-alpha), impaired cell-mediated immune response, affect both CD4+ T and CD8 + T cells. 12,13 COVID-19 patients often treated with steroids and immunomodulators which impair the immune system of the patient. So, COVID-19 patients have susceptibility towards fungal co-infections such as mucormycosis.¹⁴ Mucormycosis is a rare, fatal, angio-invasive and opportunistic fungal infection among children which can affect any organ of the body. 15 In the head and neck region, rhino-orbital-cerebral infection is common type of the mucormycosis infections. 16 Although immune deficiency is an important risk factors for co-fungal infections, there are several other diseases also provide chance for mucormycosis in children. Hematological malignancy is an important risk factor for mucormycosis.¹⁷ Other risk factors are hematopoietic stem cell transplants or solid organ transplant recipient. Solid organ cancer (without transplant) is not usually associated with mucormycosis. 18 Diabetes mellitus is also another important risk factor with 9% to 36% of the cases of mucormycosis found in diabetes. 19 Injudicious use of steroids during treatment of COVID-19 infections lower the immunity is also an important risk factor for getting mucormycosis infection. Systemic steroid not only lowers the immunity and but also increases the blood glucose level in the blood and so act as risk for getting fungal infection.²⁰ Tocilizumab is an immunomodulator which impair the immunity of the patient. Iron overload, deferoxamine therapy, intravenous drug use, kidney diseases are less common in children but remain well recognized risk factors for causing mucormycosis in children.²¹ Burns and traumatic ulcers/wounds may be associated with cutaneous mucormycosis.21 Poor oral hygiene during oxygen administration and use of unsterile, unclean oxygen providing medical devices are also responsible for cofungal infections to the COVID-19 children. So, the oral care should be done and devices giving oxygen must be maintained with optimum sterility. ¹⁶ In some children, no specific underlying risk factors are associated with mucormycosis.22 The Rhizopus species (approximately 44%) and Mucor species (approximately 15%) are most commonly found in mucormycosis infection.²³

The important factor for pathogenesis of Mucormycosis are host defense mechanism, fungal endothelial interaction and role of the iron. In case of normal immune status, mononuclear and polymorphonuclear cells produce oxidative metabolites which usually kill Mucorales. This is the cause for neutropenia and defective phagocytes being considered as risk factors for resulting mucormycosis. Diabetes patients with COVID-19 infection increases the risk for impair blood glucose levels and ketoacidosis to damage the phagocytic defense mechanism.²⁴ The hallmark for mucormycosis is extensive angioinvasion, resulting thrombosis in the vessels and

necrosis of the affected tissue. The endothelial cells result in phagocytosis of the dead fungus which results in further tissue damage. This is the rationale behind the requirement of surgical debridement in combination to antifungal treatment for CAM. The serum iron level also has role in the pathogenesis of the mucormycosis. Higher serum iron levels increase the susceptibility for mucormycosis. In patient of diabetes ketoacidosis, the iron is released from the transferrin in acidic pH, this result in predisposing for mucormycosis.25 Mucormycosis usually clinically as five forms such as rhinocerebral, pulmonary, disseminated, gastrointestinal and cutaneous. The most common form is rhinocerebral. Mucormycosis in pediatric age group is usually associated with prematurity, low birth weight, febrile neutropenia, immunodeficient states, systemic corticosteroid, broad spectrum antibiotic treatment, malnutrition and local injury in skin.²⁶ This fungal infection can occur in the rhino-orbital-cerebral part, respiratory, gastrointestinal and cutaneous forms on the basis of the sites where the spores are inhaled, ingested or inoculated.²⁷ Rhino-orbital-cerebral form of the mucormycosis in head and neck region is very fatal and can result in even death of the patient if not treated promptly. Fungi enter into the body via inhalation and the fungal hyphae may enter into lymphatics, arteries and veins results in thrombosis and eschar formation.²⁸

CLINICAL PRESENTATIONS

In head and neck region, rhino-orbital-cerebral disease is the commonest form of the mucormycosis in adult and children. The initial clinical presentations often mimic to rhinosinusitis and shows non-specific symptoms such as facial pain, nasal discharge, nasal block, headache, facial swelling (Figure 1), eye pain and orbital swelling.²⁹ Male children are more commonly affected than female with M: F is 1.6:1.³⁰



Figure 1: A 2-year-old male child with CAM presenting with right orbito-facial swelling.

Progression of the disease causes tissue infarction and formation of necrotic eschars. Spread of the infections to the eye usually occurs from the ethmoidal sinuses which manifests as eye pain and proptosis. Intra-cranial involvement often occurs from the ethmoidal and sphenoidal sinus by blood vessels to the brain and/or cavernous sinus.³¹ The warning symptoms for rhino-

orbito-cerebral mucormycosis are nasal stuffiness, foul smelling nasal discharge, epistaxis, facial swelling, periocular swelling, eye pain, facial pain, worsening headache, proptosis, sudden loss of vision, facial paresthesia, sudden ptosis, diplopia, facial palsy, fever, altered sensorium. Patients of CAM may complain toothache, loosening of maxillary teeth.³² Patient may also present with blurring of the vision or double vision in case of orbital involvement.

DIAGNOSIS

Mucormycosis is considered as a medical emergency which need early diagnostic confirmation for prompt treatment. Sometimes the early diagnosis is hampered due its non-specific symptoms. The diagnosis needs a high grade of suspicion and close interaction between the clinicians and microbiologists. Suspected patient of CAM should undergo undergoes diagnostic nasal endoscopy and tissue should be collected in sterile saline for microscopy and culture and other portion in normal saline for study. histopathological During diagnostic endoscopy, the presence of black eschar at the site of lesion usually gives first clue for the diagnosis. Prompt diagnosis can be made by direct microscopy with KOH mount and biopsy. Histopathological examination usually provides definite diagnosis. The histopathological examination can support towards the diagnosis by showing the broad aseptate hyphae and angioinvasion. Vascular thrombosis is a classical feature found in zygomycosis because of the angioinvasion by the fungus. The fungi can also be highlighted by special stains such as Gomori's methenamine silver (GMS) or periodic acid Schiff (PAS) stains. Sometimes, the immunohistochemistry zygomycete antibodies is useful for diagnosis.33 Fungal culture of the tissue sample is the gold standard for diagnosis of the mucormycosis, as it only confirms the diagnosis but also helpful for precise genus and species identification. Now days, molecular testing with tissue samples also confirm the histopathological diagnosis. Molecular technique is based on polymerase chain reaction (PCR) uses internal transcribed spacer (ITS) such as ITS1 and ITS2 regions which are variable between fungal species as target for identification of species.34 Other molecular techniques are 18S targeted semi-nested PCR and real time PCR targeting cytochrome b gene.34 One study introduced two real time quantitative PCR assays which targets 28S rRNA gene.³⁴ As histopathology and culture are time taking process, molecular assays are emerged to identify fungal pathogens and also species identification, both from fresh and formalin fixed embedded (FFPE) tissue. The wound culture usually takes time and blood culture are negative, so rarely useful.³⁵

TREATMENT

The key to effective management of the CAM is early identification, elimination of predisposing factors, aggressive surgical debridement and parenteral antifungal treatment. Pediatric patients of CAM if known case of

diabetes or diabetic ketoacidosis should be properly controlled with appropriate medication like insulin or oral hypoglycemic medications. The immunomodulators if any taken by patients should be discontinued. Surgical intervention is an essentials treatment option in mucormycosis. Aggressive debridement of the infected and necrotic part/tissue should be done promptly. The debridement of the necrotic tissue is usually done till getting bleeding tissue for enhancing penetration of the antifungal drugs into the affected areas. The highest level of successful treatment can be achieved by combination of surgery and medical management.³⁶ Surgical debridement is often associated with significant lowering of the mortality rates, specifically those with rhino-orbitalcerebral mucormycosis.³⁷ Surgical debridement include removal of the necrotic materials; if eye involved, exenteration of eye should be done. Sometimes reconstruction of the affected area may be required for functional and cosmesis purpose.

Before starting medical treatment with amphotericin B, insert peripheral inserted central catheter (PICC) or central venous catheter. Patient should maintain adequate systemic hydration, infuse normal saline IV before amphotericin B infusion. The standard medical treatment of CAM is Amphotericin B (AmB) in the dose of 1.0 to 1.5 mg/kg/day for period ranges from weeks to months depending on the clinical response.³⁵ Amphotericin B (AmB) is the corner stone in the medical management of the mucormycosis and delay in starting of AmB is a predictor for poor outcome in patients of mucormycosis. So, early initiation of AmB is associated with greater survival rates.³⁸ There is less toxic form of AmB, called liposomal form colloidal dispersible type, lipid complex given at higher dose (3 to 5 mg/kg/day) with lesser side effects. There is topical AmB has also available which is helpful but limited by its availability and cost factors. Posaconazole is a triazole and act as a broad-spectrum antifungal drug. It acts against Mucorales fungi and available in oral and intravenous formulations.39 Posaconazole is highly lipophilic and distributed to all part of the tissue easily. It is also better tolerated in comparison of AmB and has lesser toxicity. Study on posaconazole showed that oral formulation has good safety and tolerability with moderate efficacy against invasive fungal infections.40 However it is less studied in pediatric patients, so need additional studies for establishing ideal dose and its efficacy and side effects in children. In pediatric age group, it has limited role and primarily to combination therapy. Isavuconazonium sulfate is a new prodrug of the triazole isavuconazole against Mucorales molds.⁴¹ It is also available in oral or intravenous forms and has good results in adults. Isavuconazonium sulfate can be useful in conjunction with AmB in pediatric patients. Isavuconazole may be a safe and effective antifungal drug for children and adolescents.⁴² In few selected cases, hyperbaric oxygen is also helpful for controlling CAM.26 Combined surgical and medical approach are the mainstay of treatment for CAM.

PROGNOSIS

The overall mortality related to CAM is high, especially in immunocompromised pediatric patient. The mortality is associated with delayed treatment and disseminated infection in age of less one year. 43 High indexes of clinical suspicion, early diagnosis and prompt treatment can improve the survival of the children. The diagnosis is usually delayed in majority cases as clinicians are not much familiar to this disease. The case fatality rate of mucormycosis in worldwide is approximately 46%.⁴⁴ The diagnosis of the CAM in pediatric age is often difficult to diagnose early. However, the early diagnosis and management of the fatal lesion in the pediatric patient is always essential and delay pf even 6 days is associated with doubling of mortality rate from 35 % to 66%. 44 Despite early identification and aggressive treatment, the prognosis for getting recovery from the CAM is poor. In case of high-risk child, the diagnosis of CAM can be suspected if there is associated with unilateral facial swelling, facial pain, orbital swelling and proptosis. The late sign is tissue necrosis which act as a hallmark for mucormycosis, occur due to angioinvasion and vascular thrombosis. 45 Once the diagnosis of CAM is done, prompt surgical debridement is needed followed by antifungal agents. So, early diagnosis and prompt treatment are necessary for improvement of the outcome of the CAM in children.

CONCLUSION

COVID-19 infection is spreading quickly all the continents of the world and affecting all age groups including children. Currently the mucormycosis, a fatal fungal infection is associated with COVID-19 patient. Children with low immunity, diabetes mellitus or taking systemic steroids or under any immunosuppressive medication with COVID-19 are at higher susceptibility for fungal infection. Mucormycosis is a life-threatening fungal disease resulting in vascular invasion by the hyphae leading to thrombosis and necrosis of the host tissue. Although CAM is a fatal, early diagnosis and multidisciplinary approach to the treatment can lead to excellent outcome. In COVID-19 patient, the severity of the mucormycosis is due its rapid progression and angio-Pediatrician invasive nature. or clinician otorhinolaryngologist should act promptly to identify the mucormycosis particularly in immunocompromised children or poorly controlled diabetes mellitus. There should be multidisciplinary approach for this fatal clinical entity such as prompt diagnosis and early treatment with broad spectrum antifungal agents and appropriate surgical debridement plus reversal of the underlying risk factors condition.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

REFERENCES

- 1. Swain SK, Behera IC. Managing pediatric otorhinolaryngology patients in coronavirus disease-19 pandemic—A real challenge to the clinicians. Indian Journal of Child Health. 2020;7(9):357-62.
- Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis. 2012;54(1):23-34.
- 3. Vaezi A, Moazeni M, Rahimi MT, de Hoog S, Badali H. Mucormycosis in Iran: a systematic review. Mycoses. 2016;59(7):402-15.
- Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020;8(5):475-81.
- Swain SK, Jena PP. Clinical implications and future perspective of COVID-19 pandemic-a review. Int J Adv Med. 2021;8(2):334-40.
- 6. Badiee P, Arastefar A, Jafarian H. Comparison of histopathological analysis, culture and polymerase chain reaction assays to detect mucormycosis in biopsy and blood specimens. Iran J Microbiol. 2013;5(4):406-10.
- Bonifaz A, Tirado-Sánchez A, Calderón L, Romero-Cabello R, Kassack J, Ponce RM, et al. Mucormycosis in children: a study of 22 cases in a Mexican hospital. Mycoses. 2014; 57:79-84.
- 8. Kriengkauykiat J, Ito JI, Dadwal SS. Epidemiology and treatment approaches in management of invasive fungal infections. Clin Epidemiol. 2011;3:175-91.
- Kontoyiannis DP, Lionakis MS, Lewis RE, Chamilos G, Healy M, Perego C, et al. Zygomycosis in a tertiary-care cancer center in the era of Aspergillusactive antifungal therapy: a case-control observational study of 27 recent cases. The Journal of infectious diseases. 2005;191(8):1350-60.
- Sharma MC, Gill SS, Kashyap S, Kataria R, Gupta DK, Sahni P, et al. Gastrointestinal mucormycosis-an uncommon isolated mucormycosis. Indian J Gastroenterol. 1998;17:131-3.
- 11. Abedi E, Sismanis A, Choi K, Pastore P. Twenty-Five years experience treating Cerebro-Rhino-Orbital mucormycosis. The Laryngoscope. 1984;94(8):1060-2.
- Swain SK, Acharya S, Sahajan N.
 Otorhinolaryngological manifestations in COVID-19
 infections: An early indicator for isolating the
 positive cases. J Sci Soc. 2020;47(2):63-8.
- 13. Swain SK, Das S, Padhy RN. Performing tracheostomy in intensive care unit-A challenge during COVID-19 pandemic. Siriraj Medical Journal. 2020;72(5):436-42.
- 14. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia. 2020;185:599-606.

- 15. Rodden M, Zaoutis T, Buchanan W, Knudsen TA, Sarkisova TA, Schaufele RL et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis: Off Pub Infect Dis Soc Am. 2005;41(5): 634-53.
- 16. Cornely OA, Alastruey-Izquierdo A, Arnez D. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study group Education and Research Consortium. The Lancet infectious diseases. 2019;19(12):405-21.
- Swain SK, Lenka S, Das SR. Rhino-orbital Mucormycosis-A Dreaded Clinical Entity. Int J Cur Res Rev. 2020;12(24):197-203.
- 18. Kennedy KJ, Daveson K, Slavin MA, Van Hal SJ, Sorrell TC, Lee A, et al. Mucormycosis in Australia: contemporary epidemiology and outcomes. Clinical Microbiology and Infection. 2016;22(9):775-81.
- 19. Skiada A, Pagano LI, Groll A, Zimmerli S, Dupont B, Lagrou K, et al. Zygomycosis in Europe: analysis of 230 cases accrued by the registry of the European Confederation of Medical Mycology (ECMM) Working Group on Zygomycosis between 2005 and 2007. Clinical Microbiology and Infection. 2011;17(12):1859-67.
- 20. Velavan TP, Meyer CG. The COVID-19 epidemic. Tropical medicine & international health. 2020;25(3):278-80.
- 21. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clinical Infectious Diseases. 2012;54(1):23-34.
- 22. Pana ZD, Seidel D, Skiada A, Groll AH, Petrikkos G, Cornely OA, et al. Invasive mucormycosis in children: an epidemiologic study in European and non-European countries based on two registries. BMC infectious diseases. 2016;16(1):1-9.
- Zaoutis TE, Roilides E, Chiou CC, Buchanan WL, Knudsen TA, Sarkisova TA, et al. Zygomycosis in children: a systematic review and analysis of reported cases. The Pediatric infectious disease journal. 2007;26(8):723-7.
- 24. 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: 1123-29.
- 25. Agrawal P, Saikia U, Ramanaathan S, Samujh R. Neonatal small intestinal zygomyocosis misdiagnosed as intussusception in a two-day-old child with a review of the literature. Fetal and pediatric pathology. 2013;32(6):418-21.
- Dave SP, Vivero RJ, Roy S. Facial cutaneous mucormycosis in a full-term infant. Archives of Otolaryngology–Head & Neck Surgery. 2008;134(2):206-9.
- 27. Oh D, Notrica D. Primary cutaneous mucormycosis in infants and neonates: case report and review of the

- literature. Journal of pediatric surgery. 2002;37(11):1607-11.
- 28. Glazer M, Nusair S, Breuer R, Lafair J, Sherman Y, Berkman N. The role of BAL in the diagnosis of pulmonary mucormycosis. Chest. 2000;117(1):279-82.
- 29. Swain SK, Sahu MC, Baisakh MR. Mucormycosis of the Head and Neck. Apollo Medicine. 2018;15(1):6-10.
- 30. Agrawal P, Saikia U, Ramanaathan S, Samujh R. Neonatal small intestinal zygomyocosis misdiagnosed as intussusception in a two-day-old child with a review of the literature. Fetal and pediatric pathology. 2013;32(6):418-21.
- 31. McCarthy MW, Kalasauskas D, Petraitis V, Petraitiene R, Walsh TJ. Fungal infections of the central nervous system in children. Journal of the Pediatric Infectious Diseases Society. 2017;6(3):123-33.
- 32. Swain SK, Sahu MC, Banerjee A. Non-sinonasal isolated facio-orbital mucormycosis—a case report. Journal de mycologie medicale. 2018;28(3):538-41.
- Corzo-León DE, Chora-Hernández LD, Rodríguez-Zulueta AP, Walsh TJ. Diabetes mellitus as the major risk factor for mucormycosis in Mexico: Epidemiology, diagnosis, and outcomes of reported cases. Medical mycology. 2018;56(1):29-43.
- 34. Martinello M, Nelson A, Bignold L, Shaw D. "We are what we eat!" Invasive intestinal mucormycosis: A case report and review of the literature. Medical mycology case reports. 2012;1(1):52-5.
- 35. Lumbang WA, Caufield BA. Vesicular eruption on the arm of an infant. Dermatology online journal. 2010:16(5):13.
- 36. Cornely O, Arikan-Akdagli SE, Dannaoui E, Groll AH, Lagrou K, Chakrabarti A, et al. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013. Clinical Microbiology and Infection. 2014;20:5-26.
- 37. Lelievre L, Garcia-Hermoso D, Abdoul H, Hivelin M, Chouaki T. Posttraumatic mucormycosis: a nationwide study in France and review of the literature. Medicine. 2014;93(24):395-404.

- 38. Shoham S, Magill SS, Merz WG, Gonzalez C, Seibel N, Buchanan WL, et al. Primary treatment of zygomycosis with liposomal amphotericin B: analysis of 28 cases. Medical mycology. 2010;48(3):511-7.
- 39. Mehta AK, Langston AA. Use of posaconazole in the treatment of invasive fungal infections. Expert Rev Hematol. 2009;2:619-30.
- 40. Döring M, Blume O, Haufe S, Hartmann U, Kimmig A, Schwarze CP, et al. Comparison of itraconazole, voriconazole, and posaconazole as oral antifungal prophylaxis in pediatric patients following allogeneic hematopoietic stem cell transplantation. European Journal of Clinical Microbiology & Infectious Diseases. 2014(4):629-38.
- 41. Pettit NN, Carver PL. Isavuconazole: a new option for the management of invasive fungal infections. Ann Pharmacother. 2015;49:825-4.
- 42. Barg AA, Malkiel S, Bartuv M, Greenberg G, Toren A, Keller N. Successful treatment of invasive mucormycosis with isavuconazole in pediatric patients. Pediatric blood & cancer. 2018;65(10):27281.
- 43. Son HJ, Song JS, Choi S, Jung J, Kim MJ, Chong YP, et al. Risk factors for mortality in patients with pulmonary mucormycosis. Mycoses. 2020;63(7):729-36.
- 44. Chamilos G, Lewis RE, Kontoyiannis DP. Delaying amphotericin B-based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis. Clin Infect Dis. 2008;47:503-9.
- 45. Swain SK, Behera IC, Mohanty JN. Mucormycosis in head-and-neck region—Our experiences at a tertiary care teaching hospital of Eastern India. Annals of Indian Academy of Otorhinolaryngology Head and Neck Surgery. 2019;3(2):58-62.

Cite this article as: Swain SK. COVID-19 associated mucormycosis in head and neck region of pediatric patients: a life-threatening disease in current pandemic. Int J Contemp Pediatr 2021;8:1322-7.