



Rhino-Orbito-Cerebral Mucormycosis (ROCM): An Observational Case Report of Covid-19 Positive Patients Admitted in Intensive Care Unit of Community Hospital in South India

Chimezie Finian Nwadinigwe*, Mateus Sakundarno Adi**, Budi Laksono**, Dwi Sutningsih**

*St. Joseph's Hospital Mysore, India

**School of Postgraduate Studies, Diponegoro University Semarang, Indonesia

ABSTRACT

Background: Rhino-orbito-cerebral mucormycosis (ROCM) increasing incidence in the setting of COVID-19 in India and elsewhere has become a matter of immediate concern. In this observational case report we have observed the signs and symptoms of ROCM among coronavirus positive patients with reference to “Mucor code” as reported by Honavar SG 2021, we have reported cases been admitted to ICU for <2weeks in a community hospital in South India.

Method: Patient informed consent was taken, Patient's data (Medical record, medication charts, daily report) were collected using a designed data collection form, observed warning signs and symptoms, and predisposed factors was noted and ROCM is characterized with reference to the “Mucor code”.

Results: Nasal stuffiness, Foul smell and Facial pain and among others were the most coherent warning signs and symptoms observed among the patients in <2weeks of admission in ICU. Other observed predisposing risk factors were regular administration of corticosteroids, antibiotics, Diabetes Mellitus, Hypertension, and Kidney Stone.

Conclusion: All the cases on preliminary examination on the basis of observed warning signs and symptoms were “Possible” ROCM a sub-type of Covid-19 associated mucormycosis (CAM), as this was the first reported case of the hospital. Our study gave basis for further diagnosis and monitoring of Covid-19 positive patient admitted in the intensive care units.

Keywords: Covid-19; mucormycosis; rhino-orbito-cerebral mucormycosis; mucor; fungi infection.

*Corresponding author, finiancn@students.undip.ac.id

Introduction

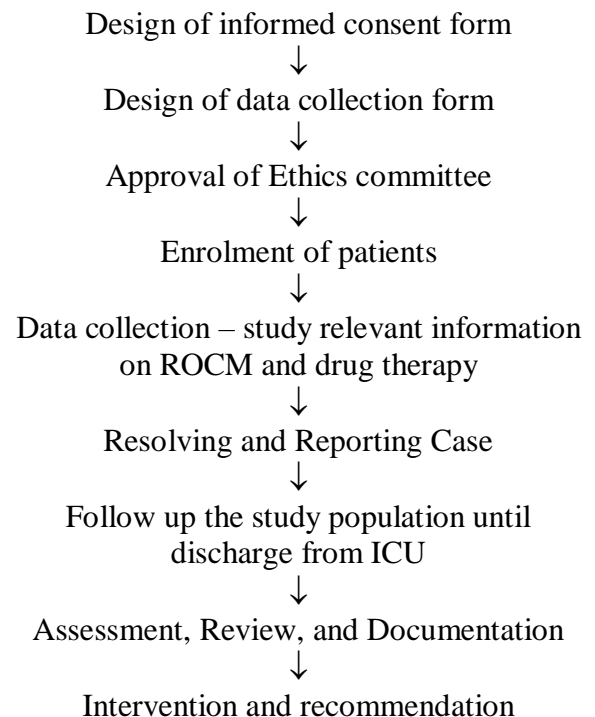
The new coronavirus disease (COVID-19) continues to exhibit uncommon reverberations worldwide along with its atypical symptoms. Recent reports of SARS-CoV-2 infection emphasize the risk of opportunistic fungi infections, including pulmonary aspergillosis and mucormycosis, that manifest with viral symptoms, leading to death by invading multi-organ systems¹. Experience from SARS patients indicated that the incidence of fungal co-infection was 14.8–27%, and it was higher in critically ill SARS patients reaching up to 33%². Furthermore, severe cases of influenza pneumonia resulting in acute respiratory distress syndrome complicated by fungal infection were reported³. 83 (19%) of 432 patients with influenza were found to have experienced invasive pulmonary aspergillosis, and it was higher in immunocompromised patients (32%)⁴.

Invasive fungal infections are mainly thought to be caused due to the weakening of inborn defense mechanisms, such as ciliary clearance, and the insufficient lymphatic immune response against fungal invasion during the pathophysiologic sequence of non-regulated immune mechanisms in coronavirus-related acute respiratory distress syndrome (ARDS)⁵. Indeed, the utilization of corticosteroids, one of the widely used medications against COVID-19 to diminish the risk of mortality, most likely causes critically ill patients in intensive care units (ICU) to be more susceptible to opportunistic infections, which in turn may lead to death. The incidence of fungal involvement is precisely not yet known due to the incapability of common bronchoscopy diagnosis in COVID-19 patients. A growing number of patients with rhino-orbito-cerebral mucormycosis (ROCM) have been reported from India recently in covid-19 settings⁶. Our study aims to report early warning signs and symptoms to serve as a basis for follow-up on patients and to prevent Covid-19 associated mucormycosis (CAM) complications among coronavirus-positive patients admitted to the

Intensive care unit of St. Joseph's Hospital Mysore, India. Experience from SARS patients showed that the incidence of fungal co-infection was 14.8–27%, and it was higher in severely ill SARS patients reaching up to 33%⁷.

Method

A form was designed for the collection of data from patients file and physicians' daily assessment, data to be collected includes, patients' history, biodata, medication history, signs and symptoms, predisposing risk factors etc. the form and the nature of the study was approved by the ethical committee. Information collection was on daily basis and reconciled with the concerned physician inputs. Data collection continues until patients were transferred to ward. Recommendation and suggestions were made.



Results

The result reflects the data collected in <2weeks of coronavirus positive patients admitted in ICU, the description of the data are as follows;

Case 1

Male Covid-19 positive patient from Bidar district, 54yrs has been in admittance for 7days in ICU, on tocilizumab and corticosteroid medication, with history of Diabetes mellitus.

Observable symptoms within this period includes; Nasal stuffiness, Foul smell, Facial pain.

Case 2

Female Covid-19 positive patient from Bidar district, 45yrs has been in admittance for a 5days in ICU, on corticosteroid medication, Mechanical ventilation with history of hypertension stage 1

Observable symptoms within this period includes; interval headaches, Nasal stuffiness, Foul smell, Facial pain.

Case 3

Male Covid-19 positive patient from Bidar district, 50yrs in admittance for 10days in ICU, on tocilizumab and corticosteroid medication and supplemental oxygen administration, with history of Diabetes mellitus and kidney stones.

Observable symptoms within this period includes; Nasal stuffiness, dental pain, nasal discharge, Foul smell, Facial pain.

Table 1. Characteristic of Covid-1 positive patients

Case	District	Sex	Age	Covid-19 Result	Code Mucor (ROCM)	Cortico-steroids	Antibiotics	Diabetes Mellitus (DM)	B.P	Kidney stone
1	Bidar	M	54	Positive	Possible	Yes	Yes	Yes	No	No
2	Bangaluru	F	45	Positive	Possible	Yes	Yes	No	Yes	No
3	Chikbalapur	M	50	Positive	Possible	Yes	Yes	Yes	No	Yes

Table 2. Warning symptoms and signs of Rhino-orbito-cerebral mucormycosis

**Warning symptoms and signs of rhino-orbito-cerebral mucormycosis category 1 “Possible”
Mucor Code (Hanovar SG, 2021)**

- Nasal stuffiness
- Foul smell
- Epistaxis
- Nasal discharge - mucoid, purulent, blood-tinged or black
- Nasal mucosal erythema, inflammation, purple or blue discoloration, white ulcer, ischemia, or eschar
- Eyelid, periocular or facial edema
- Eyelid, periocular, facial discoloration

- Regional pain – orbit, paranasal sinus or dental pain
- Facial pain
- Worsening headache
- Proptosis
- Sudden loss of vision
- Facial paresthesia, anesthesia
- Sudden ptosis
- Ocular motility restriction, diplopia
- Facial palsy
- Fever, altered sensorium, paralysis, focal seizures

According to the “Mucor code” ROCM are categorized as Possible, Probable, and Proven. A patient who has symptoms and signs of ROCM (Table 1) in the clinical setting of concurrent or recently (<6 weeks) treated COVID-19, diabetes mellitus, use of systemic corticosteroids and tocilizumab, mechanical ventilation, or supplemental oxygen is considered at the “Possible” category of ROCM⁶. When the clinical symptoms and signs are supported by diagnostic nasal endoscopy findings, or contrast-enhanced MRI or CT scan, the patient is considered as “Probable” ROCM. Clinico-radiological features, coupled with microbiological confirmation on direct microscopy or culture or histopathology with special stains or molecular diagnostics are essential to categorize a patient as “Proven” ROCM⁶.

According to the "Mucor code" ROCM are categorized as Possible, Probable, and Proven. A patient who has symptoms and signs of ROCM (Table 1) in the clinical setting of concurrent or recently (<6 weeks) treated COVID-19, diabetes mellitus, use of systemic corticosteroids and tocilizumab, mechanical ventilation, or supplemental oxygen is considered at the "Possible" category of ROCM⁶. When the clinical symptoms and signs are supported by diagnostic nasal endoscopy findings, or contrast-enhanced MRI or CT scan, the patient is considered "Probable" ROCM. Clinico-radiological features, coupled with microbiological confirmation on direct microscopy or culture or histopathology with special stains or molecular diagnostics are essential to categorize a patient as "Proven" ROCM⁶.

Discussion

Mucormycosis is associated with the invasion of blood vessels, which results in ischemic necrosis. Mucormycosis has the potential to invade various systems in the body resulting in a myriad of clinical symptoms that progress rapidly. Based on the anatomic site involved, mucormycosis can be classified into

the following forms: rhino-cerebral, pulmonary, gastrointestinal, cutaneous, and disseminated¹

Dilek A et al reported a case of a 54-year-old male, hospitalized due to severe COVID-19 pneumonia. He was given long-term, high doses of systemic steroids. He developed maxillo-fascial mucormycosis and died of sepsis⁷. COVID-19 patients with trauma, diabetes mellitus, GC use, HM, prolonged neutropenia, allo-HSCT, SOT is more likely to develop mucormycosis².

The three cases observed in the study in reference to the mucor code were categorized to be "Possible". ROCM as a rapidly progressive disease requires early diagnosis as any slightest delay in diagnosis or required management can have devastating implications on the patient's survival. However, the outcome can be maximized by early diagnosis prompted by awareness of warning symptoms and signs and a high index of clinical suspicion, confirmation of diagnosis by appropriate modalities, and initiation of aggressive medical and surgical treatment by a multidisciplinary team. Our study findings imply coronavirus patients in critical conditions require close monitoring to be able to detect these warning signs and symptoms early enough to prevent further complications, although there were not enough diagnostic data to confirm our results at the time of making this report. But our findings were successful in providing the basis for it.

Conclusion

The reported three cases included in the observation showed Nasal stuffiness, Foul smell, and Facial pain warning signs and symptoms respectively, others include interval headaches, dental pain, and nasal discharge. Corticosteroids, antibiotics, Diabetes mellitus, hypertension, and kidney stone were predisposing factors. Although more data and clinical analysis are required to confirm the latter. We also recommended proactive screening and monitoring especially for critically ill patients in the ICU which is

essential to mitigate the conditions facilitating the emergence of ROCM and prevent complications and reduce the mortality rate.

Acknowledgement

Thank you to all those who have contributed to this research and to JEKK for allowing the author to share the results of the research conducted by the author.

References

1. Bhatt, K. et al. 2021. 'High mortality co-infections of COVID-19 patients: mucormycosis and other fungal infections.', *Discoveries (Craiova, Romania)*, 9(1), p. e126. Available at: <https://doi.org/10.15190/d.2021.5>.
2. Song, G., Liang, G. and Liu, W. 2020 'Fungal Co-infections Associated with Global COVID-19 Pandemic: A Clinical and Diagnostic Perspective from China.', *Mycopathologia*, 185(4), pp. 599–606. Available at: <https://doi.org/10.1007/s11046-020-00462-9>.
3. Thevissen, K. et al. 2020 'International survey on influenza-associated pulmonary aspergillosis (IAPA) in intensive care units: responses suggest low awareness and potential underdiagnosis outside Europe.', *Critical care (London, England)*, 24(1), p. 84. Available at: <https://doi.org/10.1186/s13054-020-2808-8>.
4. Schauwvlieghe, A.F.A.D. et al. 2018. 'Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study.', *The Lancet. Respiratory medicine*, 6(10), pp. 782–792. Available at: [https://doi.org/10.1016/S2213-2600\(18\)30274-1](https://doi.org/10.1016/S2213-2600(18)30274-1).
5. Mitaka, H. et al. 2021. 'Incidence and mortality of COVID-19-associated pulmonary aspergillosis: A systematic review and meta-analysis', *Mycoses*. John Wiley and Sons Inc, pp. 993–1001. Available at: <https://doi.org/10.1111/myc.13292>.
6. Honavar, S.G. 2021. 'Code Mucor: Guidelines for the Diagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis in the Setting of COVID-19.', *Indian journal of ophthalmology*, 69(6), pp. 1361–1365. Available at: https://doi.org/10.4103/ijo.IJO_1165_21.
7. Dilek, A., Ozaras, R., Ozkaya, S., Sunbul, M., Sen, E. I., & Leblebicioglu, H. 2021. COVID-19-associated mucormycosis: Case report and systematic review. *Travel medicine and infectious disease*, 44, 102148. <https://doi.org/10.1016/j.tmaid.2021.102148>