ISSN 1949-8470 (online)

World Journal of *Radiology*

World J Radiol 2023 July 28; 15(7): 216-240

Published by Baishideng Publishing Group Inc

World Journal of Radiology

Contents

Monthly Volume 15 Number 7 July 28, 2023

MINIREVIEWS

ORIGINAL ARTICLE

Basic Study

CASE REPORT

World Journal of Radiology

Monthly Volume 15 Number 7 July 28, 2023

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Radiology*, Kıvanç Kamburoğlu, DDS, MSc, PhD, Professor, Department of Dentomaxillofacial Radiology, Ankara University, Ankara 06500, Turkey. dtkivo@yahoo.com

AIMS AND SCOPE

The primary aim of *World Journal of Radiology* (*WJR*, *World J Radiol*) is to provide scholars and readers from various fields of radiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJR mainly publishes articles reporting research results and findings obtained in the field of radiology and covering a wide range of topics including state of the art information on cardiopulmonary imaging, gastrointestinal imaging, genitourinary imaging, musculoskeletal imaging, neuroradiology/head and neck imaging, nuclear medicine and molecular imaging, pediatric imaging, vascular and interventional radiology, and women's imaging.

INDEXING/ABSTRACTING

The *WJR* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJR* as 2.5; IF without journal self cites: 2.3; 5-year IF: 2.5; Journal Citation Indicator: 0.54.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Si Zhao*; **Production Department Director:** *Xu Guo*; **Editorial Office Director:** *Jia-Ping Yan*.

NAME OF JOURNAL
World Journal of Radiology

ISSN
ISSN 1949-8470 (online)

LAUNCH DATE
January 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Thomas J Vogl

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1949-8470/editorialboard.htm

PUBLICATION DATE
July 28, 2023

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Radiology

Submit a Manuscript: https://www.f6publishing.com

World J Radiol 2023 July 28; 15(7): 234-240

DOI: 10.4329/wjr.v15.i7.234

ISSN 1949-8470 (online)

CASE REPORT

Invasive rhinocerebral mucormycosis: Imaging the temporal evolution of disease in post COVID-19 case with diabetes: A case report

Ramakrishna Narra, Shravya Rayapati

Specialty type: Radiology, nuclear medicine and medical imaging

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Jain M, India; Yu YB, China

Received: April 3, 2023
Peer-review started: April 3, 2023
First decision: May 19, 2023
Revised: June 2, 2023
Accepted: June 26, 2023
Article in press: June 26, 2023
Published online: July 28, 2023

Ramakrishna Narra, Shravya Rayapati, Department of Radiodiagnosis, Katuri Medical College, Guntur, Andhra Pradesh 522018, India

Corresponding author: Ramakrishna Narra, DNB, MD, MNAMS, Academic Editor, Professor, Department of Radiodiagnosis, Katuri Medical College, Flat No. 30, 1/2 Chandramoulinagar, Guntur, Andhra Pradesh 522018, India. narra.ramki29@gmail.com

Abstract

BACKGROUND

Rhinocerebral mucormycosis (RCM) is a rare, fatal, invasive fungal infection infecting mainly patients with immunocompromised conditions, such as diabetes mellitus, hematologic malignancies, and organ transplantations. Coronavirus disease 2019 (COVID-19) disease in these patients further weakens the immune system due to several factors, including hypoxia, corticosteroid usage (further increasing hyperglycemic status), mechanical ventilation, increased serum ferritin levels, endothelitis due to free radicals, and glucose receptor protein upregulation. Timely diagnosis, judicious treatment decisions, and diabetes control with proper treatment guidelines in patients with coexisting COVID-19 disease can reduce complication rates and improve survival.

CASE SUMMARY

A 75-year-old male patient with diabetes and hypertension diagnosed with COVID-19 presented to the emergency department. Laboratory examinations revealed elevated blood glucose levels, as well as ketone bodies in the urine. He was treated with oxygen and steroids, as well as insulin to correct blood glucose levels. He complained of a headache 10 d later, and imaging demonstrated mucosal thickening in bilateral sphenoidal, ethmoidal, and maxillary sinuses with hyperdense foci in the right maxillary sinus but without central nervous system involvement. Surgical debridement was performed, and a histopathological study revealed fungi hyphae. Systemic antifungals (amphotericin b and posaconazole) were administered. Subsequently, on 15th day he developed right lower limb weakness and left lateral rectus palsy. There was slow but steady progress, and he was discharged. However, he presented to emergency department 1mo later with altered sensorium and poor control of diabetes resulted in an intracranial spread of mucormycosis, which ultimately led to the patient's poor prognosis and slow recovery.

CONCLUSION
Prompt early diagnosis, judicious treatment decisions, and diabetes control with proper treatment guidelines are necessary in patients with COVID-19 associated invasive RCM to reduce complication rates and improve patient survival.

Key Words: Rhinocerebral mucormycosis; COVID-19 disease; Corticosteroids; Diabetes mellitus; Diabetic ketoacidosis; Case report

Core Tip: Coronavirus disease 2019 associated invasive rhinocerebral mucormycosis is potentially life threatening in patients with uncontrolled diabetes mellitus and diabetic ketoacidosis. Early diagnosis and imaging the disease progression with proper treatment guidelines are essential for reducing the morbidity and mortality in these patients.

Citation: Narra R, Rayapati S. Invasive rhinocerebral mucormycosis: Imaging the temporal evolution of disease in post COVID-19 case with diabetes: A case report. *World J Radiol* 2023; 15(7): 234-240
URL: https://www.wjgnet.com/1949-8470/full/v15/i7/234.htm
DOI: https://dx.doi.org/10.4329/wjr.v15.i7.234

INTRODUCTION

Mucormycosis is a rare opportunistic and potentially lethal infection caused by members of the family mucoraceae, order mucorales, and class zygomycetes[1]. It is caused by fungi, which may be found in decaying food, soil, or other organic matter, such as animal excreta.

Rhinocerebral mucormycosis (RCM) is the most common type, accounting for 30%-50% of cases. Its extension to the orbit and brain is usual, making it a potentially life-threatening disease. Immunocompromised patients are especially susceptible, and timely diagnosis and judicious intervention are of utmost importance for the successful management and prevention of intracranial extension. Patients with coronavirus disease 2019 (COVID-19) with uncontrolled diabetes and diabetic ketoacidosis on corticosteroid treatment are potentially susceptible to invasive RCM and need aggressive treatment to prevent further morbidity and mortality. Other reported immunocompromised conditions include blood dyscrasias, malnutrition, neutropenia, iron overload, organ transplantation, and immunosuppressive therapy[2]. Microscopic demonstration of fungal hyphae-mucormycosis with high blood glucose levels and serum ferritin and ketone levels should alert the clinician for appropriate care and aggressive treatment[3].

CASE PRESENTATION

Chief complaints

A 75-year-old male patient diagnosed with positive reverse transcription polymerase chain reaction for COVID-19 infection was admitted to the emergency department.

History of present illness

A 75-year-old male patient diagnosed with positive reverse transcription polymerase chain reaction for COVID-19 infection was admitted to the emergency department with fever, sore throat and generalized weakness for 3 d.

On 10th day he complained of frontal headache. On 15th day he complained of persistent frontal headache and left orbital pain, and a dragging sensation in the right foot. After 1 mo he progressed into altered sensorium and seizures and was admitted to emergency department.

History of past illness

He is known diabetic and hypertensive for 10 years.

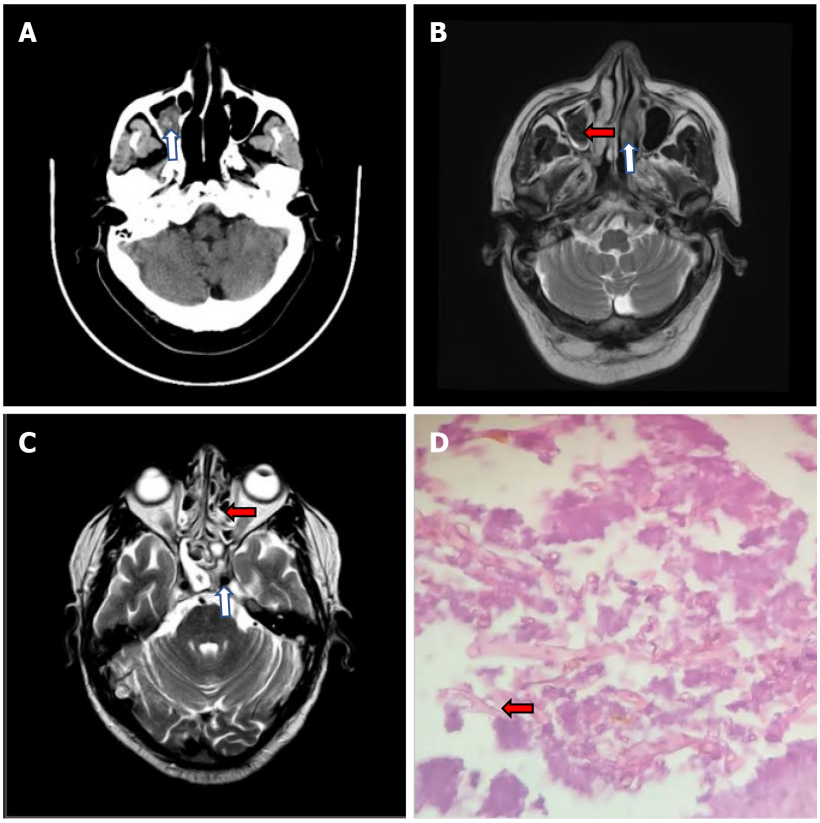
Personal and family history

No significant personal and family history.

Physical examination

On examination at admission temperature was 102.5 ^{0}F, pulse rate: 124/min, blood pressure (BP): 150/100 mmHg.

On 10th day temperature was 101.5 ^{0}F, pulse rate: 88/min, BP: 150/90 mmHg. On 15th day temperature was 99 ^{0}F, pulse rate: 108/min, BP: 130/90 mmHg, neurological examination revealed reduced power in the right lower limb (2/5) and



DOI: 10.4329/wjr.v15.i7.234 **Copyright** ©The Author(s) 2023.

Figure 1 Images of patient with post COVID-19 mucormycosis. A: Axial computed tomography image of brain, 10 d post admission demonstrating hyperdensity in right maxillary sinus (white arrow); B: Axial T2 weighted (T2W) and magnetic resonance imaging (MRI) image of brain demonstrating mucosal thickening with hypointensity within right maxillary sinus (red arrow) and hypointense left inferior turbinate (white arrow); C: Axial T2W and MRI image of brain demonstrating bilateral sphenoid and ethmoidal sinusitis (red arrow) with normal flow void within left internal carotid artery (white arrow); D: Histopathology slide demonstrating broad, aseptate ,branched hyphae of mucormycosis (red arrow).

left lateral rectus palsy. On 30th day temperature was 102 ^{0}F, pulse rate: 115/min, BP: 160/100 mmHg, glasgow coma scale was poor (8/15).

Laboratory examinations

On admission: Elevated C-reactive protein (188 mg/dL), serum ferritin (513 ng/mL), blood glucose (400 mg/dL), and glycosylated hemoglobin (16%) levels and the presence of ketone bodies (+++) in the urine. Other parameters were within the normal limits: Hemoglobin of 11 gm%; red blood cells of 5.2 × 10^{6}/μL; total leukocyte count of 9000/cumm; differential leukocyte count, including neutrophils of 75%, lymphocytes of 22%, eosinophils of 02%, and macrophages of 01%; platelets of 2.4 Lakhs/cumm; serum potassium of 3.8 mmol/L; serum sodium of 138 mmol/L; blood urea of 12 mg/dL; and serum creatinine of 0.8 mg/dL.

On 10th day C-reactive protein (106 mg/dL), serum ferritin (498 ng/mL), blood glucose (260 mg/dL), and the presence of ketone bodies (+) in the urine.

On 15th day C-reactive protein (108 mg/dL), serum ferritin (450 ng/mL), blood glucose (250 mg/dL), and the presence of ketone bodies (+) in the urine.

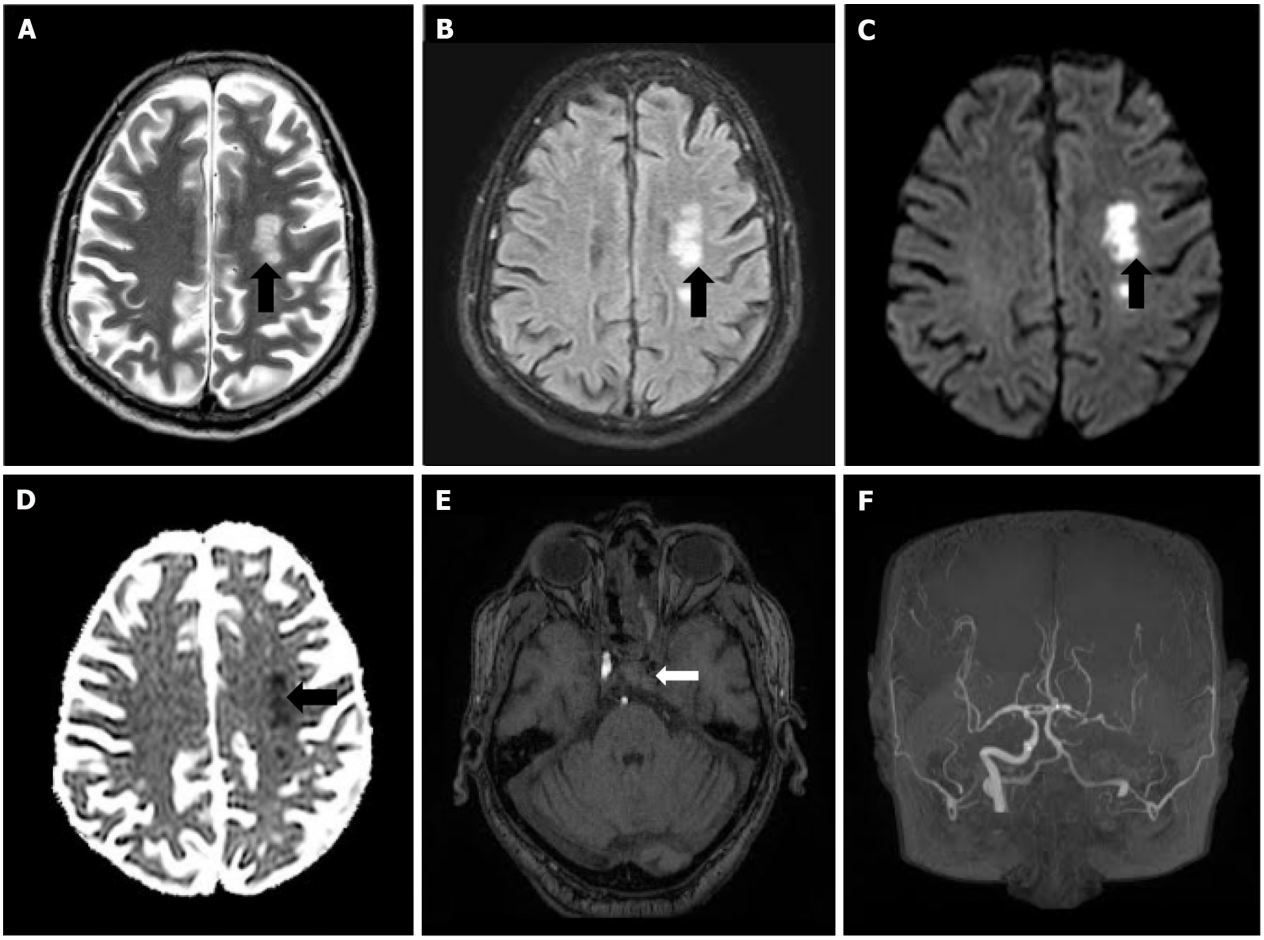
After 1 mo C-reactive protein (198 mg/dL), serum ferritin (415 ng/mL), blood glucose (450 mg/dL), and the presence of ketone bodies (+++) in the urine.

Rest of the routine laboratory investigations were within normal limits.

Imaging examinations

On 10th day post admission computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated mucosal thickening in the bilateral ethmoidal, sphenoidal and maxillary sinuses with hyperdensity (CT) and hypointensity (MRI) in the right maxillary sinus suggestive of fungal sinusitis (Figure 1A-C). The patient underwent functional endoscopic sinus surgery under general anesthesia, and a biopsy was performed for histopathological examination which revealed fungus of mucorales species (Figure 1D).

On 15th day post admission MRI scan of the brain, paranasal sinuses and the orbits with IV contrast was advised which demonstrated acute infarcts in the watershed territories of left anterior cerebral artery, middle cerebral artery and posterior cerebral arteries (Figure 2A-D) with filling defects in the left cavernous sinus suggestive of cavernous sinus thrombosis. In addition magnetic resonance angiogram demonstrated complete occlusion of left internal carotid artery (ICA) (Figure 2E and F).



DOI: 10.4329/wjr.v15.i7.234 **Copyright** ©The Author(s) 2023.

Figure 2 Images of patient with post COVID-19 mucormycosis. A and B: Axial T2-weighted and axial fluid attenuated inversion recovery images of brain 15 d post admission demonstrating acute infarcts (black arrows); C and D: In left centrum semiovale with diffusion restriction on diffusion-weighted imaging and reversal on apparent diffusion coefficient represented by black arrows; E and F: Magnetic resonance angiography (MRA) images of Brain demonstrating loss of flow signal is noted in left internal carotid artery (white arrow) on source images and absent left internal carotid artery on maximum intensity projection MRA.

After 1 mo MRI of brain with IV contrast demonstrated an hyperintense lesion on T2 Weighted and fluid attenuated inversion recovery sequence with surrounding edema and peripheral rim enhancement of approximately 21 mm × 12 mm in the right basi-frontal lobe with restriction on diffusion weighted imaging and reduced apparent diffusion coefficient suggestive of fungal abscess (Figure 3). CT and MRI of brain demonstrated destruction of cribriform plate, clivus, sphenoid sinus and magnetic resonance spectroscopy demonstrated elevated lactate peak within the lesion (Figure 4).

FINAL DIAGNOSIS

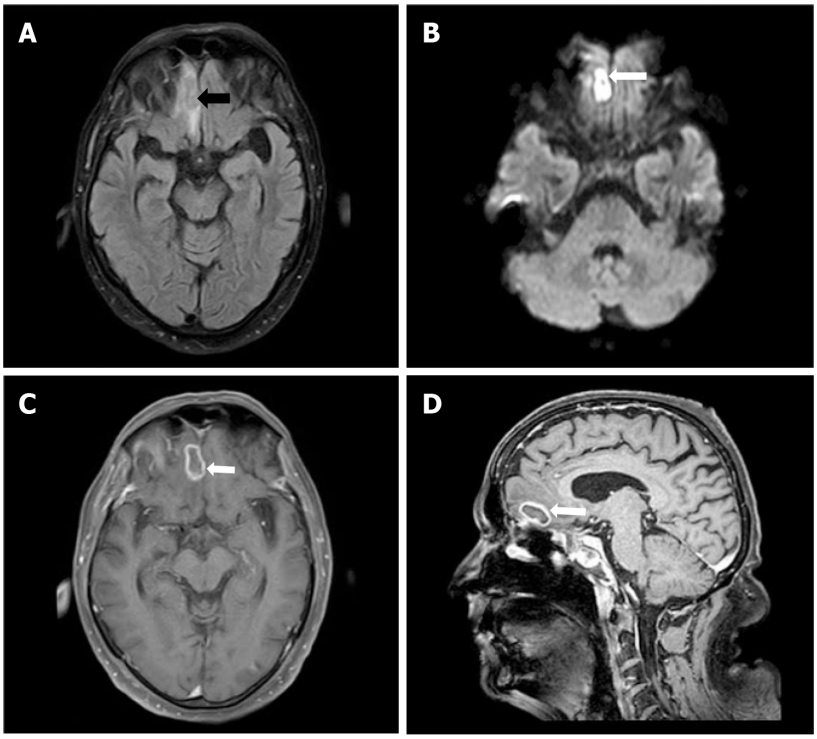
Post COVID-19 associated invasive RCM.

TREATMENT

On admission: Patient was given mechanical ventilation and oxygen support, anti-pyretics, azithromycin, remedesivir (200 mg loading dose) followed by 100 mg daily for 5 d, and intravenous dexamethasone 10 mg intravenous for 10 d. The patient was administered insulin 0.1 U/kg as an intravenous bolus dose followed by infusion of 0.1 U/kg/h for a targeted glucose level of 200 mg/dL.

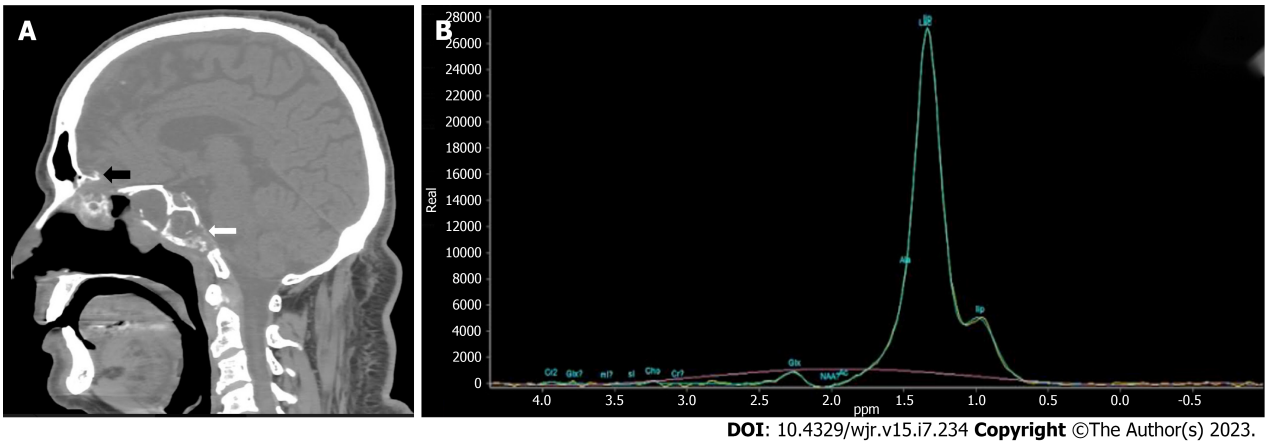
On 10th day: The patient was advised and started with amphotericin b injection at 3 mg/kg/day for 14 d and oral posaconazole at 300 mg twice daily for 6 wk. The renal profile was checked every 3 d for nephrotoxicity from amphotericin b. Poor patient tolerance was noted and steroids discontinued.

On 15th day: The patient was administered aspirin 150 mg, clopitab 75 mg, and atorvastatin 40 mg. After stabilization and rehabilitation patient was counselled for diabetes control and discharged. He was maintained on human mixtard insulin thrice daily.



DOI: 10.4329/wjr.v15.i7.234 **Copyright** ©The Author(s) 2023.

Figure 3 Images of patient with post COVID-19 mucormycosis. A and B: Magnetic resonance imaging of brain after one month demonstrating isointense area with surrounding edema (black arrow) on axial fluid attenuated inversion recovery with restriction on diffusion-weighted imaging (white arrow); C and D: Post-contrast axial and sagittal T1 weighted images demonstrating rim enhancement of the lesion-s/ofungal abscess (white arrow).



DOI: 10.4329/wjr.v15.i7.234 **Copyright** ©The Author(s) 2023.

Figure 4 Images of patient with post COVID-19 mucormycosis. A: Computerized tomography of brain after one month mid sagittal reformatted section in bone window demonstrating destruction of cribriform plate (black arrow), sphenoid sinus and clivus (white arrow); B: Magnetic resonance spectroscopy with a voxel placed in right frontal lobe fungal abscess demonstrating lactate peak at 1.33 ppm.

After 1mo: The patient was treated with antiepileptics, and insulin and anti-fungal treatment was continued with supportive treatment.

OUTCOME AND FOLLOW-UP

After stabilization there was very slow recovery of the patient with residual neurological deficits and increased morbidity.

DISCUSSION

RCM is a rare invasive infection caused by fungi of the class phycomycetes commonly involving the nasal and sinus mucosae of immunocompromised patients and spreads rapidly to the orbit and brain. Diabetes mellitus (especially with ketoacidosis) and hematologic malignancies with neutropenia are the principal predisposing factors. High blood glucose levels and ketoacidosis in diabetes enhance fungal growth. The altered number or function of neutrophils increases the risk of infection because they are responsible for defense against fungi[3]. COVID-19 disease in these patients further weakens the immune system due to several factors, including hypoxia, corticosteroid usage (further increasing hyperglycemic status), mechanical ventilation, increased serum ferritin levels, endothelitis due to free radicals, and glucose receptor protein upregulation, increased iron reduces the function of gamma interferon which prevents phagocytic function on fungus[4]. Other identified risk factors are steroid therapy, organ transplantation, chemotherapy, and chronic kidney disease[5-7]. Extensive angioinvasion is considered the main cause of vascular thrombosis and tissue necrosis. Vascular involvement is a more common cause of increased morbidity and mortality, resulting in ICA thrombosis causing brain ischemic infarcts and infiltrating the cavernous sinus and orbital apex, causing facial cellulitis and vision loss. Histopathological examination of the thrombus demonstrated the fungus in some cases of ICA thrombosis following thrombectomy[8]. Mucormycosis may spread intracranially from the paranasal sinuses along the cribriform plate into the anterior cranial fossa, leading to a cerebral abscess.

Brain and paranasal sinus MRI provides a better evaluation of intracranial and soft tissue involvement, skull base invasion, perineural spread, and vascular obstruction. MRI contrast study demonstrates orbital soft tissue invasion, skull base infiltration, perineural spread, intracranial complications, and vascular obstruction, involving the ICA[9,10].

At present, antifungal therapy and aggressive surgical debridement are used in active mucormycosis treatment. The overall mortality of patients with mucormycosis remains high and approaches 40% in patients with diabetes with invasive mucormycosis despite antifungal therapy and surgical debridement. Prophylactic treatment with antiplatelet drugs, including aspirin, clopitab, and statins, should also be initiated in aggressive cases where complications, such as ICA occlusion, thrombosis, and angioinvasion may develop.

Our case report explains the disease progression from infection initially involving the paranasal sinuses to subsequent brain involvement. Mucosal thickening of the bilateral sphenoidal, ethmoidal, and maxillary sinuses was initially noted on imaging in the present report, with no central nervous system involvement with a normal ICA and without any bony involvement. However, ICA thrombosis causing ischemic infarcts was noted on subsequent imaging, probably due to poor patient compliance to antifungal drugs causing increased fungal growth. The patient was stabilized and treated with aspirin 150 mg, clopitab 75 mg, and atorvastatin 40 mg and rehabilitation. However, the patient was readmitted to the hospital with seizures and altered consciousness after a few days, and subsequent imaging revealed the spread of infection through the destruction of the cribriform plate and clivus to the brain causing a cerebral abscess. This was due to poor diabetes control and diabetic ketoacidosis after patient discharge, which caused the intracranial spread of the disease.

CONCLUSION

Invasive RCM is a rare but fatal fungal infection that primarily affects immunocompromised patients. Early diagnosis and prompt management with aggressive surgical intervention and antifungal therapy are crucial for improving patient outcomes. This case report highlights the importance of close monitoring and imaging in patients with post-COVID-19 treated with oxygen therapy and corticosteroids, as well as diabetes, and ensuring optimal glycemic control to prevent rapid disease progression and intracranial spread. Regular monitoring of serum ferritin levels, lymphocyte count and further strengthening the immune system with regular follow-up imaging is essential to monitor disease progression and identify potential complications.

ACKNOWLEDGEMENTS

Dr Rama Krishna Gorantla for his expert advice and guidance.

FOOTNOTES

Author contributions: Narra R reviewed the manuscript and designed the study; Rayapati S prepared the manuscript, and collected materials for the study.

Informed consent statement: Informed written consent was obtained from the patient and his relatives for the publication of this report and any accompanying images.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016) and the manuscript was prepared and revised according to the CARE Checklist (2016).

Country/Territory of origin: Mayotte

ORCID number: Ramakrishna Narra 0000-0002-1850-6136.

S-Editor: Qu XL
L-Editor: A
P-Editor: Zhao S

REFERENCES

1 **Kim JG**, Park HJ, Park JH, Baek J, Kim HJ, Cha IH, Nam W. Importance of immediate surgical intervention and antifungal treatment for rhinocerebral mucormycosis: a case report. *J Korean Assoc Oral Maxillofac Surg* 2013; **39**: 246-250 [PMID: 24471053 DOI: 10.5125/jkaoms.2013.39.5.246]
2 **Mallis A**, Mastronikolis SN, Naxakis SS, Papadas AT. Rhinocerebral mucormycosis: an update. *Eur Rev Med Pharmacol Sci* 2010; **14**: 987-992 [PMID: 21284348]
3 **Dilek A**, Ozaras R, Ozkaya S, Sunbul M, Sen EI, Leblebicioglu H. COVID-19-associated mucormycosis: Case report and systematic review. *Travel Med Infect Dis* 2021; **44**: 102148 [PMID: 34454090 DOI: 10.1016/j.tmaid.2021.102148]
4 **Aggarwal SK**, Kaur U, Talda D, Pandey A, Jaiswal S, Kanakan A, Singh A, Chakrabarti SS. Case Report: Rhino-orbital Mucormycosis Related to COVID-19: A Case Series Exploring Risk Factors. *Am J Trop Med Hyg* 2021; **106**: 566-570 [PMID: 34902834 DOI: 10.4269/ajtmh.21-0777]
5 **Spellberg B**, Edwards J Jr, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clin Microbiol Rev* 2005; **18**: 556-569 [PMID: 16020690 DOI: 10.1128/CMR.18.3.556-569.2005]
6 **Bhansali A**, Bhadada S, Sharma A, Suresh V, Gupta A, Singh P, Chakarbarti A, Dash RJ. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. *Postgrad Med J* 2004; **80**: 670-674 [PMID: 15537854 DOI: 10.1136/pgmj.2003.016030]
7 **Onyango JF**, Kayima JK, Owen WO. Rhinocerebral mucormycosis: case report. *East Afr Med J* 2002; **79**: 390-393 [PMID: 12638836 DOI: 10.4314/eamj.v79i7.8845]
8 **Kashyap S**, Bernstein J, Ghanchi H, Bowen I, Cortez V. Diagnosis of Rhinocerebral Mucormycosis by Treatment of Cavernous Right Internal Carotid Artery Occlusion With Mechanical Thrombectomy: Special Case Presentation and Literature Review. *Front Neurol* 2019; **10**: 264 [PMID: 30972005 DOI: 10.3389/fneur.2019.00264]
9 **McDevitt GR Jr**, Brantley MJ, Cawthon MA. Rhinocerebral mucormycosis: a case report with magnetic resonance imaging findings. *Clin Imaging* 1989; **13**: 317-320 [PMID: 2598114 DOI: 10.1016/0899-7071(89)90065-x]
10 **Parsi K**, Itgampalli RK, Vittal R, Kumar A. Perineural spread of rhino-orbitocerebral mucormycosis caused by Apophysomyces elegans. *Ann Indian Acad Neurol* 2013; **16**: 414-417 [PMID: 24101833 DOI: 10.4103/0972-2327.116921]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com