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Journal of Global Scientific Research (ISSN: 2523-9376)
6 (5) 2021/ 1369-1374

Journal of Global Scientific Research
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Rhinocerebral Mucormycosis as a COVID-19-Related Complication: A Case Report from Basra City, Southern Iraq

Hassan Ala Farid[1], Ali Rahim Hashim[2], Nareen Haikaz Hasrat[3]

[1]Neurology, College of Medicine, University of Basra, Basra Teaching Hospital, Basra, Iraq.
[2]Internal Medicine and Neurology, College of Medicine, University of Basra, Basra Teaching Hospital, Basra, Iraq.
[3]Medical Physiology, College of Medicine, University of Basra, Basra Health Directorate, Basra, Iraq.

Email Address:
Correspondence should be addressed to Hassan Ala Farid hasbuttosan@gmail.com

Received: 4 Apr 2021, Revised: 10 Apr 2021, Accepted: 22 Apr 2021, Online: 17 May 2021

Abstract

Mucormycosis is a fungal infection mainly caused by Rhizopus species and has been reported to develop in patients with immunocompromised conditions. In Al-Mawani teaching hospital, a specialised centre for coronavirus disease (COVID-19), a 53-year-old man with type 2 diabetes mellitus and COVID-19 infection complicated by diabetic ketoacidosis (DKA) was admitted on 25th August, 2020. Despite the effective management of DKA, the patient started to develop altered conscious levels, third, fifth, and seventh cranial nerves palsies with periorbital cellulitis, which eventually progressed to skin necrosis. Although rhinocerebral mucormycosis was diagnosed and treatment with systemic antifungal medication initiated, the patient died.

Keywords: Rhinocerebral Mucormycosis, COVID-19

1. Introduction

Mucormycosis refers to different diseases caused by fungal infection-the most common organism is the Rhizopus species. [1,2] The main risk factor for mucomycosis is the immunocompromised status, especially uncontrolled diabetes mellitus, and those with ketosis are at higher risk, in addition to patients with cancer and patients on immunosuppressive therapy as glucocorticoids. [3,4] The major route of infection is through inhalation, and when the spores are deposited in the nasal turbinates, rhinocerebral disease developed. [5,6,7] This disease is rare and thus scarcely reported, [1] but the incidence appears to be increasing secondary to the rising number of immunocompromised persons. [8,9] The rhinocerebral mucormycosis causes significant morbidity and requires rapid diagnosis with aggressive medical and surgical therapy; despite the aggressive treatment, it carries a high mortality rate, reaching up to 70% or above. [10,11].

2. Case Presentation

We considered a 53-year-old married man (with three children, a taxi driver from Basra, southern Iraq), who had a past medical history of type 2 diabetes mellitus diagnosed in the last three years but not well controlled on oral medications (Metformin 500mg twice daily and Glibenclamide 5 mg once daily) with poor compliance to treatment, having hypertension without treatment diagnosed accidentally for about one year. This man had a history of dry cough with mild shortness of breath in addition to palpitation, mild fever, headache, hypogeusia, and malaise for a few days, and for these symptoms, he kept himself on outpatient medications, including injectable steroids and antibiotics, without any medical prescription.

A few days later, his medical condition deteriorated more, and he started to develop increasing shortness of breath with rapid breathing as well as become more lethargic and fatigue, was complaining also from increasing thirst and his family noticed that he became drowsy with unawareness. For this reason, his family decided to seek medical advice and consulted the emergency department in a nearby hospital in which both brain and chest computed tomography (CT) was conducted for him, which revealed normal CT brain, and highly confident CT chest for COVID-19 (peripheral bilateral basal ground glass opacities) with 20% lung involvement. Polymerase chain reaction (PCR) for COVID-19 was negative; immediately, he was referred to the Al-Mawani teaching hospital.

He was received at the Al-Mawani emergency room, general and systemic assessment were conducted. The general examination reveals confused patient with severe dehydration status, rapid acidotic breath, dyspnic, tachypnic with disorientation to time, place and person and irritability. His vital signs showed pulse of 98 beats per minutes, the respiratory rate was around (36 cycle/minutes). His temperature was 38.3°C and his blood pressure was (150/90 mmHg), the oxygen saturation was above (93%) at room air. the cardiovascular, respiratory and abdominal examination were normal, neurological examination showed that the Glasgow coma scale of around 10 (Eye 4, Verbal 2, and Motor 4) with normal fundoscopy, normal cranial nerves examination and negative meningeal signs and normal tone, power and reflexes. The blood sugar was assessed using a glucometer, which revealed high result (above 500 mg/dl). The diagnosis of diabetic ketoacidosis (DKA) was suspected. Initial investigations and arterial blood gases was done for the patient and the results was summarized in the table below.

Table 1: The results of laboratory investigations

Laboratory test	Value	Reference range
pH	7.1	7.35 – 7.45
Hco3 (bicarbonate)	12 mEq/L	22 – 28
Serum creatinine	1.64 mg/dl	0.7 – 1.1
Blood urea	18 mmol/L	2.5 – 10.7
White blood cell count (WBC)	23.000 Cell/m3 / severe lymphopenia	< 11.000
Serum ferritin	1200 ng/ml	< 250
Lactate dehydrogenase (LDH)	560 U/L	< 280
C-reactive protein (CRP) titre	1/96	Negative

Aspartate aminotransferase (AST)	33 U/L	5 – 40
Alanine aminotransferase (ALT)	35 U/L	5 – 40
Urine for ketones was	+++	Negative
Serum sodium (Na)	139 mEq/L	135 - 145
Serum potassium (k)	4.9 mEq/L	3.5 – 5.5

Foley catheter was inserted to assess the urine output, and the management of the DKA started in the form of fluid, insulin infusion, potassium chloride, and supportive treatment in addition to the initiation of antiviral therapy in the form of favipiravir, anticoagulants, and antibiotics. Strict follow-up was performed for him to resolve the DKA and control his blood sugar and to normalise his pH and bicarbonate level, thereby improving his hydration status and urine output and these goals were achieved, however, his consciousness level was still disturbed.

Furthermore, after two days of admission, the patient started to develop swelling around the right eye with ptosis and chemosis (first picture in Figure-1) in addition to right-sided facial palsy of the upper motor neuron pattern, right sided oculomotor nerve palsy, and trigeminal nerve palsy. Consequently, magnetic resonance imaging (MRI) with magnetic resonance venography and angiography (MRA/MRV) was done. While MRI showed normal cerebral hemisphere with both maxillary sinuses with air fluid level and normal MRA study, the MRV showed loss of flow-related signal at the left transverse sinus with suspension of thrombosis or stenosis. Although the patient was kept on heparin infusion, no improvement in clinical condition was observed. Three days later, the patient started to develop a skin lesion below the right eye (as shown in picture 2) with increasing eye redness; therefore, Mucormycosis diagnosis was highly suspected clinically and microbiological conformation was done. Amphotericin therapy was initiated, and the neurosurgical consultation was performed, but the family refused any surgical intervention. The patient's condition deteriorated more, and the necrosis of skin became more obvious (as in picture 3), and the patient died after 10 days of hospitalisation.

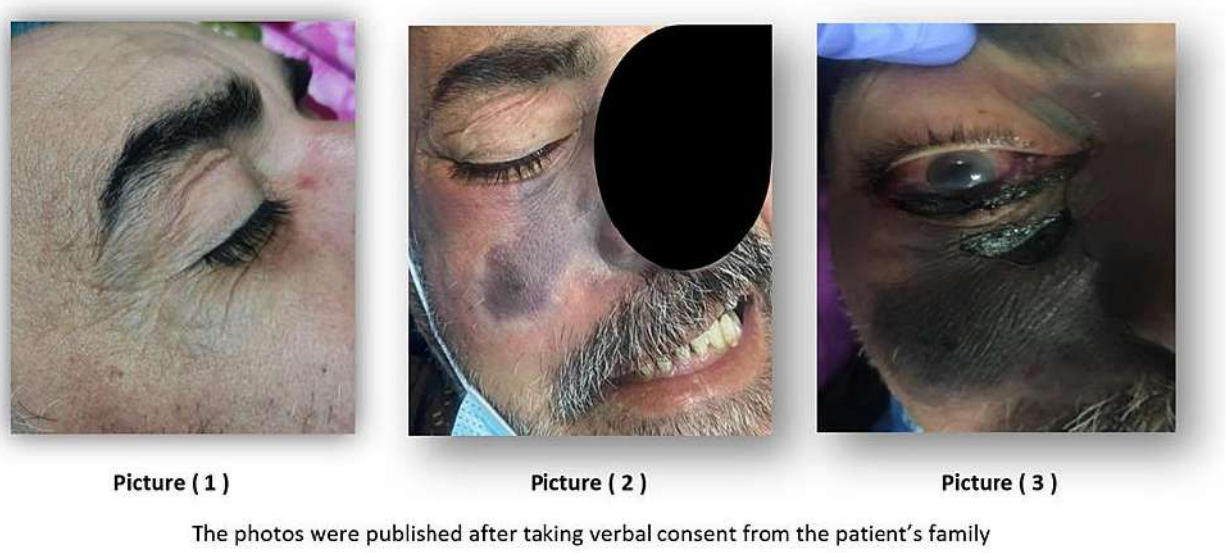

Figure 1: The skin changes in the patient

3. Discussion

According to the anatomic localisation, mucormycosis can be classified as rhinocerebral, pulmonary, cutaneous, gastrointestinal, and disseminated. [12] Rhinocerebral disease may manifest as unilateral headache, facial pain, numbness, fever, hyposmia, and nasal congestion, which progresses to black discharge. Late symptoms that indicate invasion of the orbital nerves and vessels include diplopia and visual loss. These late symptoms are usually followed by a reduced level of consciousness. Most patients with rhinocerebral disease have diabetes (especially with ketoacidosis), [13,14] and this was typically observed in our patient as he was developing COVID-19 infection, which was eventually complicated by DKA in addition to the side effects of steroids that the patient was taken. Collectively, the patient became a typical victim of mucormycosis. Orbital swelling and facial cellulitis were progressive. Necrotic eschars with a black purulent discharge can be noted in the nasal cavity and on the face (as shown in the pictures above). Proptosis, ptosis, and chemosis were also noticed in our patient, and ophthalmoplegias occurred, which may have indicated retro-orbital extension of the disease. Cranial nerves V and VII were mostly affected in our patient because the patient had right-sided facial palsy of the upper motor neuron pattern and trigeminal nerve palsy with brisk jaw jerk. A reduced level of consciousness state denoted brain involvement, which was possibly unclear in the early MRI study, and as the consciousness level deteriorated through the days of hospitalisation, it became difficult to perform the second MRI due to the patient's unstable condition.

When evaluating our patient with suspected rhinocerebral mucormycosis, especially in the early days of admission before the appearance of the cutaneous manifestation, the picture was queried, and both the bacterial orbital cellulitis and cavernous sinus thrombosis were a strong differential diagnosis. Therefore, we kept the patient on aggressive antibiotic treatment with "vancomycin" and "meropenem" and continous heparin infusion.

Patients with suspected rhinocerebral disease should undergo emergent computed tomography (CT) imaging of the paranasal sinuses and an endoscopic examination of their nasal passages with

biopsies of any suggestive lesions. [15] In our situation, this was not feasible and easy because of limited facilities and family disapproval.

It was suggested that the pathogenesis of secondary fungal infection In patient with COVID-19 was attributes to two main causes, the 1st mechanism is related to the immune dysregulation and the reduction in the count of T lymphocyte (CD4 and CD8) in addition to alteration of the innate immunity. The 2nd mechanism is related to degree of pulmonary damage that may enhance the risk of invasive fungal infection. [16]

Patients with mucormycosis should be treated in a tertiary care centre with subspecialty units experienced in managing this condition and its underlying risk factors. Correction of the underlying abnormality, prompt initiation of "liposomal amphotericin B" therapy, and surgical resection are critical. [1,10,11] Although we tried our best to treat all the associated comorbidities, such as DKA, acute kidney injury, and COVID-19 infection, by initiating amphotericin therapy as early as possible, the patient died. As it was shown that the mortality rate of rhinocerebral mucormycosis is possibly reaching 50-70%, and the mortality rate associated with disseminated diseases is approaching 100%. [17] Only a limited number of cases of secondary mucormycosis with COVID-19 have been previously reported. Hanley et al. have reported a case of a 22-year-old male from UK with COVID-19 pneumonia which discover accidentally disseminated mucormycosis involving the lungs and brain at post-mortem study. [18] Werthman-Ehrenreich reported the case of a 33-year-old Somali female who presented with left-sided ptosis and proptosis with altered sensorium. Investigations revealed diabetic ketoacidosis with COVID-19 infection and Mucor was demonstrated via a nasal biopsy and subsequent culture. [19] Salil Mehta et al reported also a case of Rhino-Orbital Mucormycosis associated With COVID-19 from india. A 60- year-old male patient with a longstanding diabetes mellitus who developed signs of orbital cellulitis with nasal biopsy revealed broad aseptate filamentous fungal hyphae suggestive of mucormycosis, which was confirmed on culture. [20]

4. Conclusions

Rhinocerebral Mucormycosis is a serious and life threatening condition specially if follow COVID-19 infection in immunocompromised patients with coexisting medical illnesses as diabetes mellitus, and further imposed by heavy use of steroids, we need to ruminate on whether the patient develops the skin lesion and necrosis or neurological manifestation.

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