

Case Report

COVID-19 associated rhino orbital mucormycosis : Single center experience of 21 cases

De Alwis ASR¹  Weerakkody WPL², Kirihena KDRA³

¹ Senior Registrar in ENT, National Hospital of Sri Lanka

² Registrar in ENT, National Hospital of Sri Lanka


³ Consultant ENT and Head & Neck Surgeon, National Hospital of Sri Lanka

Abstract

Intensifying the burden of the second wave of COVID-19 in Sri Lanka, invasive mucormycosis started emerging in numbers among COVID-19 recovered patients. It was commonly found among immunocompromised patients. Prompt initiation of antifungals and aggressive surgical debridement contributes immensely for the overall prognosis.

Key words - mucormycosis, rhino-orbital, post-COVID , diabetes

Copyright: © 2022 De Alwis ASR et al.

This is an open access article distributed under the [Creative Commons Attribution License \(CC BY 4.0\)](https://creativecommons.org/licenses/by/4.0/) . This license lets others distribute, remix, tweak, and build upon the work, even commercially, as long as they credit the original author for the creation.

Funding: None

Competing interest: None

Correspondence: Dr. ASR De Alwis (2shashini@gmail.com)

Accepted Date: 14th Jan 2022

Published Date: 26th February 2022

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with a range of bacterial and fungal co-infections. A considerable increase in the number of cases of mucormycosis is observed during the second wave of COVID 19 in Sri Lanka leading to high morbidity and mortality. This air bone infection, mainly affecting the upper or lower airways, leads to sinusitis with or without orbital and cerebral involvement or pulmonary infection. Even though cutaneous and cerebral manifestations are less common, dissemination can occur leading to high mortality rates¹.

The fungi order of Mucorales which is angio-invasive includes Mucor, Rhizopus, Rhizomucor, Absidia and Cunninghamella². Even though its prevalence in Sri Lanka is low, we have had 42 recorded cases in 2019, 24 cases in 2020 and 24 recorded cases upto May 2021². Uncontrolled DM, Prior steroids, immunosuppression by the virus have been proposed as causative factors, the exact mechanism yet to be revealed³.

Case Presentations

Socio Demographic data

Twenty-one patients presented to the ENT unit at NHSL with a mean age of 58.3 years with a male preponderance(n=13). Major comorbidities were Diabetes mellitus (100%), chronic kidney disease (55%) while the minority had hypertension, dyslipidemia, post Kidney Transplant, ischemic heart disease and bronchial asthma. All had impaired glucose level on admission. None of them received steroids for their COVID 19 treatment. 53% received two doses of COVID 19 vaccine. Only 9.5% had the vaccine 6 weeks prior to COVID 19 infection.

Clinical manifestations

Majority had orbital symptoms (95%). Almost all had proptosis (95%), 33.3% had complete blindness of an eye on admission while one had bilateral involvement. 57% had headache. Facial pain was found in 24% with paresthesia over the cheek. Only 38% had nasal symptoms such as nasal block, discharge, epistaxis, hyposmia on admission. Two patients had cutaneous manifestations, and one had multiple cranial nerve palsies (CN II-VII). All underwent rigid nasal endoscopic assessment at presentation (Figure 1).

Clinical Manifestations on Admission

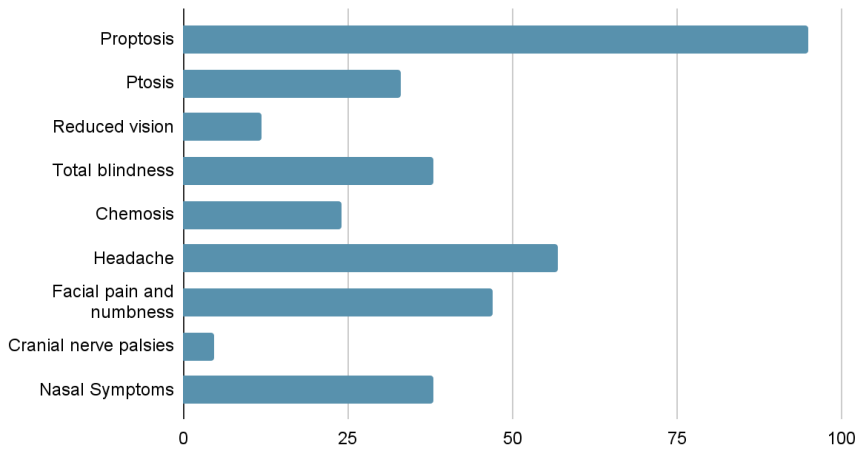


Figure 1 : Clinical Manifestations on Admission

Microbiological Examination

Mycological evaluation of the tissue biopsies from the nasal cavity revealed broad ribbon-like aseptate fungi on KOH wet mount suggestive of Zygomycetes. Culture on Sabouraud dextrose agar showed *Rhizopus* in 19 % but the culture was negative in majority (81 %). Histology with Grocott's fungal staining further confirmed the fungal invasion.

Radiological Assessment

In the Contrast Enhanced CT scan, only 62% had a Lund Mackay grade 2 haziness of the paranasal sinuses of the affected side while the rest had only grade 1 haziness. The commonest sinuses involved are the maxillary, ethmoid and sphenoid. Bilateral involvement is observed in 19% with maxillary sinus being the commonest. Further, the CT scan demonstrated fat stranding in premaxillary, infratemporal and pterygopalatine regions. MRI scans were carried out on all patients to rule out cerebral involvement. 42.8% noted to have orbital cellulitis. Optic neuritis was found in 9.5%. Cerebral involvement was observed in 25%.

Surgical Intervention and findings

All patients underwent extensive surgical debridement with Full house FESS unilaterally in 65% and bilateral in 14 % of patients. Orbital decompression was carried out in 71.42% and optic nerve decompression in Two underwent debridement of the facial muscles due to extensive cutaneous involvement. Intracranial abscess was drained in three patients. Surgical findings include blackish crusting in the nasal cavities, nasal polyposis, purulent discharge from maxillary, ethmoid and sphenoid sinuses, pale necrotic mucosa, erosions of the posterior maxillary wall and nasal septum.

Treatment

Almost all the patients (95%), were started on IV amphotericin B. Switching between conventional amphotericin and liposomal variants was carried out depending on the availability and serum creatinine levels. Even though the majority (61.9%) got commenced on amphotericin within 2-3 days of clinical suspicion, the median lag period is 7.1 days. The serum creatinine was raised in all the subjects from the baseline level and 23.8% developed acute kidney injury. Other side effects observed are thrombocytopenia(10%), myocardial infarction, nausea, vomiting, loss of appetite and general malaise. While 14.2% succumbed to the disease, 42.8% had their treatment completed (Figure 2).

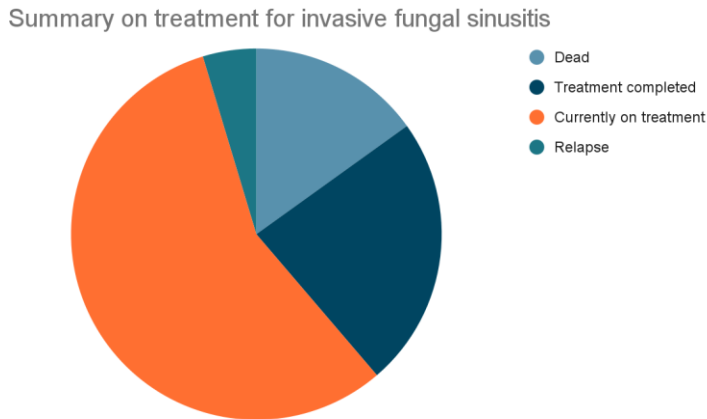


Figure 2 : Summary on treatment for invasive fungal sinusitis

Discussion

Mucormycosis is a rare opportunistic infection which leads to angioinvasion causing necrosis and infarction of the involved tissues. Characteristic blackish crusting denotes its name “Black Fungus”⁴. It can cause a wide spectrum of diseases involving sinuses, nasal cavity, orbit, cerebral tissues, skin, GI tract, lungs or a dissemination.

Lymphopenia caused by COVID-19 infection acts as a risk factor for invasive fungal infection. The Mucorales specific T-cells produce interleukins (IL 4, IL-10, IL-17) and IFN- γ which can damage fungal hyphae. Hence the recovery of lymphocyte count will control the infection⁵. Furthermore, uncontrolled diabetes will lead to worsening host response. None of the patients received prior steroids although it was considered a risk factor.

Majority of the patients presented with orbital symptoms such as eye pain, periorbital swelling, proptosis or loss of vision to an ophthalmologist, or with headache and facial pain and numbness to a neurologist. Keeping a higher level of suspicion and prompt referral for early diagnostic nasal endoscopy is vital.

The imaging findings include a rim like soft tissue thickening or opacification of the sinuses. The fat stranding of the facial, retroantral, infratemporal and orbital tissue is an early sign of extra sinus spread⁶.

38% had only mucosal thickening of grade 1 amidst the RNE findings. This also justifies the early diagnostic endoscopy even though the CT findings are minimal in suspected cases. MRI findings include lack of enhancement with restricted diffusion of the involved tissues⁶.

Angioinvasion of the fungi causes vascular thrombosis leading to pale mucosa with sparse bleeding, cutaneous involvement of the premaxillary tissues, and the necrosis of the underlying bone. Loss of vision is owing to infarction in the central retinal or ophthalmic artery and involvement of the orbital apex.

The intracranial spread occurs through direct extension or via angioinvasion. The pterygopalatine fossa is considered the main foci for the transmission of infection to the cerebrum, orbit and facial tissues⁷. Hence the pterygopalatine fossa clearance was carried out. Those who had cerebral involvement also had orbital involvement. Cutaneous involvement warranted extensive debridement of premaxillary tissues and maxillectomy, with reconstruction later. The intracranial spread is indicated by focal neurological signs⁸. Despite maximum surgical debridement and antifungal therapy 60 % mortality rate was observed in patients with cerebral involvement⁹.

Prompt pharmacological therapy is recommended on suspicion with Amphotericin B. Even though the liposomal formulations of amphotericin B have a favorable side effect profile, the lack of availability led to commencement of conventional preparation. According to Dekkers et.al. there is no difference between the three formulations of the drug apart from its side effect profile. Even Though Posaconazole is recognized as a second line agent with an effect on survival in the refractory cases, the unavailability warrants its use in our patients¹⁰.

Conclusion

Key for successful management of fulminant disease is rapid commencement of multidisciplinary treatments. Treatment at a tertiary care center with the collaboration of otorhinolaryngology, microbiology, ophthalmology, neurosurgery, plastic surgery, endocrine and nutrition units is beneficial. We feel that prompt initiation of medical treatment on suspicion and aggressive surgical debridement contributes immensely for the overall prognosis and propose treating mucormycosis as any other medical emergency.

References

1. Sugar AM. Mucormycosis. Clinical infectious diseases. 1992 Mar 1;14(Supplement_1):S126-9. https://doi.org/10.1093/clinids/14.Supplement_1.S126.PMid:1562684
2. Sri Lanka News: ColomboPage - Original News from Sri Lanka [Internet]. Sri Lanka : 'Black fungus' is not new to Sri Lanka, don't panic - Dr. Primali Jayasekara; [cited 2022 Jan 15]. Available from: http://www.colombopage.com/archive_21A/May24_1621874353CH.php
3. Mitra S, Janweja M, Sengupta A. Post-COVID-19 rhino-orbito-cerebral mucormycosis: a new addition to challenges in pandemic control. European Archives of Oto-Rhino-Laryngology.

2021 Jul 26;1-6.<https://doi.org/10.1007/s00405-021-07010-1>

4. Awal SS, Biswas SS, Awal SK. Rhino-orbital mucormycosis in COVID-19 patients-a new threat?. *Egyptian Journal of Radiology and Nuclear Medicine*. 2021 Dec;52(1):1-6. <https://doi.org/10.1186/s43055-021-00535-9>.PMid:PMC8217789
5. Revannavar SM, Supriya PS, Samaga L, Vineeth VK. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world?. *BMJ Case Reports CP*. 2021 Apr1;14(4):e241663.<https://doi.org/10.1136/bcr-2021-241663>. PMid:33906877
PMid:PMC8088249
6. Jindal G, Sethi A, Bhargarva K, Sethi S, Mittal A, Singh U, Singh S, Shrivastava A. Imaging findings in invasive rhino-orbito-cerebral mucormycosis in post-COVID-19 patients. In *Baylor University Medical Center Proceedings 2021 Sep 17 (pp. 1-3)*. Taylor & Francis. <https://doi.org/10.1080/08998280.2021.1981100>.PMid:34970028 PMid:PMC8682837
7. Sugar AM. Mucormycosis. *Clinical infectious diseases*. 1992 Mar 1;14(Supplement_1):S126-9. https://doi.org/10.1093/clinids/14.Supplement_1.S126.PMid:1562684
8. Pai V, Sansi R, Kharche R, Bandili SC, Pai B. Rhino-orbito-cerebral Mucormycosis: Pictorial Review. *Insights into Imaging*. 2021 Dec;12(1):1-7.<https://doi.org/10.1186/s13244-021-01109-z>. PMid:PMC8587501
9. Palejwala SK, Zangeneh TT, Goldstein SA, Lemole GM. An aggressive multidisciplinary approach reduces mortality in rhinocerebral mucormycosis. *Surgical neurology international*. 2016;7.<https://doi.org/10.4103/2152-7806.182964>.PMid:27280057 PMid:PMC4882964
10. Dekkers BG, Bakker M, van der Elst KC, Sturkenboom MG, Veringa A, Span LF, Alffenaar JW. Therapeutic drug monitoring of posaconazole: an update. *Current fungal infection reports*. 2016 Jun;10(2):51-61.<https://doi.org/10.1007/s12281-016-0255-4>. PMid:27358662
MCid:PMC4896980