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Case Report of Rhino-Orbital Mucormycosis in a Diabetic, with Excellent Outcome

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Acute sinusitis secondary to virulent organisms can initially be subtle, or might be misdiagnosed as viral sinusitis. It is one of the most common diagnoses we face in clinical practice. Among all the variable etiologies, fungal sinusitis is the most obscure with devastating consequences. The purpose of this case report is to increase the awareness of health care professionals about invasive fungal sinusitis as an under-diagnosed disease, and emphasize that excellent outcome can be achieved by early employment of different therapeutic modalities. In this case report, we review an older adult male, with significant cardiac and diabetes history, who presented with acute rhino-orbital mucormycosis, and was successfully treated with prompt endoscopic surgical debridement, dual IV antifungals, local amphotericin B nasal washing, and hyperbaric oxygen therapy. All of the above led to extremely favorable outcome for such an aggressive infection.

Keywords: Rhino-orbital-cerebral mucormycosis; nasolaryngoscopy; hyperbaric oxygen therapy.

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1. CASE REPORT

A 54 years old Emirati male, presented with severe left sided facial pain, left orbital swelling and lid ptosis of 2 days duration. Nine days prior to presentation, he had routine follow up nasolaryngoscopy post epiglottal cyst resection done two years ago. Rhinoscopy was discontinued due to pain and mild bleeding from the left nostril. Few hours later, the patient experienced bad odor in the left nostril, swelling in the left side of the face, impaired vision in the left eye with gradual ptosis. He described thick nasal discharge from the left nostril as well.

Our patient is overweight, and known to have diabetes mellitus type II since 6 years with diabetic neuropathy, hypertension since 6 years, ischemic heart disease with previous stenting three times in 2002, 2005, and 2010, with ischemic cardiomyopathy and systolic heart failure, Left ventricular ejection fraction (LVEF) = 40%. In addition, he had chronic kidney disease (CKD) stage 3, and gouty arthritis, latest flare up was few weeks before presentation for which he was getting weekly betamethasone injections.

Screening colonoscopy done 1.5 years ago was normal. He is married, father of 9 children, ex-smoker 40 pack-years, quit 4 years ago, and ex-alcohol consumer (> 5 times/week), quit 8 years ago. No history of recent travel.

On examination, patient had all clinical features of left orbital cellulitis/sinusitis: left eye proptosis, ipsilateral complete ophthalmoplegia, and lids' edema, hyperemia and warmth, left pupil dilated and non reactive (Images 1-4). There was also loss of sensation along the distribution of the ophthalmic branch of the trigeminal nerve. No overt nasal discharge noted. Slit lamp examination showed only light perception in the left eye, normal visual acuity in the right eye. Other systemic examination was normal, including vital signs.

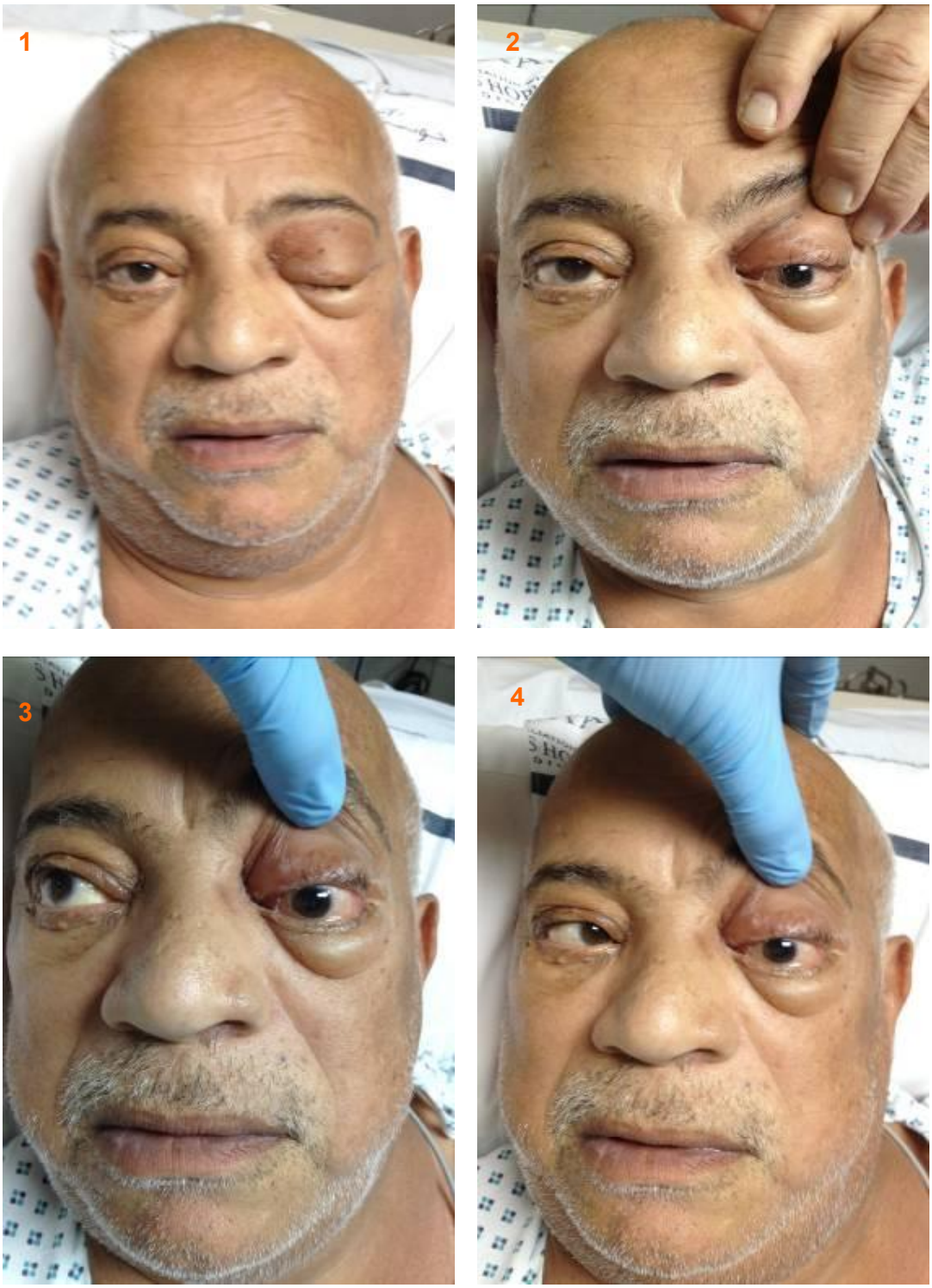
Significant blood tests results were: creatinine of 65 micromol/L, random blood glucose of 14.5 mmol/L without any evidence of ketoacidosis, WBC=10.9*10^9/L with neutrophilia of 86%, hemoglobin=86 g/L normochromic normocytic, and a platelet count of 305* 10^9/L.

CT brain revealed changes of pansinusitis (more so on left side), without associated bony destruction. Inflammatory fat stranding was present in the left orbital cavity, without obvious evidence of subperiosteal or intraorbital abscess formation (Images 5-6). A chest x-ray showed clear lung fields and cardiomegaly.

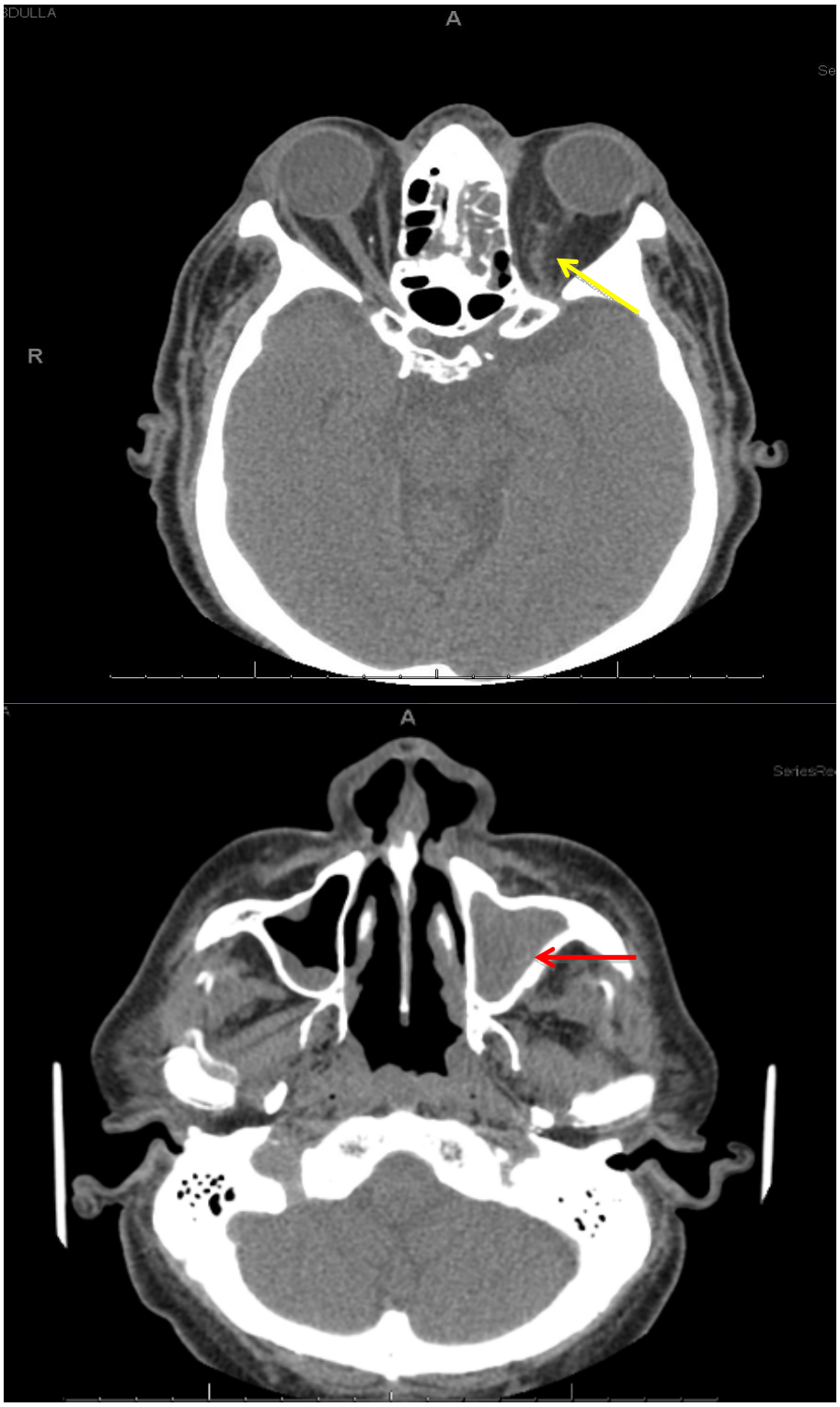
Within 8 hours, patient was taken for diagnostic and therapeutic Functional Endoscopic Sinus Surgery (FESS) under general anesthesia. Intraoperatively, the diagnosis of fungal sinusitis on the left side was made, and the pattern of involvement was suggestive of mucormycosis; gangrenous lateral nasal and orbital walls with blocked maxillary sinus ostium. Transorbital, endoscopic ethmoidectomy done, and a subperiosteal orbital abscess was incised and drained. In addition, endoscopic maxillary antrostomy with debridement helped the evacuation of the left maxillary sinus inflammatory and gangrenous tissue content. Tissue samples were taken cautiously and sent for histopathology, bacterial and fungal stain and culture. MRI brain was negative for cerebral lesions or venous sinus thrombosis. He was started on Ceftriaxone & Metronidazole then changed to Piperacillin/tazobactam & Vancomycin, with IV steroid for 3 days to reduce orbital swelling. Liposomal Amphotericin B with voriconazole was added to treatment due to the high suspicion of fungal sinusitis from the intraoperative findings.

Debrided tissue culture and histopathology initially revealed Aspergillus spp., MSSA, and Proteus mirabilis. However, final culture results about 1 week later showed Rhizomucor spp. (sections 1-4). Patient was then continued on IV liposomal Amphotericin B, and switched from Voriconazole to Caspofungin as per infectious disease department input. Patient after starting the latter drugs developed: severe recurrent hypoglycemia, hypomagnesaemia, AKI despite liposomal amphotericin B dose reduction, and several exacerbations of heart failure.

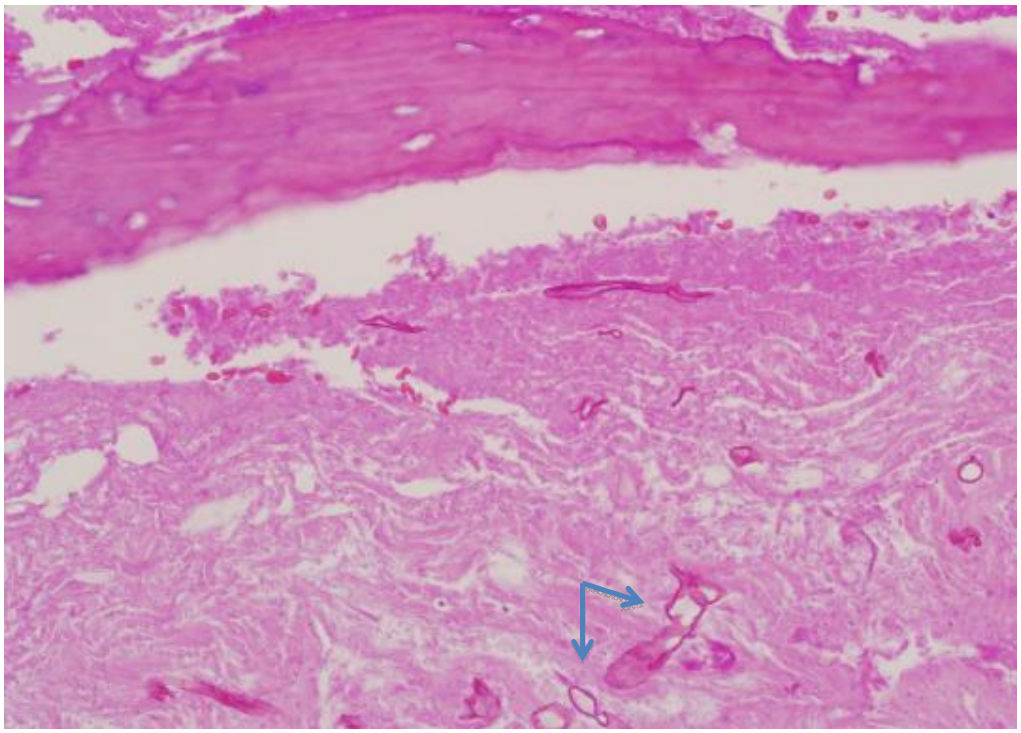
The option of hyperbaric oxygen therapy (HBOT) was discussed with the patient, and he was very enthusiastic about it. He received around 32 sessions of HBOT. However, he developed gout exacerbation, which we attributed in part to dietary habits and in part to the HBOT [1]. HbA1c level checked after 1 month from start of therapy was 6.1%. The treating team suggested the use of intranasal amphotericin B lavage daily for 3-4 weeks, as it had led to improved outcomes with previous similar cases. This was initiated after explanation, counseling and teaching the patient on how to use it.



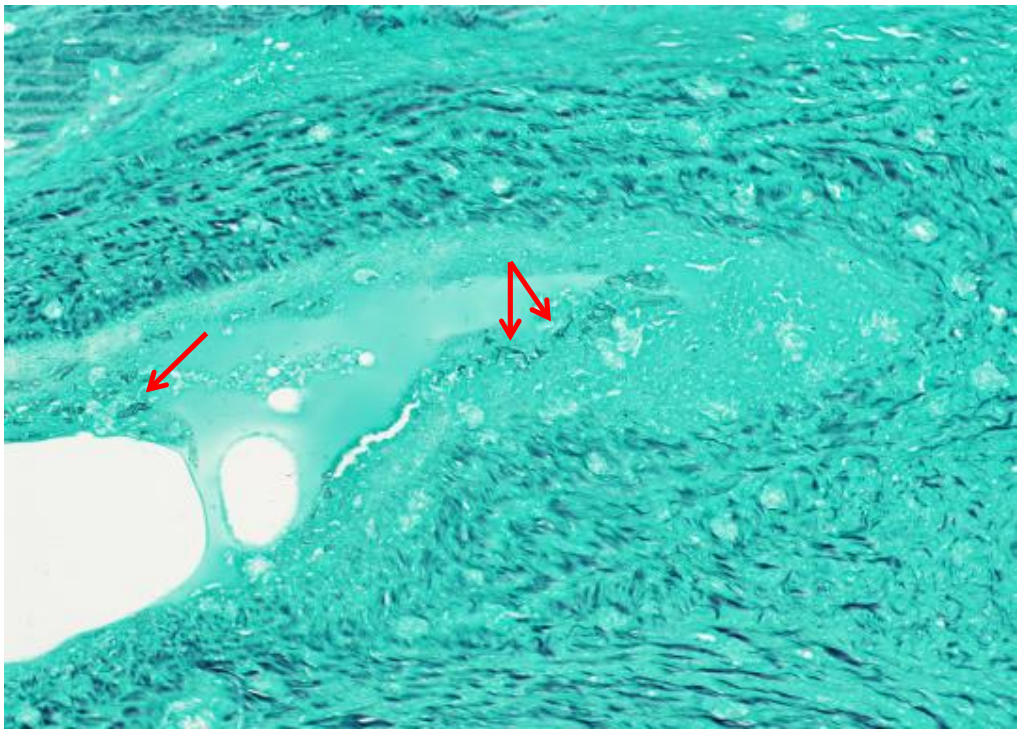
Images 1-4. Complete ptosis & proptosis of the left eye (1), Patient attempting forward gaze (2), right conjugate gaze (3), and left conjugate gaze (4)



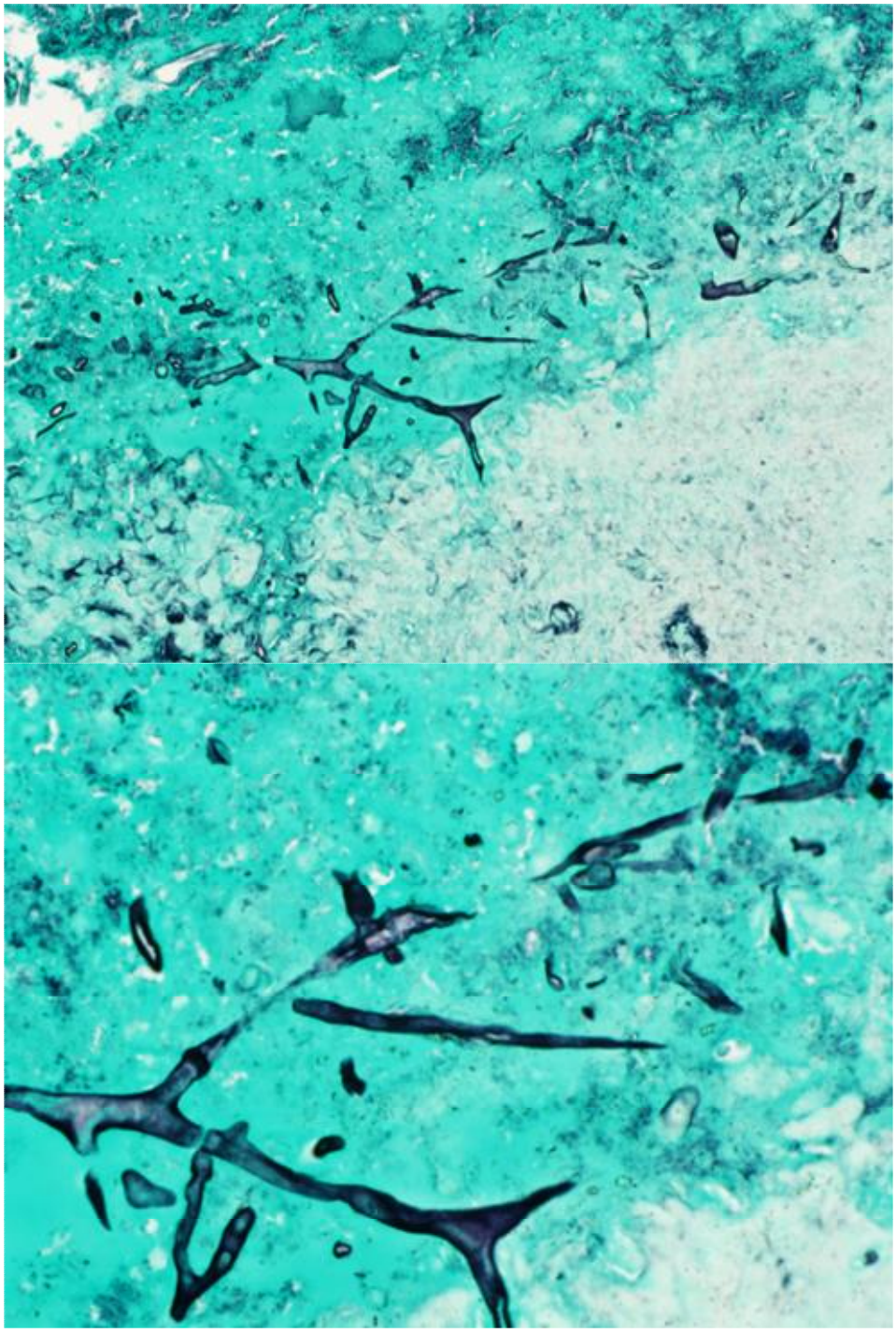
Images 5-6. CT scan head upon presentation to hospital; inflammatory fat stranding in the left orbital cavity (yellow arrow) without clear abscess formation; Sinusitis apparent on both sections more clear on the Left side, with opacified left maxillary sinus (red arrow) without bony destruction



Section 1. H&E staining of necrotic bone and soft tissue sample from the medial orbital wall. Note at the lower half of the section (arrow) the dark pink staining, thin irregular walled organisms (Mucor)



Section 2. Silver Stain (Grocott Gomorii Stain) of a blood vessel at low magnification; In the middle of the section (vessel lumen) are the dark color staining Rhizomucor spp. (arrows)



Sections 3 and 4. Higher magnification of section 2, showing in the middle the black staining broad, predominantly nonseptate hyphae, branching at wide angles and seldom at acute angles (Rhizomucor). The organism has been confirmed on tissue culture.

After 8 weeks of therapy, patient had no more eye proptosis, but the ptosis, loss of vision, and complete ophthalmoplegia in the left eye persisted. He continued to have frequent debridements almost every 2 weeks for 8 weeks, most of them being under local anesthesia.

On his first follow up visit in clinic after 10 weeks, patient was able to actively open his left eye and was able to adduct his left eyeball. Follow up MRI brain showed persistent inflammatory changes in the paranasal sinuses, without brain tissue involvement.

At 4 months follow up, patient lost about 20 kgs over 5 months with dietary adjustment, BMI became 25, and his chronic diseases became more controlled. His left eye blinks just like the right eye, he regained the left oculomotor nerve function, the sensation along the ophthalmic branch of the trigeminal nerve, but still had left abducens nerve palsy. He did not have any facial deformity (Image 7). Rhinoscopy revealed only minimal crust and predominantly regenerating, healthy nasal mucosa.

2. DISCUSSION

Fungal rhinosinusitis is often a rapidly invading infection, in which 50% of the cases have orbital, oral, or brain involvement. Inhalation of fungal spores is not equivalent to getting infected; colonized individuals with competent immune systems do not often develop overt infections. Those who progress to infection are usually immunocompromised, most commonly having malignancy, or organ transplant, advanced HIV, diabetes, or on long-term steroids [2]. However, there is until now more than 200 cases published worldwide of mucormycosis infection in immunocompetent, otherwise healthy patients. This group was found to have relatively better survival rate even with delayed diagnosis or treatment [3,4].

Mucor & Rhizopus grow in soil in dry to humid climate, reproduce very rapidly and spread in the form of spores. They invade blood vessels, nurturing on glucose and acid, thus making uncontrolled diabetics their favorite preys. Another attraction site for these organisms are patients with iron overload on deferoxamine therapy, as this deferoxamine-iron compound is another favored supply for the multiplying fungus [5].

Mucormycosis is getting more readily diagnosed over the past 2 decades. The increasing number of cases can be attributed in part to the increasing prevalence of type 2 diabetes, especially in our region. However, there is definitely a lot more cases that are undiagnosed due to difficult culture of this organism. This - among many other factors- contributes to difficult determination of exact incidence of the disease [4]. Most encountered form of this infection is rhino-orbital or rhino-orbital-cerebral mucormycosis (ROCM). Other rare forms of this opportunistic infection are cutaneous, pulmonary, gastrointestinal, disseminated, renal, and mandibular after dental extraction [3,5].

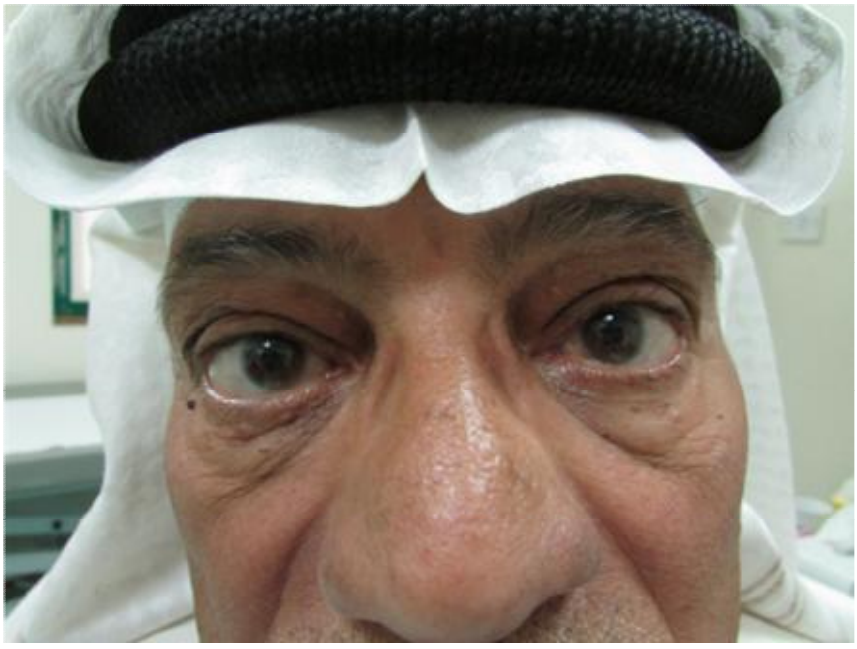


Image 7. The patient at 4 months follow up

ROCM infection hallmark is the rapidity of onset in most cases, although some patients still present with subacute illness. The shared feature in all cases is the rapid invasion of blood vessels thus tissue infarction, and likely poor outcomes [5]. Roden et al. in his review of 929 published cases of mucormycosis infection over few decades, have identified 36% to be diabetics, out of which 44% the infection has killed [6].

The triggers of ROM infection in this patient can be explained by uncontrolled diabetes and general immunosuppression status attributed to the betamethasone injections received 2 weeks prior to presentation. Our patient –however- had excellent outcome compared to most cases of ROCM, especially with his background comorbidities. After reviewing ROCM literature, most patients either died, retained facial deformity, had evisceration surgery of the eyeball, or had sustained neurological deficit from fungal invasion of the brain or intracerebral bleed [7-10]. In contrast, our patient had no facial deformity, no significant cerebral involvement, and regained extra ocular muscles' movement and eye opening. His pain scale throughout the illness never exceeded 5/10.

We attribute this success to several elements: first is the use of combination systemic antifungal therapy. In a major article published by Reed C, et al. it was proven that combination therapy with polyene-caspofungin had significantly improved outcomes 30 days from discharge and better long term survival, compared to population using polyene monotherapy. This is explained by the molecular and laboratory data that R. oryzae genus express the target enzyme for echinocandins, thus allowing them to exert pharmacological action on this genera [11,12]. Also, the synergistic action of lipid polyene-echinocandin combination and their safety profile supports their use for treating this life-threatening infection. The more severe, invasive and disseminated the mucormycosis infection was, the more did this dual combination therapy improve survival [12].

Second, we used intranasal amphotericin B in his treatment for at least 3 weeks, based on the improved outcomes shown in several studies. It has been proven that such therapy reduced mucosal thickening and signs of inflammation on rhinoscopy and repeat CT scanning in such patients [13]. The local instillation of amphotericin B directly onto the infected tissues has already been adopted by many practitioners; due to its observed benefit [14,15]. In addition, he received very frequent and vigilant surgical debridements up to 2 months from admission and on follow up visits in ENT clinic as well.

Third, our patient was keen on hyperbaric oxygen therapy. The latter helps to suppress fungal growth, reduce tissue edema, enhance tissue regeneration, revascularization and healing. A small retrospective study was conducted more than 15 years ago in Duke University Medical Center on patients with ROCM who received HBOT versus those who did not. It showed evidence of mortality reduction without side effects [16]. However, this promising adjunctive therapy is not yet present all around the world.

It is also noteworthy that there is an observed seasonal pattern for this infection. Several observational studies conducted in the Middle East demonstrated the seasonal preference of mucormycosis to summer and autumn [17]. Our patient presented with mucormycosis at the end of August.

3. CONCLUSION

Early diagnosis is the first step in saving the lives of patients with ROCM. When offered the comprehensive and multidisciplinary management needed in timely manner, patients with invasive mucormycosis infection can survive with minimal morbidity and excellent outcomes.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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