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Case of Rhino-orbital-cerebral mucormycosis post COVID-19 infection

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ABSTRACT

Mucormycosis used to be a rare fungal infection that could affect the craniofacial area among other regions in the body. However, after COVID19 era it became more common especially in older individuals with systemic co morbidities like diabetes. Rhino-orbital-cerebral mucormycosis is a severe and a serious complication of COVID-19 infection that has a high morbidity and mortality rate despite proper medical and surgical management. Here we report a case of Rhino-orbital-cerebral mucormycosis post covid infection in a 66-year-old female patient who presented with a fungating eye lesion.

Keywords: Mucormycosis, Rhino-orbital-cerebral mucormycosis, COVID-19

1. INTRODUCTION

With the current SARS-Cov-2 pandemic the world facing, there has been a rise in COVID-19 associated Mucormycosis cases and other fungal superinfections especially among patients with medical comorbidities. Risk factors predisposing patients to Rhino-orbital-cerebral mucormycosis ROCM include, but are not limited to uncontrolled diabetes, neutropenia, organ transplant, cancer, corticosteroids and immunosuppressive therapy. Diabetes mellitus type II is associated with two-fold increase in mortality and severity of COVID-19 comparing to non-diabetic patients (Werthman-Ehrenreich, 2021; Saldanha et al., 2023).

Clinical signs and symptoms in ROCM patients include facial pain, paresthesia, swelling of malar area, dental pain, nasal discharge, periorbital swelling and headache. When ROCM is suspected, an urgent intervention is warranted due to the progressive and destructive nature of the infection. The mortality rate of Rhino-orbital-cerebral mucormycosis (ROCM) reaches up to 50% even with treatment (Werthman-Ehrenreich, 2021).

Randomized clinical trials have shown the important role of steroids in the management of patients with COVID-19. Both clinical outcomes and mortality were improved in hospitalized patients (Sarma et al., 2020). However, immunosuppression in diabetic patients with COVID-19 places them at risk of ROCM. Within that context we report a rare case of ROCM in a diabetic patient post COVID-19 infection.

DISCOVERY SCIENTIFIC SOCIETY

2. CASE REPORT

Presentation of the case

A 66-year-old female patient with a past medical history significant for diabetes mellitus DM type II and hypothyroidism, was referred to the infectious diseases department at King Abdulaziz University Hospital KAUH from another medical facility in the city of Jeddah, with an established diagnosis of right cavernous sinus thrombosis and ROCM post COVID-19 and received treatment at our facility in the period between January 2021 to May 2022. The patient recovered from her COVID-19 infection four months before her presentation at our center. She received the treatment for her COVID-19 infection in her home country and the family was not sure whether steroids were used in her treatment or not.

She started to complain of headache and developed right eye redness, proptosis and ptosis with ophthalmoplegia and 6th cranial nerve palsy. The oral and maxillofacial surgery service at KAUH was consulted on the case for the surgical management of her ROCM. Upon clinical examination the patient was alert, oriented and vitally stable. Her right globe was swollen, proptotic (>1cm) with a fungating growth (Figure 1). Intra oral examination was within normal limits with no signs of infection. Ocular examination revealed complete loss of vision and ocular motility in the right eye.

Her CBC results on admission were WBC 12.08 cmm, Hb 9.9 g/dl, Hct 32%, Plt 337 cmm; liver function test and chemistry were within normal limits. Yet her HbAIC was high at 9.2%. The patient was not complaining of any pain related to her right eye. She was started on IV Amphotericin B (0.5 mg/kg slow IV daily) and Apixaban 5 mg taken orally twice daily upon arrival to KAUH along with her other regular medications.

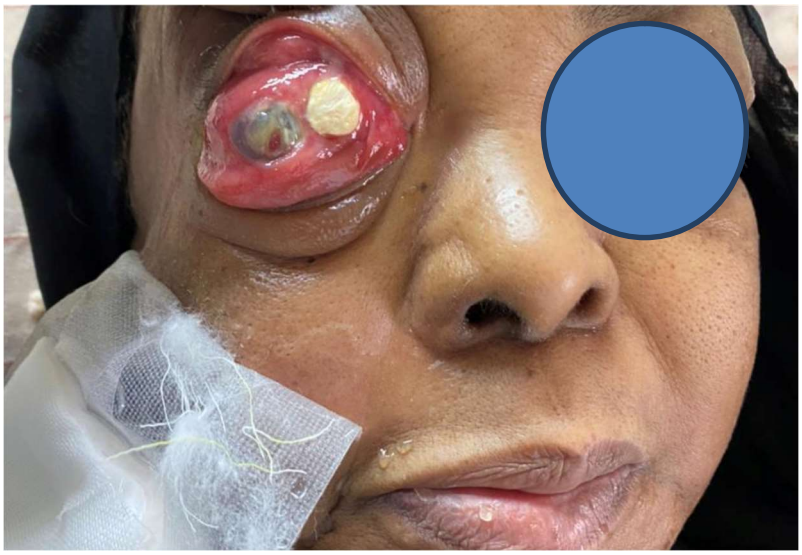

Figure 1 Preoperative clinical photo showing proptotic necrotic right eye

Management and in hospital course

MRI brain and orbit was done and showed thickening and increased enhancement of the walls of the right myofascial cone with associated intraconal and extracoronal fat stranding. The extraocular muscles are thickened and of decreased density, proptosis and stretching of the optic nerve sheath complex was seen (Figure 2a, 2b). The fat stranding extended to the orbital apex, inferior and superior orbital fissures. There was intracranial involvement with thickening and increased enhancement along the lateral wall of the right cavernous sinus and adjacent meninges of the right middle cranial fossa. However, there were no cerebral lesions or collection.

After clinical and radiographic examination, the decision was made to perform orbital exenteration under general anesthesia. After removal of the orbital content the medial orbital wall was noticed to be destructed and the ethmoidal mucosa was swollen and inflamed. An ethmoidectomy procedure with debridement of the sinus mucosal lining was done, the diseased eyelid skin was excised along with the orbit, yet primary closure was achieved due to skin laxity, closure done using 4-0 nylon. No skin grafts or free flaps were needed (Figure 3a, 3b).

The collected specimen including the orbital content and the sinus mucosa was submitted for histopathology and culture sensitivity. Postoperatively, the patient was placed on IV Vancomycin (500 mg IV every 6 hours) and meropenem (1,000 mg every 8 hours) in addition to Amphotericin B. Histopathological examination of the right orbit revealed necrotizing granulomatous

inflammation with invasive fungal elements, morphologically consistent with mucormycosis. The medial orbital wall and the sinus mucosa showed unspecific inflammation with no evidence of fungal elements (Figure 4).

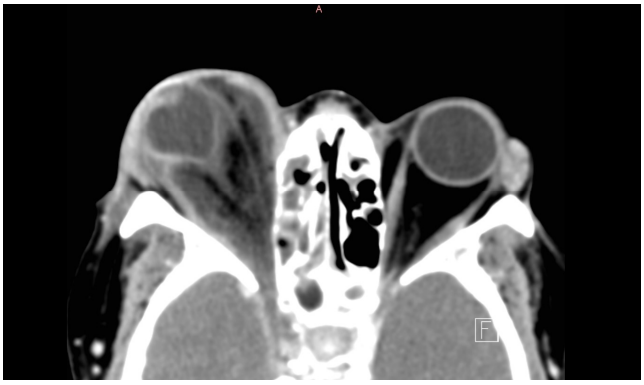

Figure 2a The right globe is distorted in contour with posterior tenting, there is proptosis and stretching of the optic nerve sheath complex

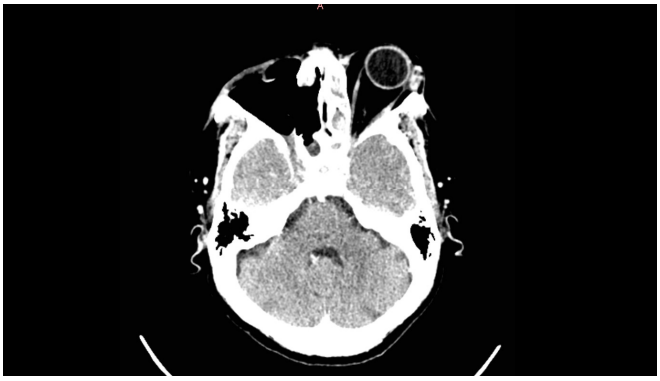

Figure 2b Postoperative CT scan with IV contrast

Figure 3a Intraoperative photo after orbital exenteration

Postoperative CT scan showed stable appearance of right maxillary sinus mucosal thickening with complete opacification of the frontal, sphenoidal and left ethmoidal sinuses. However, no enhancing intracranial lesion was depicted. The patient underwent functional endoscopic sinus surgery for the frontal, left ethmoidal sinuses specimens came negative for fungal growth. During her hospital stay the patient developed an ischemic stroke and seizure disorder post her ROCM. The patient was discharged one month later, in a vitally stable clinical condition after insertion of PICC line to continue her amphotericin B doses.

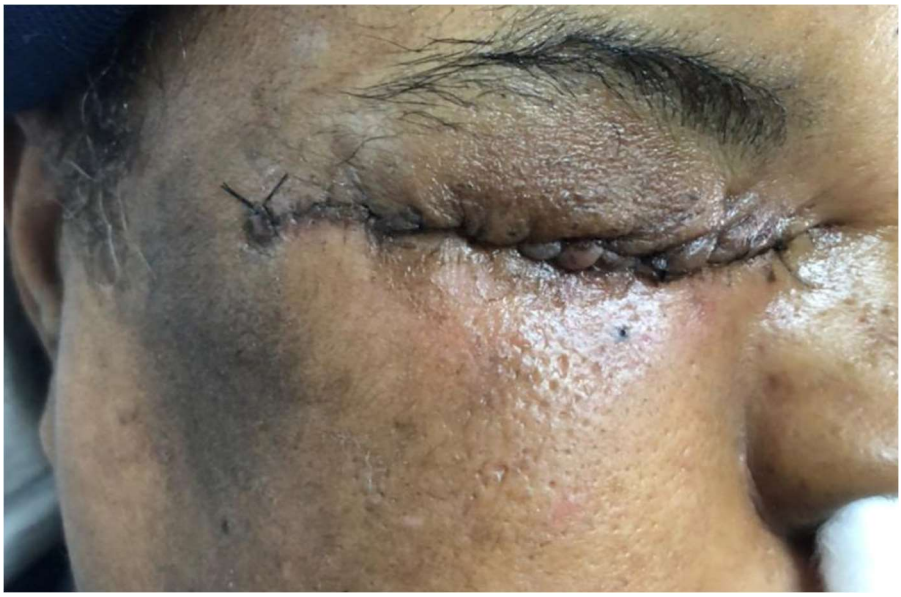

Figure 3b Primary closure, no spacer or skin graft were used

The patient presented to the emergency department two months after discharge, febrile with altered mental status. The family gave history of decreased oral intake in the last three days with fluctuation in the level of consciousness, vomiting and diarrhea. Her labs were WBC: 40.18 cmm, Hg: 7.8 g/dl, Na: 140 mmol/L, K: 3.9 mmol/L, Creatinine: 176, PH: 7.24, CO2: 38.4, PO2:53.4, HCO3:16.4, lactate: 8. Urine and wound culture showed klebsiella KP CRE NDM Oxa48, MRI brain showed a fungal cyst. The patient was admitted to the ICU as a case of septic shock secondary to urosepsis and was started on meropenem, vancomycin, colistin, amphotericin b. Her condition was complicated with hospital acquired pneumonia and herpes zoster ophthalmicus in the left eye.

When the patient condition stabilized, she was shifted to the floor under the care of the medical team. However, after few weeks her level of consciousness dropped from her baseline (9 GCS) to 3 GCS and was febrile at 39°c. At that point the patient was intubated, placed on mechanical ventilation and admitted back to the ICU. An MRI was taken at the time and showed a new parenchymal fungal lesion; Caspofungen (day 1 loading dose: 70 mg/m² IV, day 2 and thereafter: 50 mg/m² IV qday) was started as a salvage therapy. Her cultures came back positive again for klebsiella KP CRE NDM Oxa48 and VRE Enterobacter, she was placed back on meropenem, colistin and linezolid. The patient condition was highly unstable on pressors; eventually she developed multi organ failure and died few days after.

Microbiology and histopathology

Microbiological studies were performed on tissue biopsies obtained from the orbital exenteration procedure. Special histochemistry for fungal hyphae: PAS and GMS were positive. Histopathology showed necrotizing granulomatous inflammation with invasive fungal elements, morphologically consistent with mucormycosis (non septated branching hyphae). Orbital nerve was involved with the fungal process (Figure 4, 5).

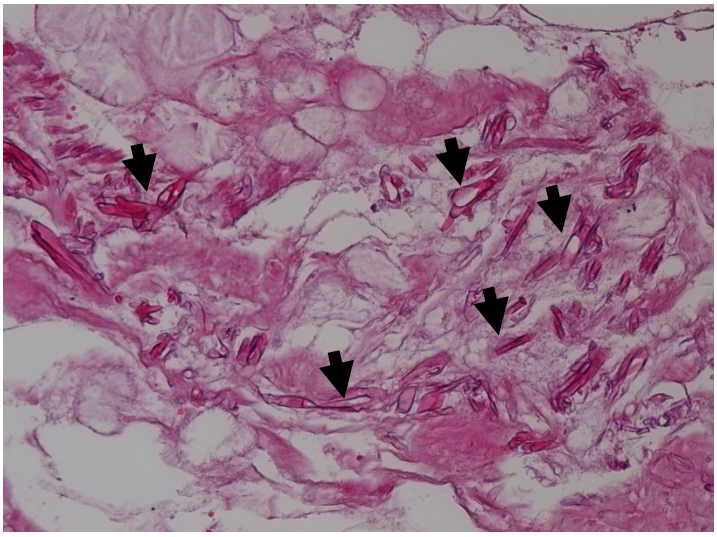

Figure 4 The hematoxylin and Eosinophil-stained section shows board irregular non-septate branching hyphae at 90-degree angle morphologically consistent with mucormycosis. The fungal hyphae lay within necrotic tissue (20X magnification)

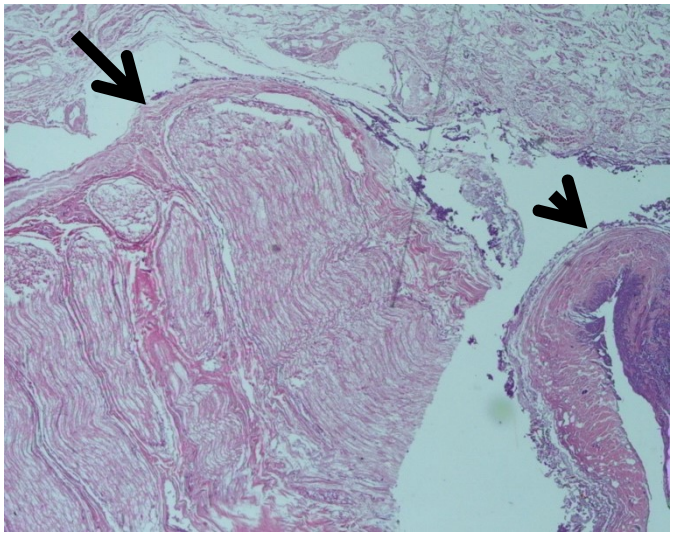

Figure 5 The hematoxylin and Eosinophil-stained section shows the optic nerve (long arrow) with necrotic tissue at the periphery (short arrow) (4X magnification)

3. DISCUSSION

Since the COVID-19 pandemic started, there has been an increase of mucormycosis cases (Patel et al., 2021; Sarkar et al., 2021). The clinical presentation of mucormycosis has been linked to the underlying comorbidity; for example, patients with diabetes are more likely to have ROCM, while patients with hematological malignancies such as leukemia or lymphoma develop pulmonary mucormycosis.

Symptoms of ROCM might be concurrent with COVID-19 or become evident later. In our patient, it started around 4 months after her recovery from COVID-19, interval time reported in the literature is between 1-90 days (Pakdel et al., 2021; Shah et al., 2022) to our knowledge this is the first case to report symptoms 120 days after recovery from COVID-19. ROCM associated with COVID19 has become a healthcare challenge complicating the recovery of COVID-19 infection in diabetic patients (Sarkar et al., 2021).

The mortality rate remains high even with proper medical care. Diabetes as a risk factor for mucormycosis is well documented in cases with and without COVID-19. Unfavorable outcomes in such cases are associated with uncontrolled diabetes and involvement of the orbital apex and CNS (Dave et al., 2021; Patel et al., 2021) which was the case in our patient. She was above 60 years old and her HbA1c was higher than 8 at presentation, both of these factors are associated with increased mortality rate (Yadav et al., 2022).

The current literature supports that using of steroids in the treatment of COVID-19 subject patients to the risk of mucomycosis (Hoang et al., 2020; Sharma et al., 2021) the glucose rich environment resulting from diabetes and the use of steroids provide an opportunity for mucor to become invasive as it compromises the phagocytic immune cell response; one of the major defenses against mucormycosis (Chen et al., 2020; Song et al., 2020; Moorthy et al., 2021; Spellberg et al., 2005).

Given that in this case the COVID-19 infection was treated in the patient country of origin we didn't have a clear history whether steroids were used in her treatment and in what capacity. However, the use of steroids in severs COVID-19 infection is the standard of care, therefore it is reasonable to say they were utilized. Therefore, COVID-19, uncontrolled DM, +/- use of steroids are the main risk factors for developing mucomycosis in our late patient.

4. CONCLUSION

The poor outcome in this case is mainly attributed to her uncontrolled DM, old age, aggressive nature of the disease, late diagnosis and therefore delayed treatment, as the patient already had necrotic fungating lesion in her right eye at initial presentation at our hospital. Early diagnosis and aggressive surgical and medical therapy are key elements for survival in mucormycotic cases.

Acknowledgement

We thank the participants who were all contributed samples to the study.

Author Contributions

The primary/single author of this work contributed by treating the patient, data collection and writing the full manuscript.

Ethical approval

The study was approved by the Ethics Committee of King Abdulaziz University, Faculty of Dentistry, Jeddah, Saudi Arabia (Ethical approval code: 44107279).

Informed consent

Written & Oral informed consent was obtained from the patient family.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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