Advances in Health Sciences Research, volume 38
Proceedings of the 1st International Ninevah Conference on Medical Sciences (INCMS 2021)

Mucormycosis in COVID-19 Diabetic Patient A Review and Case Report

Wassan Nori [*1] Sanaa Norri [2]

[1] *Department of Obstetrics and Gynecology, Mustansiriyah University*
[2] *Endocrine department, Child Welfare Teaching Hospital*
[*]*Corresponding author. Email:* Dr.wassan76@uomustansiriyah.edu.iq

ABSTRACT

Mucormycosis is an unusual and potentially lethal invasive infection of fungi that most commonly affects diabetes and other immunocompromised individuals. This infection showed high morbidity and mortality rate. Furthermore, the rapidity with which mucormycosis spreads is an extraordinary phenomenon; even a minor delay in diagnosis can be lethal. COVID-19–associated mucormycosis has been documented more frequently recently, notably among cases with uncontrolled diabetes. Patients with type I diabetes mellitus and hyperglycemia often have an inflammatory condition exacerbated by suppressed immunity triggered by SARS-CoV-2, making secondary infections more likely. Reports of mucormycosis in Iraq is scrutinized; therefore, we aimed to discuss the infection's epidemiological criteria, risk factors, and pathogenesis as we present a young child case report who suffered from a tragic course.

Keywords: *COVID 19, Mucormycotic, Diabetes.*

1. INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)is causing a disastrous pandemic around the globe [1]. Furthermore, COVID-19-associated mucormycotic is a new type of opportunistic mycotic infection that's still unappreciated. Mucormycotic (MM)is an angioinvasive deadly fungal infection caused by Rhizopus Oryzae spp, which represents the most frequent type causing nearly 90% of MM cases in human and accounts for 90.5 per cent of the Rhino-orbital-cerebral macrocytosis [2,3].

1.1. Risk Factors

The traditional predisposing factors for infection in patients have altered immunity like AIDS, patients suffering from hematologic malignancies like leukaemia, patients treated by organs allograft or stem cell, Diabetic mellitus (DM) and those on steroids [4].

However, recently COVID 19 cases showed an increased incidence of the disease since dexamethasone is indicated for SARS COV 2 patients hospitalized, thereby escalating the chance of invasive mould infection. MM incidence ranged from 0.005 to 1.7 per million people; in the era of COVID 19, it raised approximately 80 multiple higher (0.14 per 1000), particularly in India, which is regarded as (the world's capital of diabetes). In Europe and the United States, blood malignancies and transplantation take the lead [5,6].

1.2. Course of Infection

Historically MM was first discussed in 1885 by Paltauf and only later was given the name (Mucormycosis) in 1957 by Baker, the American pathologist [7]. The infection occurs by inhaling the spores of mold located in the soil and organic compounds. These will spread through the oral and nasal cavity, to the retro-orbital area via the orbital arteries, and finally, access the brain. The primary nested site is a pterygopalatine fossa, where the infraorbital nerve gets involved, manifested as pain and paresthesia early in the affected cases[8].

Involvement of the vessels disturbs the blood supply; the necrotic process begins, where the characteristic mycotic dark patch is noticed, demonstrated in figure 1. Mucormycosis can be subdivided into five types; the most frequently seen is Rhino-orbital-cerebral [9,10]. Other types include pulmonary, cutaneous, gastrointestinal, and disseminated MM.

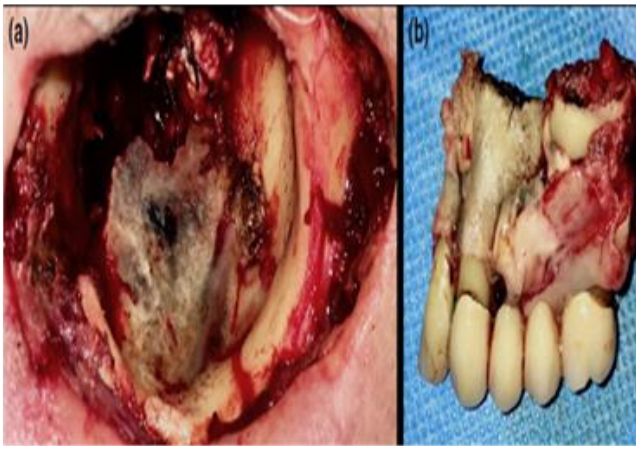

Figure 1 (a)Typical mycotic dark patches with Necrotic floor of the orbit floor after exenteration /before orbital floor resection (b) and complete avital bone and soft tissue after partial maxillectomy by Beiglboeck FM et al. [10].

1.3. Diagnosis

The hallmark of Mucomycosis involves; necrosis of the underlying tissue by eosinophilic infiltration, giant cell invasion, and thrombosis. The gold criteria for diagnosing Mucomycosis are black, necrotic area mistaken for crusted dried blood, bloody nasal discharge, facial pain and swelling, and ptosis of the eyelid alongside periorbital swelling [11].

Definitive diagnosis of mucormycosis relies on microbiological and histopathological confirmation, although the latter is more conclusive. This infection carries high mortalities and morbidities rate[12]. Therefore, early diagnosis and prompt, aggressive surgical debridement and antimycotic therapy are essential for survival. MM prevalence has recently increased among COVID-19 cases, particularly those with diabetes [11,12].

This review and case report examine the youngest MM infection case reported in Iraq, which took a tragic turn. We aimed to provide an appropriate description, assessment, and physiological explanation for why mucormycosis is increasingly correlated to COVID-19, especially in diabetic patients.

2. CASE PRESENTATION

Mr.M. is a 13years old boy with two years history of type I Diabetes mellitus who was admitted to our ER department complaining of dyspnea and a fever of 2 days. On examination, the patient was restless feverish, and have acidotic breathing. He was sent for a complete blood picture (CBC), ESR, random blood sugar (RBS), urine for sugar and ketone bodies, blood gas analysis and C-reactive protein (CRP). Results confirmed severe diabetic ketoacidosis (DKA), the blood Ph was 7.10, and he was put on DKA regime treatment hourly. The blood urea was increased up to 5.70 mg/dl.

CBC showed leukocytosis;$16*10^6$ predominantly neutrophils suggested superadded infection. Haemoglobin was 10 mg/dl, Platelets 700 fl/dl; it was very high; normal level up to 450. The ESR was very high, up to 107. Moreover, CRP was 76, which alerts for COVID 19 possibility. An oropharyngeal swab by PCR confirmed the case. Intravenous Ceftriaxone 100mg/kg /day with IV fluid and symptomatic treatment was initiated. After two days of admission, he complained of worsening headache, increased blood pressure, left-sided facial swelling and unilateral loss of sight in the left eye.

An urgent CT scan was done for suspicion of cerebral oedema, revealed to be normal. Therefore, a Mutidisplenary approach was implemented in management. The ophthalmologist confirmed papilloedema and signs of raised intracranial pressure; mannitol was added to the treatment. Still, the vision did not improve, implying ischemic injury by a stroke. The neurosurgeon later confirmed that by the associated cranial nerve palsies of the 3rd,5th and 7th Cranial nerve.

Fasiciomaxillay surgeons strongly suspected fungal mucormycosis; he intended to do an urgent surgical debridement and biopsy from the necrotic tissue. However, the high blood sugar made the case unfit for general anaesthesia, so it was done under local anaesthesia, alongside daily irrigation of the area. Again, the response of the case was reasonable. Finally, the ENT surgeon examined the patient and ensured that the nasal bone was intact and no invasion had occurred to the sinuses.

MRV(Magnetic Resonance Venography);a technology that utilizes intravenous (IV) contrast dye to visualize the veins; showed occlusion of the left retinal artery by thrombus. Enoxaparin was added to the treatment with a dose of 1mg/kg/day; systemic anti-fungal Amphotercine B was given in a dose of 3mg /Kg for a 4-6 weeks, in addition to the triple anti-biotic regime of ceftriaxone, metronidazole and vancomycin. Five days later, the fever had subsided, the headache was resolved. Unfortunately, he lost his left eye.

3. DISCUSSION

The SARS-CoV-2 infection has been associated with many opportunistic bacterial and fungal illnesses; Mucomycosis is reported as one of the most prevalent fungal infections. Among the participating factors for mucormycosis in COVID 19 cases are the hypoxic state caused by primary lung involvement and injury [13].

In addition, high serum iron is another risk factor for mucormycosis; it represents an ideal resource for invading mold [14]. Increased serum iron is partially accredited to the hyperglycemia state that enhances transferrin and ferritin glycosylation; further, it reduces the chelating activity of transferitein. Another point; is the cytokine release, which raises free iron levels via increased production and decreased transport [15].COVID 19 is further known for its ability to produces endothelialitis, endothelial damage, and thrombosis. In addition, it suppresses the immunity by lymphopenia and a decrease in CD4+ and CD8+ T-cell levels [16].

Our case was known to be diabetic, a metabolic disorder that was an independent risk factor to COVID 19 and Mucormycosis. COVID 19 infection caused hyperglycemia, and DKA's acidic state was a major precondition for the fungus to thrive with COVID 19's reduced immunity, putting the patient at risk for subsequent mycotic infections.

DM, remains the greatest predisposing factor for MM worldwide, with a 46 per cent overall death rate. However, recently a meta-analysis recruited 851 patients with seldom occurring MM, declared that DM was an independent predisposing factor [Odds ratio 2.68; 95 per cent confidence interval 1.76–3.54; P 0.001] [17].

On the other hand, glucocorticoid use has been linked to opportunistic fungal infections such as aspergillosis and mucormycosis; corticosteroid use for 1-2 weeks has been associated with MM, particularly in patients with diabetes. Interestingly, in the European Federation of Medical Mycology Research, 46 per cent of the cases were given corticosteroids a month pAl-rior to MM diagnosis [18,19].

The thrombotic event in our case was triggered by SARS COV-2 thrombotic effects, mucormycosis-related thrombosis, and the patient's pre-existing comorbidity, such as fever and reduced fluid intake, which induced blood stasis [2,6]. MM has been documented with COVID 19 in other countries, but we believe this is the youngest case reported to date.

Singh AK et al. investigated the anthropometric criteria of cases with macrocytosis worldwide, including 105 patients; his result highlighted that 79% of those affected were male, having a history of COVID 19 infection 40% for past and 60% for current infection. DM was associated in 80 per cent of the cases, while DKA was in 15%. Steroid was seen in 76 per cent of the cases. Mucormycosis of the nose showed the highest percentage, followed by Rhino-orbital-cerebral MM . The age range in their study was 60-27 years [20]. No cases were reported at such young age as in the current study.

4. CONCLUSION

The lethal trinity of COVID 19, mucormycosis, and DM resulted in a tragic loss of sight in this young boy. Therefore, to reduce the incidence of deadly MM in diabetic cases, we recommend maintaining good glycemic control in conjunction with antithrombotic medications.

AUTHORS' CONTRIBUTIONS

Both authors contributed equally and approved the final version.

ACKNOWLEDGMENTS

To our beloved University, Al Mustansiriyah, for continuous support.

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