



Brunei International Medical Journal

OFFICIAL PUBLICATION OF
THE MINISTRY OF HEALTH
AND
UNIVERSITI BRUNEI DARUSSALAM

Volume 17

1 September 2021 (23 Muharram 1443H)

RHINO-ORBITAL MUCORMYCOSIS IN A POST COVID 19-INFECTED PATIENT: A CASE REPORT AND REVIEW OF LITERATURE.

Nurul Anis MOHD FAUZI^{1,2}, CHUA Hui Heng^{2,3}, Zaleha KAMALUDIN^{2,3}, Sakinah MOHAMAD^{1,2}, Baharudin ABDULLAH^{1,2}, Ramiza Ramza RAMLI^{1,2}, Norasnieda MD SHUKRI^{1,2}

¹Department of Otorhinolaryngology-Head & Neck Surgery, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.

²Hospital Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.

³Department of Pathology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.

ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV 2), was first identified in Wuhan, China, in December 2019 and the outbreak which rapidly spread around the world was officially declared a global pandemic by WHO on March 11, 2020. Covid-19 is associated with bacterial and fungal secondary infection or co-infection but has been inadequately investigated or reported thus far. We present a case of rhino-orbital mucormycosis in a 50-year-old man with multiple comorbidities who was recently infected with COVID-19. He presented with a history of blurring of vision and diplopia of the right eye with right-sided nasal blockage and rhinorrhea. He was treated with intravenous (IV) Amphotericin B, IV Caspofungin and oral Itraconazole and underwent multiple operations for fungal deloading. In this case, we want to emphasize that the clinicians should be aware that the patients with COVID-19 infection who have received steroid therapy may have a high risk of contracting a secondary fungal infection.

Keywords: COVID-19, Fungi, Amphotericin B, Mucormycosis, Surgery.

Brunei Int Med J. 2021;17:109-115

Brunei International Medical Journal (BIMJ)

Official Publication of The Ministry of Health and Universiti Brunei Darussalam

EDITORIAL BOARD

Editor-in-Chief	Ketan PANDE
Sub-Editors	Vui Heng CHONG William Chee Fui CHONG
Editorial Board Members	Muhd Syafiq ABDULLAH Alice Moi Ling YONG Ahmad Yazid ABDUL WAHAB Jackson Chee Seng TAN Pemasiri Upali TELISINGHE Pengiran Khairol Asmee PENGIRAN SABTU Dayangku Siti Nur Ashikin PENGIRAN TENGAH

INTERNATIONAL EDITORIAL BOARD MEMBERS

Lawrence HO Khek Yu (Singapore)	Chuen Neng LEE (Singapore)
Wilfred PEH (Singapore)	Emily Felicia Jan Ee SHEN (Singapore)
Surinderpal S BIRRING (United Kingdom)	Leslie GOH (United Kingdom)
John YAP (United Kingdom)	Ian BICKLE (United Kingdom)
Nazar LUQMAN (Australia)	Christopher HAYWARD (Australia)
Jose F LAPENA (Philippines)	

Advisor

Wilfred PEH (Singapore)

Past Editors-in-Chief

Nagamuttu RAVINDRANATHAN
Kenneth Yuh Yen KOK
Chong Vui Heng
William Chong Chee Fui

Proof reader

John WOLSTENHOLME (CfBT Brunei Darussalam)

Aim and Scope of Brunei International Medical Journal

The Brunei International Medical Journal (BIMJ) is a six monthly peer reviewed official publication of the Ministry of Health under the auspices of the Clinical Research Unit, Ministry of Health, Brunei Darussalam.

The BIMJ publishes articles ranging from original research papers, review articles, medical practice papers, special reports, audits, case reports, images of interest, education and technical/innovation papers, editorials, commentaries and letters to the Editor. Topics of interest include all subjects that relate to clinical practice and research in all branches of medicine, basic and clinical including topics related to allied health care fields. The BIMJ welcomes manuscripts from contributors, but usually solicits reviews articles and special reports. Proposals for review papers can be sent to the Managing Editor directly. Please refer to the contact information of the Editorial Office.

Instruction to authors

Manuscript submissions

All manuscripts should be sent to the Managing Editor, BIMJ, Ministry of Health, Brunei Darussalam; e-mail: editor-in-chief@bimjonline.com. Subsequent correspondence between the BIMJ and authors will, as far as possible via should be conducted via email quoting the reference number.

Conditions

Submission of an article for consideration for publication implies the transfer of the copyright from the authors to the BIMJ upon acceptance. The final decision of acceptance rests with the Editor-in-Chief. All accepted papers become the permanent property of the BIMJ and may not be published elsewhere without written permission from the BIMJ.

Ethics

Ethical considerations will be taken into account in the assessment of papers that have experimental investigations of human or animal subjects. Authors should state clearly in the Materials and Methods section of the manuscript that institutional review board has approved the project. Those investigators without such review boards should ensure that the principles outlined in the Declaration of Helsinki have been followed.

Manuscript categories

Original articles

These include controlled trials, interventional studies, studies of screening and diagnostic tests, outcome studies, cost-effectiveness analyses, and large-scale epidemiological studies. Manuscript should include the following; introduction, materials and methods, results and conclusion. The objective should be stated clearly in the introduction. The text should not exceed 2500 words and references not more than 30.

Review articles

These are, in general, invited papers, but unsolicited reviews, if of good quality, may be considered. Reviews are systematic critical assessments of

literature and data sources pertaining to clinical topics, emphasising factors such as cause, diagnosis, prognosis, therapy, or prevention. Reviews should be made relevant to our local setting and preferably supported by local data. The text should not exceed 3000 words and references not more than 40.

Special Reports

This section usually consist of invited reports that have significant impact on healthcare practice and usually cover disease outbreaks, management guidelines or policy statement paper.

Audits

Audits of relevant topics generally follow the same format as original article and the text should not exceed 1,500 words and references not more than 20.

Case reports

Case reports should highlight interesting rare cases or provide good learning points. The text should not exceed 1000 words; the number of tables, figures, or both should not be more than two, and references should not be more than 15.

Education section

This section includes papers (i.e. how to interpret ECG or chest radiography) with particular aim of broadening knowledge or serve as revision materials. Papers will usually be invited but well written paper on relevant topics may be accepted. The text should not exceed 1500 words and should include not more than 15 figures illustration and references should not be more than 15.

Images of interest

These are papers presenting unique clinical encounters that are illustrated by photographs, radiographs, or other figures. Image of interest should include a brief description of the case and discussion with educational aspects. Alternatively, a mini quiz can be presented and answers will be posted in a different section of the publication. A maximum of

three relevant references should be included. Only images of high quality (at least 300dpi) will be acceptable.

Technical innovations

This section include papers looking at novel or new techniques that have been developed or introduced to the local setting. The text should not exceed 1000 words and should include not more than 10 figures illustration and references should not be more than 10.

Letters to the Editor

Letters discussing a recent article published in the BIMJ are welcome and should be sent to the Editorial Office by e-mail. The text should not exceed 250 words; have no more than one figure or table, and five references.

Criteria for manuscripts

Manuscripts submitted to the BIMJ should meet the following criteria: the content is original; the writing is clear; the study methods are appropriate; the data are valid; the conclusions are reasonable and supported by the data; the information is important; and the topic has general medical interest. Manuscripts will be accepted only if both their contents and style meet the standards required by the BIMJ.

Authorship information

Designate one corresponding author and provide a complete address, telephone and fax numbers, and e-mail address. The number of authors of each paper should not be more than twelve; a greater number requires justification. Authors may add a publishable footnote explaining order of authorship.

Group authorship

If authorship is attributed to a group (either solely or in addition to one or more individual authors), all members of the group must meet the full criteria and requirements for authorship described in the following paragraphs. One or more authors may take responsibility 'for' a group, in which case the other group members are not authors, but may be listed in an acknowledgement.

Authorship requirement

When the BIMJ accepts a paper for publication, authors will be asked to sign statements on (1) financial disclosure, (2) conflict of interest and (3) copyright transfer. The correspondence author may sign on behalf of co-authors.

Authorship criteria and responsibility

All authors must meet the following criteria: to have participated sufficiently in the work to take public responsibility for the content; to have made substantial contributions to the conception and de-

sign, and the analysis and interpretation of the data (where applicable); to have made substantial contributions to the writing or revision of the manuscript; and to have reviewed the final version of the submitted manuscript and approved it for publication. Authors will be asked to certify that their contribution represents valid work and that neither the manuscript nor one with substantially similar content under their authorship has been published or is being considered for publication elsewhere, except as described in an attachment. If requested, authors shall provide the data on which the manuscript is based for examination by the editors or their assignees.

Financial disclosure or conflict of interest

Any affiliation with or involvement in any organisation or entity with a direct financial interest in the subject matter or materials discussed in the manuscript should be disclosed in an attachment. Any financial or material support should be identified in the manuscript.

Copyright transfer

In consideration of the action of the BIMJ in reviewing and editing a submission, the author/s will transfer, assign, or otherwise convey all copyright ownership to the Clinical Research Unit, RIPAS Hospital, Ministry of Health in the event that such work is published by the BIMJ.

Acknowledgements

Only persons who have made substantial contributions but who do not fulfill the authorship criteria should be acknowledged.

Accepted manuscripts

Authors will be informed of acceptances and accepted manuscripts will be sent for copyediting. During copyediting, there may be some changes made to accommodate the style of journal format. Attempts will be made to ensure that the overall meaning of the texts are not altered. Authors will be informed by email of the estimated time of publication. Authors may be requested to provide raw data, especially those presented in graph such as bar charts or figures so that presentations can be constructed following the format and style of the journal. Proofs will be sent to authors to check for any mistakes made during copyediting. Authors are usually given 72 hours to return the proof. No response will be taken as no further corrections required. Corrections should be kept to a minimum. Otherwise, it may cause delay in publication.

Offprint

Contributors will not be given any offprint of their published articles. Contributors can obtain an electronic reprint from the journal website.

DISCLAIMER

All articles published, including editorials and letters, represent the opinion of the contributors and do not reflect the official view or policy of the Clinical Research Unit, the Ministry of Health or the institutions with which the contributors are affiliated to unless this is clearly stated. The appearance of advertisement does not necessarily constitute endorsement by the Clinical Research Unit or Ministry of Health, Brunei Darussalam. Furthermore, the publisher cannot accept responsibility for the correctness or accuracy of the advertisers' text and/or claim or any opinion expressed.

RHINO-ORBITAL MUCORMYCOSIS IN A POST COVID 19-INFECTED PATIENT: A CASE REPORT AND REVIEW OF LITERATURE.

Nurul Anis MOHD FAUZI^{1,2}, CHUA Hui Heng^{2,3}, Zaleha KAMALUDIN^{2,3}, Sakinah MOHAM-AD^{1,2}, Baharudin ABDULLAH^{1,2}, Ramiza Ramza RAMLI^{1,2}, Norasnieda MD SHUKRI^{1,2}

¹Department of Otorhinolaryngology-Head & Neck Surgery, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.

²Hospital Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.

³Department of Pathology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.

ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV 2), was first identified in Wuhan, China, in December 2019 and the outbreak which rapidly spread around the world was officially declared a global pandemic by WHO on March 11, 2020. Covid-19 is associated with bacterial and fungal secondary infection or co-infection but has been inadequately investigated or reported thus far. We present a case of rhino-orbital mucormycosis in a 50-year-old man with multiple comorbidities who was recently infected with COVID-19. He presented with a history of blurring of vision and diplopia of the right eye with right-sided nasal blockage and rhinorrhea. He was treated with intravenous (IV) Amphotericin B, IV Caspofungin and oral Itraconazole and underwent multiple operations for fungal deloading. In this case, we want to emphasize that the clinicians should be aware that the patients with COVID-19 infection who have received steroid therapy may have a high risk of contracting a secondary fungal infection.

Keywords: COVID-19, Fungi, Amphotericin B, Mucormycosis, Surgery.

INTRODUCTION

COVID-19 is linked to several disease patterns, from mild to life-threatening pneumonia. Patients under intensive care due to influenza and respiratory viral infections, including COVID pneumonia, are at a higher risk of getting invasive pulmonary fungal infections, possibly because of their low immu-

nological competence.¹ Acute invasive fungal rhinosinusitis (AIFR) is a rare, life-threatening infection that exhibits a high rate of mortality, hence the need for prompt diagnosis and treatment.² It is identified by mycotic infiltration of the mucosa of the nasal cavity and paranasal sinuses. It primarily affects immunocompromised patients, mainly those with hematologic malignancies, especially in patients who have received bone marrow transplantation.

Other immunocompromised patients at risk are those on chronic steroids, poorly

Correspondence: Dr Norasnieda Md Shukri, Department of Otorhinolaryngology-Head & Neck Surgery, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia.
Email address: asnieda@usm.my; Telephone number: +60129002810

controlled diabetics, patients with acquired immunodeficiency syndrome (AIDS), and patients undergoing chemoradiation therapy. Symptoms are generally non-specific, including facial pressure and swelling, nasal congestion, epistaxis, fever, headache, proptosis, paresthesias, ophthalmoplegia, vision changes, seizures, or altered mental status.³ Here, we report a case of a patient with rhino-orbital mucormycosis who was recently infected with COVID-19. He had received steroid therapy as a part of treatment for COVID-19, and we believed that the COVID-19 infection, together with the use of steroids, had predisposed him to secondary fungal infection.

CASE REPORT

A 50-year-old male patient with a past medical history of diabetes mellitus type 2, hypertension, chronic kidney disease, and ischemic heart disease presented to the emergency department with a history of right eye diplopia and blurring of vision for four days, associated with right-sided nasal blockage, rhinorrhea, and right-sided facial pain. It occurred one day following the right upper molar tooth extraction.

He had a history of recent admission for COVID-19 stage 4 and was just discharged from the ward seven days before developing the eye symptoms. At that time, he had a fever with cough and also anosmia. He was hospitalized for 20 days for COVID-19, and there was no history of admission to the intensive care unit. He was given high-dose intravenous (IV) Methylprednisolone during admission for COVID-19. Upon discharge, he had no more fever and cough but anosmia persisted. His exit COVID-19 Antigen Rapid test kit (RTK-Ag) prior to discharge was noted to be negative. As it had been more than 14 days from when he was first tested positive for COVID-19 and he was asymptomatic

at time of discharge, there was no further home quarantine order needed.

Physical examination showed right optic and abducens nerve palsy with right maxillary sinus tenderness. Right nasoendoscopy showed crusting with blackish discoloration of the inferior turbinate, middle turbinate with pus discharge seen at the osteomeatal complex region. Baseline investigations showed a haemoglobin value of 9.3 g/dL, white cell count of $9 \times 10^9/L$, C-reactive protein of 42 mg/L, sodium of 111 mmol/L, urea of 7.3 mmol/L, and creatinine of 272 $\mu\text{mol/L}$.

Computed Tomography (CT) of paranasal sinus initially revealed non-enhancing mucosal thickening, most prominent at the right maxillary sinus and the right ethmoid, right frontal, and bilateral sphenoid sinus (Figure 1). It was associated with obliteration of the right osteomeatal complex, erosion of the right uncinate process and part of the medial wall of the maxillary sinus.

He was diagnosed with Acute Invasive Fungal Rhinosinusitis with Right Orbital Apex Syndrome and underwent multiple surgical debridements. Intraoperatively, there



Figure 1: Non-enhancing mucosal thickening seen most prominently at the right maxillary sinus and also at the right ethmoid and bilateral sphenoid sinus. (Click on image to enlarge.)

were eschars seen over the right ethmoid sinus, right sphenoid sinus, right middle and inferior turbinate (Figure 2). Histopathological examination of sinus tissue revealed inflamed, necrotic tissue with numerous fungal bodies, highlighted with fungal stains, Periodic Acid-Schiff (PAS), and Grocott Gomori Methenamine-silver (GMS). The fungus are large, non-septate hyphae with 90 degree of angle branching (Figure 3). *Pseudomonas aeruginosa* was found on tissue culture. The tissue for fungal culture was negative. He was given intravenous (IV) Tazocin for two weeks, IV liposomal Amphotericin B and IV Caspofungin for six weeks for possible Mucormycosis. Post-surgical debridement, his right vision remained poor despite improved diplopia. His repeated CT scan three weeks after initiation of treatment revealed erosion of the lateral wall and body of the right sphenoid with enhancing soft tissue density lesion extending into the right orbital apex. There was also poor demarcation between the soft tissues with the intracanalicular segment of the right optic nerve (Figure 4). Following the CT scan, he was then subjected to another surgical debridement three more times.

After he completed IV Amphotericin B and IV Caspofungin for six weeks, he was

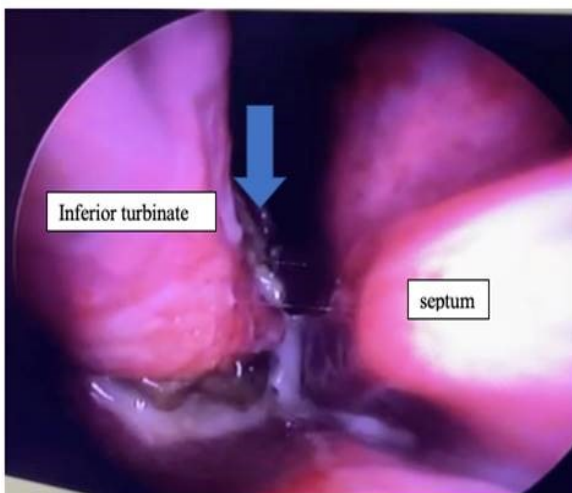


Figure 2: Eschar of the right inferior turbinate (blue arrow) with mucopus discharge in the right nasal cavity seen intraoperatively. (Click on image to enlarge.)

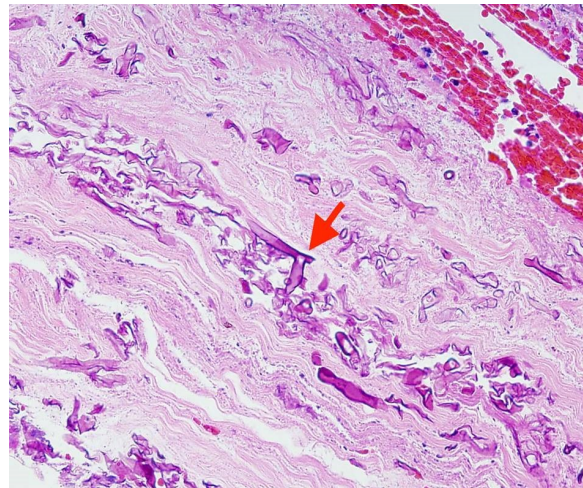


Figure 3: Image shows the tissue is infiltrated by aseptate fungal exhibit broader hyphae with irregular branching. Some of the branches exhibit a 90-degree angle (red arrow). (H&E 400X). (Click on image to enlarge.)

finally discharged home after remaining afebrile with improved right eye vision and diplopia, and his sense of smell began to return. He was discharged with oral Itraconazole for three months. On follow up, the patient was well with his right eye vision almost completely returned to normal with no diplopia.

DISCUSSION

Rhino-orbital mucormycosis is a rare, acute invasive fungal infection which is uncommon in pre-COVID-19 era. Unusually, a significant

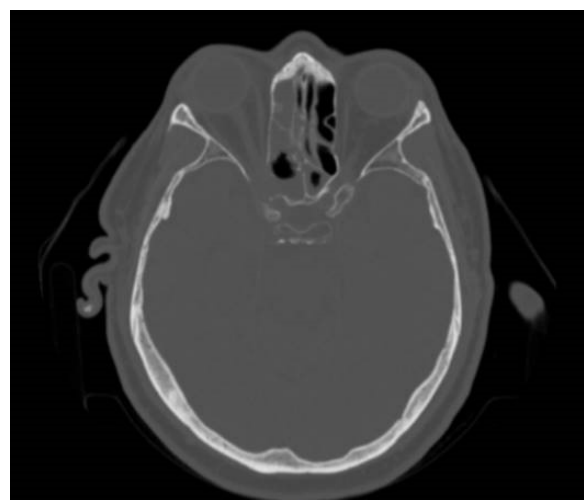


Figure 4: Erosion of the lateral wall and body of the right sphenoid seen with enhancing soft tissue density lesion extending into right orbital apex. (Click on image to enlarge.)

increasing number of this infection has been documented recently in COVID-19 patients.⁴ As many as 44.4% of post-COVID-19 patients with acute invasive fungal rhinosinusitis (AIFR) were diabetics, compared to 28.9% in AIFR patients with non-COVID-19.⁵ COVID-19 positivity and concurrent corticosteroid administration further decreased the immunity in 61.2% of patients.⁶ Corticosteroid-induced diabetes may manifest in otherwise healthy persons who are receiving long-term steroid therapy, hence increasing the risk of mucormycosis.⁷ The associated COVID-19 infection itself may be a predisposing factor in the development of mucormycosis, as some patients with COVID-19 developed new onset diabetes mellitus without receiving steroids. This emphasizes the diabetogenic role of the Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).⁸ Apart from that, the immune dysregulation associated with COVID-19, with a decreased amount of T lymphocytes, CD4+T, and CD8+T cells, may affect innate immunity.⁹

The clinical symptoms of AIFR in non-COVID-19 patients are not specific, and they include fever, nasal blockage, headache, and purulent rhinorrhea with nasal crusting.³ Orbital involvement may show clinical signs, including periorbital swelling, ophthalmoplegia, loss of vision, proptosis and impaired intraocular movements.³ These signs and symptoms are more or less the same seen in AIFR patients with COVID-19. A study done by El-Kholy *et al* showed that the most common presenting symptoms of AIFR in COVID-19 patients were headache and facial pain (75%), facial numbness (66.7%), and ophthalmoplegia and visual loss (63.9%).⁴ The COVID-19 care teams must be aware of these warning symptoms and signs of AIFR. If a patient who is receiving treatments for COVID-19 or on follow-up post COVID-19 infection shows any of the mentioned symptoms or signs, there must be a high index of suspicion for AIFR, and an immediate otorhinolaryngol-

ogy and ophthalmology consultation is warranted.

CT scan is the imaging modality of choice for the detection of bony erosion. Its characteristics include unilateral opacification of multiple sinuses, usually with focal bony erosion, soft tissue thickening, subtle infiltration of premaxillary fat, sinus and lateral nasal wall oedema, and orbital invasion.³ Whereas MRI better depicts vascular occlusion with infarct and cerebritis, leptomeningeal involvement, intracranial granulomas and pseudoaneurysms.¹⁰

Histopathological examination (HPE), direct microscopy and culture from clinical specimens are the primary diagnostic investigations for mucormycosis.¹¹ HPE shows fungi invading nasal tissue and hyphae formation within the nasal mucosa, blood vessels, or bones near the paranasal sinus. AIFR most commonly begins as mucosal inflammation around the middle turbinate. The most commonly identified pathogens are *Aspergillus* and fungi of the order *Mucorales* (*Zygomycetes*).¹⁰ Zygomycetes class are primarily found in diabetic patients, whereas *Aspergillus* is the most identified species in patients with neutropenia.¹⁰

Treatment requires multiple approaches including antifungal therapy, surgical debridement and reversal of immunosuppression.² Combining surgical debridement of necrotic tissue and antifungal treatment using liposomal Amphotericin B or combination therapy with Amphotericin B and Posaconazole or Caspofungin has been proven to prolong survival.² This was seen in our patient who had a great outcome from a combination of surgical debridement, IV Amphotericin B, IV Caspofungin and oral Itraconazole. Aggressive debridement of affected tissues is essential to prevent the spread of necrosis and decrease the fungal load. The prognosis for patients with invasive fungal rhinosinusitis

is poor. Mortality is seen in around 10% to 40% of patients and is mainly associated with the absence of host immune reconstitution and the extent of the disease.¹¹ HbA1c \geq 8 mmol/mol and cerebral involvement were linked with high death rate.⁵ In addition, cases of mucormycosis that received steroid therapy as part of COVID-19 treatment are shown to be linked with poorer outcomes.⁷ It is noted that out of seven patients infected with COVID-19, only one patient had survived (14.3%) ([Table I](#)). Table I also summarized the clinical characteristics, relevant investigations, treatment details and outcomes of cases of COVID-19 with AIFR found in literature up-to-date. However, in another study done by El-Kholy *et al*, the survival rate of AIFR patients associated with COVID-19 infection was 63.89%, which was higher than in non-COVID AIFR cases as reviewed by Turner *et al*, which was 49.7%.⁴ This could be due to early diagnosis during observation in the follow-up period post COVID-19 recovery, aggressive surgical debridement, and immediate use of antifungal treatments.

CONCLUSION

COVID-19 is strongly linked to secondary infections, including fungal likely due to immune dysregulation from the infection. Therefore, it should be of note as an emerging new risk factor for AIFR. Furthermore, the widespread use of steroids as part of treatment for COVID-19 may exacerbate the fungal disease. Early detection and diagnosis and prompt treatment for secondary fungal infection in patients with COVID-19, are of utmost importance to reduce morbidity and mortality.

CONFLICT OF INTEREST

No conflict of interest has been disclosed by the authors.

FUNDING STATEMENT

This case report did not receive any special funding.



TABLE I: Reported cases of COVID-19 with acute invasive fungal rhinosinusitis.

Author/Year	Age (Years) Sex	Comorbidity	Clinical presentation	Fungal C&S	Diagnosis	Treatment	Outcome
Mekonnen ZK et al, 2021 ²	60 Male	Diabetes mellitus Asthma, Hypertension, Hyperlipidemia	Dyspnea and hypoxia - treated as COVID-19 Pneumonia and intubated, the following day noted prominence of the right eye	Rhizopus species	Acute Invasive Rhinoorbital Mucormycosis	IV Liposomal Amphotericin B, then changed to Posaconazole (due to acute kidney injury), IV Vancomycin IV Cefepime, IV Dexamethasone	Expired
Mehta S et al, 2020 ⁹	60 Male	Diabetes mellitus	Severe shortness of breath Pyrexia Tachypnea Generalized malaise 10 days later, patient had bilateral lid edema with right eye proptosis	Mucormycosis	Rhinoorbital Mucormycosis	IV Imipenem Oral Oseltamivir IV Methylprednisolone IV Dexamethasone IV Amphotericin B IV Meropenem IV Vancomycin	Expired
Waizel-Haiat S et al, 2021 ¹²	24 Female	Obesity	Shortness of breath Pain in the left midface region Progressive left lid swelling Maxillary hypoesthesia	Lichteimia (Absidia)	Rhinoorbital Mucormycosis	IV Imipenem IV Linezolid IV Amphotericin B	Expired
Sebastian SK et al, 2021 ¹³ Case 1	59 Male	Ischemic heart disease Diabetes mellitus	Nasal blockage Facial and periorbital swelling Blackening of middle turbinate with thick dirty nasal discharge	Aspergillus fumigatus and Rhizopus	COVID-19 associated Invasive Fungal Sinusitis	IV Liposomal Amphotericin B then Voriconazole	Expired
Sebastian SK et al, 2021 ¹³ Case 2	60 Male	Diabetes mellitus Chronic kidney disease	Under ICU care for COVID-19; Developed right eye pain Periorbital swelling Restricted eye movement Diminution of vision	Zygomycosis	COVID-19 associated Invasive Fungal Sinusitis	IV Liposomal Amphotericin B	Expired
Sebastian SK et al, 2021 ¹³ Case 3	64 Male	Diabetes mellitus Peptic Ulcer	Treated as COVID-19 Pneumonia with ARDS; Developed proptosis of right eye with periorbital bluish discoloration on ninth day of admission	Not done	COVID-19 associated Invasive Fungal Sinusitis	Antifungal could not be started as patient developed massive peptic ulcer bleed and expired	Expired
Alekseyev K et al, 2021 ¹⁴	41 Male	Diabetes mellitus Type 1	Loss of taste and cough Deep aching pain in the nose radiating to the throat - pain exacerbated with eating	Mucormycosis	Rhinocerebral Mucormycosis	IV Cefepime IV Abelcet and surgical debridement	Survived

REFERENCES

- 1: Song G, Liang G, Liu W. [Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China.](#) *Mycopathologia.* 2020;31:1-8. [Accessed on 2021 August 29].
 - 2: Mekonnen ZK, Ashraf DC, Jankowski T, Grob SR, Vagefi MR, Kersten RC, Simko JP, Winn BJ. [Acute invasive rhino-orbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome.](#) *Ophthalmic Plastic and Reconstructive Surgery.* 2021;37(2):e40. [Accessed on 2021 August 29].
 - 3: Dwyhalo KM, Donald C, Mendez A, Hoxworth J. [Managing acute invasive fungal sinusitis.](#) *Journal of the American Academy of PAs.* 2016;29(1):48-53.
 - 4: El-Kholy NA, Abd El-Fattah AM, Khafagy YW. [Invasive fungal sinusitis in post COVID-19 patients: a new clinical entity.](#) *Laryngoscope.* 2021 May 19;10.1002/lary.29632. doi: 10.1002/lary.29632. [Accessed on 2021 August 29].
 - 5: Ismaiel WF, Abdelazim MH, Eldsoky I, Ibrahim AA, Alsobky ME, Zafan E, Hasan A. [The impact of COVID-19 outbreak on the incidence of acute invasive fungal rhinosinusitis.](#) *American journal of otolaryngology.* 2021;42(6):103080. [Accessed on 2021 August 29].
 - 6: Ravani SA, Agrawal GA, Leuva PA, Modi PH, Amin KD. [Rise of the phoenix: Mucormycosis in COVID-19 times.](#) *Indian journal of ophthalmology.* 2021;69(6):1563-8. [Accessed on 2021 August 29].
 - 7: Pakdel F, Ahmadikia K, Salehi M, Tabari A, Jafari R, Mehrparvar G, Rezaie Y, Rajaeih S, Alijani N, Barac A, Abdollahi A. [Mucormycosis in patients with COVID-19: A cross-sectional descriptive multicentre study from Iran.](#) *Mycoses.* 2021 Jun 7;10.1111/myc.13334. doi: 10.1111/myc.13334. [Accessed on 2021 August 29].
 - 8: Nair AG, Adulkar NG, D'Cunha L, Rao PR, Bradoo RA, Bapaye MM, Kothari A, Dave TV, Shinde CA. [Rhino-orbital mucormycosis following COVID-19 in previously non-diabetic, immunocompetent patients.](#) *Orbit.* 2021;1-6. [Accessed on 2021 August 29].
 - 9: Mehta S, Pandey A. [Rhino-orbital mucormycosis associated with COVID-19.](#) *Cureus.* 2020;12(9):e10726. [Accessed on 2021 August 29].
 - 10: Mossa-Basha M, Ilica AT, Maluf F, Karakoç Ö, İzbudak İ, Aygün N. [The many faces of fungal disease of the paranasal sinuses: CT and MRI findings.](#) *Diagnostic and Interventional Radiology.* 2013;19(3):195-200. [Accessed on 2021 August 29].
 - 11: Thompson III GR, Patterson TF. [Fungal disease of the nose and paranasal sinuses.](#) *Journal of allergy and clinical immunology.* 2012;129(2):321-6. [Accessed on 2021 August 29].
 - 12: Waizel-Haiat S, Guerrero-Paz JA, Sanchez-Hurtado L, Calleja-Alarcon S, Romero-Gutierrez L. [A case of fatal rhino-orbital mucormycosis associated with new onset diabetic ketoacidosis and COVID-19.](#) *Cureus.* 2021;13(2):e13163. [Accessed on 2021 August 29].
 - 13: Sebastian SK, Kumar VB, Gupta M, Sharma Y. [Covid Associated Invasive Fungal Sinusitis.](#) *Indian Journal of Otolaryngology and Head & Neck Surgery.* 2021:1-4. [Accessed on 2021 August 29].
 - 14: Alekseyev K, Didenko L, Chaudhry B. [Rhino-cerebral mucormycosis and COVID-19 pneumonia.](#) *Journal of Medical Cases.* 2021;12(3):85-89. [Accessed on 2021 August 29].
-