Indian Journal of Pharmacy Practice., 2024; 17(1):78-82.
https://www.ijopp.org

Case Report

Cerebral Mucormycosis: Navigating Fungal Intrusion, Immune Challenges and Vascular Consequences: A Multifaceted Case Report

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ABSTRACT

A 63-years-old male patient with a medical history of Hypothyroidism and T2DM, who had been irregularly adhering to his medication regimen, was admitted to a nearby hospital. He presented with complaints of altered sensorium and weakness on the left side of his body over the past three days and was subsequently diagnosed with a cerebrovascular accident, commonly known as a stroke. Notably, his recent medical records indicated a total loss of vision and double vision. This prior episode had been attributed to invasive Fungal Sinusitis, for which he had received treatment with Inj. Liposomal Amphotericin B. Upon physical examination, the patient was found to be drowsy and unresponsive. Laboratory investigations revealed abnormalities in WBC, Leucocyte levels, Neutrophil and Lymphocyte counts, as well as random blood glucose levels. Imaging studies confirmed the diagnosis of a CVA. In response to his condition, the patient underwent a comprehensive treatment regimen, which included the administration of Glucocorticoids, lipid-lowering medications, antibiotics, oral hypoglycaemic agents, and vitamin supplements. Following the course of treatment, the patient's condition stabilized, and he was eventually discharged from the hospital. During his discharge, he received thorough counselling regarding the importance of adhering to his medication regimen. This case emphasizes the difficulties in treating cerebral mucormycosis in a patient with a history of chronic alcoholism, smoking, Type 2 Diabetes Mellitus, and hypothyroidism. Promptly recognizing and treating Cerebral mucormycosis, while also addressing underlying health condition like CVA, UTI, electrolyte imbalance and Drug induced Hyperthyroidism are crucial for improving patient outcomes.

Keywords: Fungal sinusitis, Liposomal Amphotericin-B, Cerebralmucormycosis, Cerebrovascular Accident, Adverse Drug Reaction, Hyponatremia, Hypocalcaemia, Hypokalaemia.

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Received: 13-09-2023;
Revised: 05-10-2023;
Accepted: 23-10-2023.

INTRODUCTION

Fungal sinusitis is an uncommon but serious condition which characterized by the invasion of fungal pathogens into the sinus cavities, leading to inflammation and tissue damage. The pathophysiology of fungal sinusitis involves a complex interplay between the host immune response, underlying risk factors, and fungal virulence factors. In immunocompromised individuals, such as those with chronic alcoholism and diabetes mellitus, the immune system's ability to defend against fungal pathogens is compromised.[1] This impaired immune response allows opportunistic fungi to colonize and invade the sinus tissues more easily. Additionally, chronic alcoholism and diabetes mellitus can alter the local microenvironment in the sinuses, creating favourable conditions for fungal growth and survival. Diabetes mellitus, especially uncontrolled or poorly managed, can lead to immunological dysfunction and impaired neutrophil function.[2] Neutrophils play a crucial role in the defence against fungal infections. Their impaired function compromises the ability to eliminate fungal pathogens, allowing them to proliferate in the sinus cavities.[3] This also cause vascular complications such as invasion of the blood vessels, thrombosis formation, vasculitis.

Invasion of the blood vessels

The invasive fungal infection can infiltrate and invade the walls of the blood vessels in the sinus and adjacent regions, leading to vascular damage.

Thrombosis formation

Fungal invasion and inflammation can trigger the formation of blood clots within the affected blood vessels. These blood clots

DOI: 10.5530/ijopp.17.1.12

can occlude the vessel, leading to reduced blood flow or complete blockage, resulting in ischemia and stroke.

Vasculitis

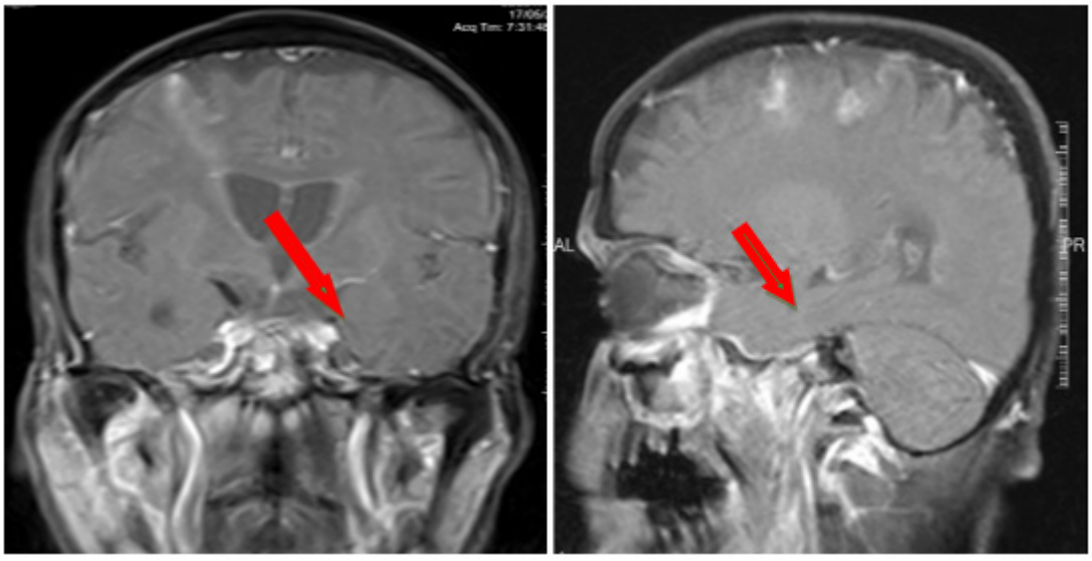
The inflammatory response elicited by the fungal infection can cause vasculitis, which is the inflammation of blood vessels. Inflammation can weaken the vessel walls, leading to vessel wall damage, narrowing, or rupture, which can ultimately result in stroke.[4]

This context delves into the situation of an immunocompromised individual who initially experienced fungal sinusitis. Unfortunately, the condition escalated to a challenging state referred to as cerebral mucormycosis, accompanied by infarction.

CASE DESCRIPTION

A 63-years-old male patient came to the hospital with complaints of altered sensorium. The patient was drowsy and not arousable to pain due to Neuroglycopenia. His past medical history showed that he recently went to another hospital with a history of vision loss and double vision over the right eye for more than one week. He underwent FESS and Sinus debridement and was diagnosed with Invasive fungal sinusitis. Currently, he is still undergoing treatment with Inj. Liposomal Amphotericin-B. The patient had a chronic history of alcoholism and smoking for the past 20 years, along with Type 2 Diabetes mellitus and hypothyroidism for the past 13 years. During the past medication history interview, he mentioned being on irregular treatment with Tab. Sitagliptin+Metformin 50/500 mg BD, Cap. Multivitamin-BD, Tab. Thyroxine 12.5 mcg-OD. Laboratory investigations, including Complete blood count, Blood glucose level, and Thyroid Function Test, showed increased Total WBC, neutrophils, lymphocytes, ESR, and random blood glucose levels. His TSH level was decreased, indicating Hyperthyroidism (Table 1). MRI-Brain plain showed Fungal invasion of the brain and right orbit, and MRI-Brain contrast angiogram and venogram revealed focal narrowing in the cavernous segment of the right internal carotid artery, indicating Cerebro vascular accident. Mucosal thickening in the bilateral maxillary, bilateral ethmoid,spenoid and frontal with hyperdense content within the sinus-residual pan sinusitis and right orbital cellulitis as represented in Figures 1, 2 and 3

The treatment goals for this patient are to minimize fungal infection and vascular recanalization, treat underlying conditions-Diabetes Mellitus and hyperthyroidism, prevent secondary infection, minimize disability, improve QoL, and minimize the incidence of drug-related problems due to polypharmacy, ADR, and drug interactions. After the administration of 25% Dextrose, the patient regained consciousness, orientation, and the ability to move his upper and lower limbs. Thyroxine 12.5 mcg-OD was stopped to reverse hyperthyroidism caused due to thyroid medication. Then the patient was advised with Inj. Liposomal Amphotericin-B 50 mg-OD, Inj. Cefoperazone+Sulbactam 1.5 mg-BD, Inj. Pantoprazole 40 mg-OD, Inj. Ondansetron 4 mg-BD, Inj. Methylcobalamin 100 mcg-OD, Inj. Thiamine 200 mg OD, Tab. Metformin 500 mg-OD, Tab. Levetiracetam 500 mg-BD, Tab. Aspirin 150 mg-OD, Tab. Atorvastatin 40 mg-OD. During the treatment, the patient was diagnosed with a urinary tract infection due to the febrile condition and abnormal urine analysis. Inj. Piperacillin+Tazobactam 4.5 mg TDS, were added to the treatment chart. The patient also had abnormal electrolyte imbalance, and Tab. Tolvaptan 15mg-BD, Inj. Calcium gluconate 10 mL l-OD, Syp. KCL 10 mL I-BD was included in the treatment to treat hyponatremia, hypocalcaemia, hypokalaemia. Gradually, the patient's condition improved and stabilized, and then he got discharged.



Figures 1 and 2: Mucosal thickening in the bilateral maxillary, bilateral ethmoid,spenoid and frontal with hyperdense content within the sinus-residual pan sinusitis and right orbital cellulitis.

Table 1: Laboratory Investigation of the patient during the days of admission.

Laboratory investigation	Parameters	Normal value	On the day of admission	On the day of discharge
Complete Blood Count	Total wbc	4,000 - 11000 million/mL	15,2000 million/mL	8500 million/mL
	Neutrophils	40-80 %	85 %	61 %
	Lymphocytes	20-40 %	12 %	25 %
	Platelet	1.40-4.50 Lakhs/cmm	3.36 Lakhs/cmm	2.55 Lakhs/cmm
	ESR	0-20 mm/hr	70 mm/hr	30 mm/hr
Blood Glucose Level	Random blood sugar	70-170 mg/dL	306 mg/dL	168 mg/dL
Urine Analysis	Sodium	135-145 mg/dL	143 mg/dL	137 mg/dL
	Potassium	3.5-4.5 mg/dL	3.7 mg/dL	3.9 mg/dL
	Sugar	Negative	Positive	Negative
	PUS	0-5/hpf	3-5/hpf	0-5/hpf
	Epithelial	<10 /hpf	8-10 /hpf	<10 /hpf
	Blood	Negative	Negative	Negative
Biochemistry	Serum calcium	8.5-10.5 mg/dL	9 mg/dL	8.9.mg/dL
	Serum phosphorus	2.5-4.5 mg/dL	2.2 mg/dL	2.7 mg/dL
TFT	TSH	0.35-5.5 ulu/ML	0.0493 ulu/ML	Drug induced Hyperthyroidism Drug withdrawn

Table 2: Adverse Drug Reaction Probability Scale (Naranjo) in Drug Induced Hyperthyroidism.

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
	Total Score: 5 (Probable)			

CASE DISCUSSION

Firstly, the primary focus was to treat Neuroglycopenia caused by hypoglycaemia, the primary approach is to raise the blood glucose levels to a safe range. Neuroglycopenia occurs when the brain is deprived of its primary fuel source, glucose, which is necessary for normal brain function. When blood glucose levels drop too low, the brain's cells do not receive sufficient energy, leading to neurological symptoms such as confusion, drowsiness, altered mental status, and, in severe cases, seizures and loss of consciousness.[5] Further treatment was done for vascular recanalization to prevent further complications.[1] The patient continued to receive Inj. Liposomal Amphotericin-B, targeting the fungal pathogen. Additionally, Inj. Cefoperazone with Sulbactam

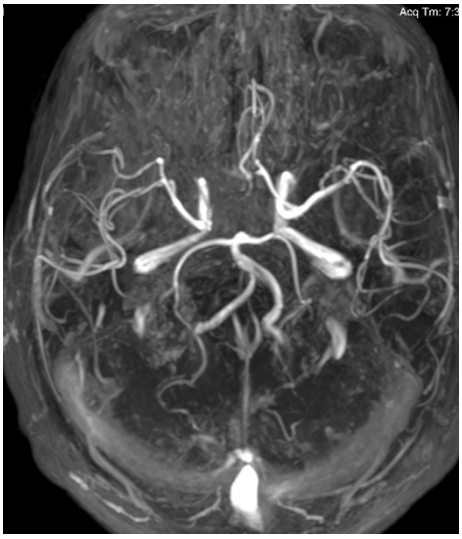


Figure 3: Focal narrowing in cavernous segment of right internal carotid artery.

was administered to address bacterial superinfection, which can commonly occur in cerebral mucormycosis.[2] Supportive care including Inj. Pantoprazole, Inj. Ondansetron was provided to manage associated symptoms. The patient's treatment also addressed the underlying conditions, including Type 2 Diabetes Mellitus, hypothyroidism. On the day of admission, the patient presented with a complaint of "Drug-induced Hyperthyroidism". This particular adverse drug reaction falls into the Type A category, resulting from an amplification of a drug's typical pharmacological effects when administered at the standard therapeutic dosage. A Naranjo causality assessment was conducted and determined that the likelihood of this reaction being caused by the drug was PROBABLE (Table 2). Consequently, the treatment with Tab. Thyroxine 12.5 mcg-OD was discontinued.[6]

Tab. Metformin, a commonly prescribed medication for diabetes management, was continued. Tab. Levetiracetam was included to manage seizures, which can occur in the context of cerebral involvement in fungal sinusitis.[2] Additionally, Tab. Aspirin, Tab. Atorvastatin were prescribed to manage Cerebro vascular accident. In order to treat the diagnosed urinary tract infection, Inj. Piperacillin + Tazobactam were added to the treatment regimen.[1] The patient also presented with electrolyte imbalances, which were managed through medications such as Tab. Tolvaptan, Inj. Calcium gluconate, and Syp. KCL. These interventions aimed to restore electrolyte balance and prevent complications associated with abnormal electrolyte levels. The gradual improvement and stabilization of the patient's condition allowed for discharge from the hospital. It is important to note that the management of Cerebral mucormycosis requires a multidisciplinary approach, involving otolaryngologists, neurologist, neurosurgeon, infectious disease specialists, and other healthcare professionals. The collaboration and expertise of these specialists are crucial in addressing the complex challenges posed by cerebral mucormycosis in immunocompromised patients with multiple comorbidities.

CONCLUSION

Mucormycosis is a serious and fast-progressing fungal infection caused by fungi in the Mucorales order. It predominantly affects individuals with poorly managed diabetes and those with weakened immune systems. This case emphasizes the difficulties in treating cerebral mucormycosis in a patient with a history of chronic alcoholism, smoking, Type 2 Diabetes Mellitus, and hypothyroidism. Promptly recognizing and treating Cerebral mucormycosis, while also addressing underlying health condition like CVA, UTI, electrolyte imbalance and Drug induced Hyperthyroidism are crucial for improving patient outcomes. A comprehensive approach involving anti-fungal treatment, surgery, management of underlying conditions, and supportive care is essential to reduce infection, prevent complications, and enhance the patient's overall well-being.

ACKNOWLEDGEMENT

First and foremost, we would like to express our thanks to the Almighty for providing us the strength and guidance. We are very grateful to acknowledge our Principal Dr. G. Murugananthan, M. Pharm., Ph.D., and Dr. P. Sharmila Nirojini, Head, Dept of pharmacy practice of Swamy Vivekananda College of Pharmacy for their valuable guidance and suggestions for this Case study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

T2DM: Type 2 Diabetes Mellitus; **CVAL:** Cerebrovascular; **FESS:** Functional Endoscopic Sinus Surgery; **WBC:** White Blood Cell count; **Tab.:** Tablet; **OD:** Once Daily; **BD:** Twice Daily; **TDS:** Three times daily; **Cap:** Capsule; **Inj.:** Injection; **Syp:** Syrup; **KCL:** Potassium Chloride; **ESR:** Erythrocyte Sedimentation Rate; **TFT:** Thyroid Function Test; **TSH:** Thyroid Stimulating Hormone; **million/mL:** Million per millilitre; **Lakhs/cmm:** Lakhs per cubic millimetre; **mm/hr:** Millimetres per hour; **hpf:** High-power field; **ulu/ML:** Micro-international units per millilitre; **%:** Percentage; **QoL:** Quality of Life; **ADR:** Adverse Drug Reaction; **UTI:** Urinary Tract Infection.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This case was reported during the study which was approved by Institutional Ethics Committee. The study was carried out after taking permission from the Institutional Ethics Committee of Vivekanandha Medical Care Hospital (Ref.: SVCP/IEC/OCT/2023/35). The consent was taken from the patient to participate in the study.

SUMMARY

A 63-years-old male with hypothyroidism and type 2 diabetes, who wasn't consistent with his medications, was hospitalized due to altered mental state and left-sided weakness. He was diagnosed with a stroke and had previously experienced vision issues from fungal sinusitis treated with Inj. Liposomal Amphotericin B. The patient had abnormal blood counts and glucose levels. Treatment involved glucocorticoids, lipid-lowering drugs, antibiotics, oral hypoglycemic agents, and vitamins. His condition improved, and he was discharged with medication adherence counseling. This case underscores the challenges of treating cerebral mucormycosis in a patient with a history of alcoholism, smoking, diabetes, and hypothyroidism. Prompt recognition and treatment of cerebral mucormycosis, along with addressing other health issues like stroke and infections, are crucial for better outcomes.

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Cite this article: Vangiliappan K, Raju N, Rajan RJ, Kartik NS. Cerebral Mucormycosis: Navigating Fungal Intrusion, Immune Challenges and Vascular Consequences: A Multifaceted Case Report. Indian J Pharmacy Practice. 2024;17(1):78-82.