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Case Report

Subglottic mucormycosis in a COVID-19 patient: a rare case report

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Abstract

Mucormycosis is an opportunistic fungal infection caused by fungi of Mucorale order. Uncontrolled diabetes mellitus and other immunosuppressive conditions such as neutropenia and corticosteroid therapy are known risk factors. A new risk factor for this infection is COVID-19 which facilitates mucormycosis by different mechanisms. The rhino-orbito-cerebral involvement is the most common form. Involvement of other anatomical regions may occur in rare situations. As we presented here, a 51-year-old woman presented with respiratory distress and subglottic lesion during COVID-19 (Delta variant) treatment which was diagnosed by histopathological examination as a subglottic mucormycosis postoperatively. The patient underwent tracheostomy and debridement of the necrotic tissues followed by antifungal treatment. New manifestations of COVID-19 are appearing over time. The association between coronavirus and mucormycosis of the laryngeal and airway region must be given serious consideration. Current guidelines recommend a combined medical and surgical approach for achieving the best outcome.

INTRODUCTION

Mucormycosis is a rare fungal infection caused by Mucorale order [1]. The rhino–orbito–cerebral form of mucormycosis is the most common form which is most commonly seen in patients with diabetes mellitus (DM). Although, pulmonary mucormycosis is a rare manifestation detected in patients with hematological malignancies and transplant recipients [2]. Diagnosis of mucormycosis is characterized by the presence of angioinvasion of Mucorales hyphae and also with culture confirmation [3–5]. Mucormycosis is an opportunistic infection and usually a rare condition. Uncontrolled DM and other immunosuppressive conditions such as neutropenia and corticosteroid therapy are known risk factors [6]. A new recognized risk factor for this opportunistic infection is the rampant use of corticosteroids in a background of coronavirus disease of 2019 (COVID-19), which facilitates mucormycosis by different mechanisms including, low oxygen and acidotic environment, high iron and glucose level and impaired function of phagocytosis [7]. Although it affects most commonly the paranasal sinuses, the presence of mucormycosis in the laryngeal tract is a very rare condition. In this context, we review a rare case of subglottic invasive mucormycosis.

CASE REPORT

A 51-year-old woman presented with malaise, fever and shortness of breath 4 weeks before admission. She had a history of DM and hypothyroidism and was treated with Metformin and Levothyroxine. She had no history of COVID-19 exposure. Physical examination revealed a conscious woman with no respiratory distress. Vital signs were as follows: blood pressure 105/70 mmHg, heart rate 92 beats/min, body temperature 38.2°C, respiratory rate 16 breaths/min and no pulmonary rales nor crackles. Although, the initial laboratory test showed poor controlled DM (fasting blood sugar: 245 mg/dl and HbA1C: 11). A Chest computed tomography (CT) scan was done and revealed multilobar ground glass opacification, which was in favor of COVID-19 infection (Fig. 1). She was admitted to the ward based on peripheral oxygen saturation (SpO2) of 88% and received 4–5 l

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per minute of oxygen nasally. Dexamethasone 8 mg twice a day/IV and Remdesivir 200 mg stat and then 100 mg daily/intravenous (IV) were started. Also, she was given regular and NPH insulin, and they were adjusted every day to control plasma glucose. RT-PCR from the nasopharyngeal swab was positive for severe acute respiratory syndrome coronavirus 2 (SARS-COV 2; COVID-19 Delta variant). During the course of treatment, on September 22 at 4:00 P.M„ she developed mild hot potato speech, dyspnea and subtle respiratory distress. Indirect laryngoscopy could not be done due to severe pooling and lack of patient's cooperation. As her symptoms worsen over time, a spiral chest, PNS and neck CT scan with IV contrast was done and revealed normal paranasal sinuses and the lung parenchyma, with resolved pulmonary opacities. Soft tissue swelling of the right side of the supraglottis, glottis and subglottis were depicted on the neck CT scan. A non-enhancing soft tissue in favor of necrosis was visible in the posterior subglottis, with extra laryngeal extension posterior to the upper trachea (Fig. 2). Based on the initial impression of bacterial subglottis infection, empiric broad-spectrum antibiotics (ceftriaxone and clindamycin) were started giving an infectious disease consultation, other treatment was continued with close observation. Initially, her respiration got better, but over the next 2 days, her breathing became progressively labored. Video laryngoscopy was done and revealed a yellowish lesion in the subglottic area (Fig. 3). She underwent an emergency awake tracheostomy. Following tracheostomy, direct laryngoscopy revealed ~1*1.5 cm white to yellowish lesion similar to crusting and necrosis in the subglottis. Multiple biopsies were taken and sent to the laboratory for histopathological and mycological evaluations. Microscopic examination showed scattered areas of necrosis infiltrated by numerous large, branching non-septate hyphae. The hyphae mostly demonstrated significant branching at 90-degree angles. Also, scattered inflammatory cells infiltration was seen in surrounding vital tissue. Additional ancillary histochemical staining (Periodic Acid Schiff—PAS- and Grocott's Methenamine Silver—GMS) confirmed the presence of the fungal hyphae throughout the specimen, in favor of mucormycosis (Fig. 4). Dexamethasone was discontinued and she was given liposomal amphotericin B 250 mg/IV/daily. The follow-up laryngoscopy showed a subglottic lesion about 1-week post-operation. Therefore, she underwent another direct laryngoscopy with debridement of the subglottic necrosis. The following indirect video laryngoscopy after about 1 week after the second debridement showed no sign of any necrosis or lesion. The general condition of the patient was completely improved after 4 weeks of liposomal amphotericin B and there was no evidence of recurrence during the outpatient follow-ups after 4 weeks of oral Posaconazole (5 cc/every 6 h) (Fig. 5).

DISCUSSION

We reported a rare case of isolated subglottic mucormycosis in a COVID-19 patient. There are only a few reports that described subglottic mucormycosis [8–11] and its prevalence is unknown. Depending on the underlying conditions and the risk factors, mucormycosis have a specific predilection to affect common anatomic sites like sinus, orbit and respiratory tracts in rare cases [12]. Wolf *et al.* reported a poor control DM patient with an intraluminal mucormycosis in the first tracheal ring that was treated after infected tissue resection and prolonged amphotericin B [11]. In another report Mohindra *et al.* described a female DM patient with tracheal mucormycosis after H1N1 influenza [10]. It seems that like our case DM is the main predisposing condition correlated with upper respiratory mucormycosis.

The differential diagnosis for the necrotic lesion in subglottis includes secondary ischemic injury to the tracheal wall due to prolonged intubation, neoplastic lesions (chondrosarcoma, adenoid cystic carcinoma and lymphoproliferative disorders), inflammatory diseases (Wegener's granulomatosis and sarcoidosis) and infectious disease (bacterial, tuberculosis, aspergillosis and mucormycosis; [11]). Biopsy of the lesion is important for precise diagnosis and treatment.

Current guidelines recommend a combined medical and surgical approach for achieving the best outcome [13]. Liposomal amphotericin B is the mainstay antifungal treatment for mucormycosis. Surgical debridement of the involved area in conjunction with antifungal treatment is also necessary as performed in this case and the in older reports [10, 11, 14].

The mortality rate and survival of the patients with mucormycosis depend on several factors. Although, many studies reported a high mortality rate for these patients [14–16] but the severity of underlying medical disorders, early initiation of antifungal therapy and effective surgical debridement have key roles in the prognosis of the patients. Surgical debridement without reversing the immunocompromised conditions is not adequate and may lead to disseminated disease and also required repeated debridement. Even one study demonstrated that controlling the underlying DM, and antifungal therapy without surgical debridement is a good treatment option in localized diseases [9]. Therefore, special consideration should be given to the underlying immunosuppression status and stop the rampant use of corticosteroid because mucormycosis usually do not affect an immunocompetent person. Furthermore, it has been shown that patients with tracheal mucormycosis and limited pulmonary involvement have better survival [17]. Our patients had isolated subglottis involvement without rhino–orbito–cerebral or pulmonary mucormycosis. Fortunately, early diagnosis and combined antifungal therapy and serial surgical debridement of necrotic tissues in conjunction

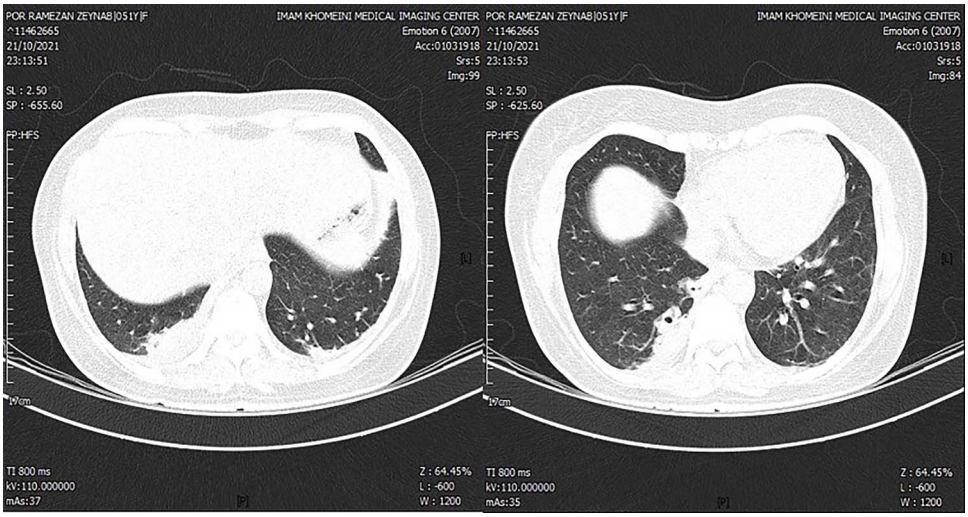

Figure 1. Chest CT scan was done and revealed multilobar ground glass opacification, which was in favor of COVID-19.

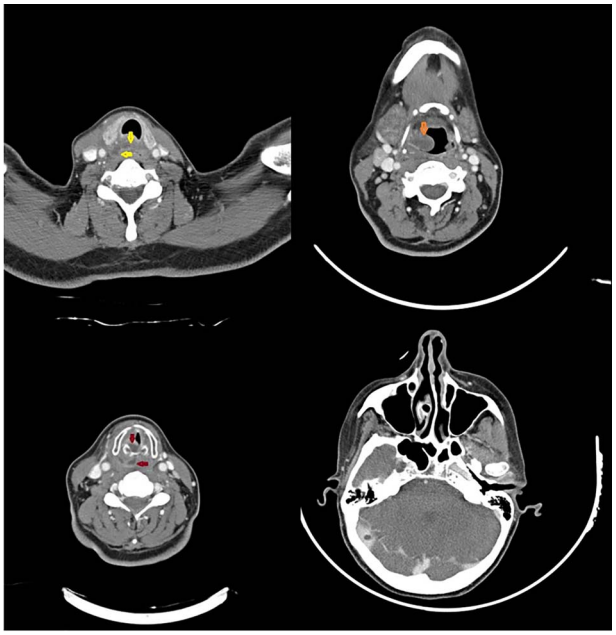

Figure 2. Axial contrast-enhanced CT scan of the neck depicts soft tissue swelling of the right side of the supraglottis, the glottis and the subglottis. Non-enhancing tissue in the posterior aspect of swollen subglottis is present surrounding the right side of the upper cricoid cartilage. An extension of non-enhancing tissue is seen in post-cricoid mucosa/hypopharynx and visceral space posterior to the trachea. The mentioned non-enhancing tissue could represent an abscess cavity or necrotic tissue. All paranasal sinuses are clear, and there is no peri-antral fat stranding.

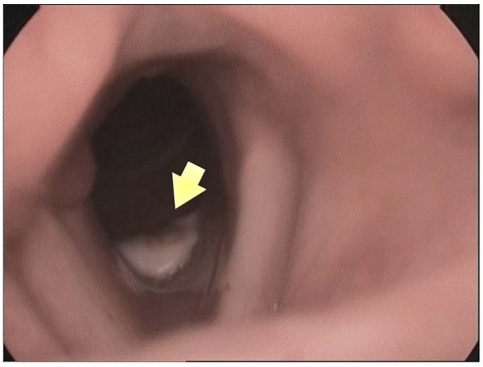

Figure 3. Video laryngoscopy revealed a yellowish lesion in the subglottic area (yellow arrow).

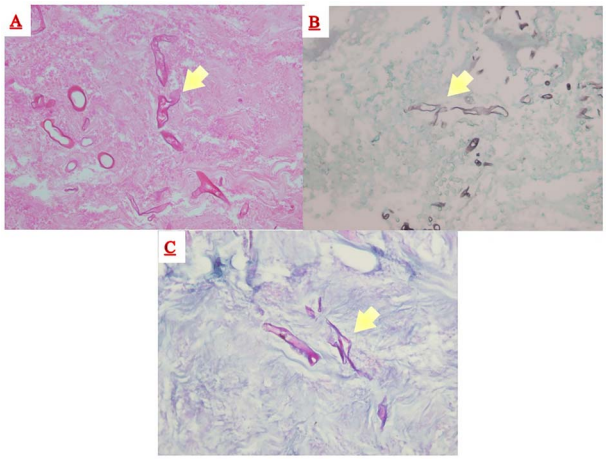

Figure 4. Non-septate fungal elements (yellow arrows) in a necrotic stroma are evident using H&E (**A**), GMS (**B**) and PAS (**C**) staining.

with aggressive control of the blood glucose and also, discontinuation of dexamethasone are the keys to our successful outcome.

The interesting aspects of this case were the presence of mucormycosis in a rare anatomical site with atypical clinical presentation. The patient developed the symptoms in a period of active COVID-19 (Delta variant) disease. The management of the patient was similar to current guidelines.

During the COVID-19 era, any necrotic tissue in the airways in immunocompromised patients should raise suspicion of mucormycosis and be diagnosed early with a rapid biopsy of the affected area.

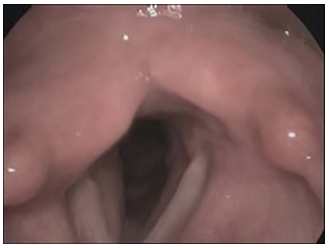

Figure 5. Video laryngoscopy of the patient 2-weeks post-operation. This showed no sign of any necrosis nor lesion in the subglottic area.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The project received institutional research ethics board approval prior to the beginning of the study from the Otolaryngology Research Center, Imam Khomeini Hospital Complex Ethics Board.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY

Not applicable.

FUNDING

None declared.

AUTHORS' CONTRIBUTIONS

MSZ and BA did the tracheostomy, tissue debridement of the patient and gathered the necessary data and were the major contributor in writing the manuscript. MJ did the secondary debridement. PA and SKh performed the histological examination of the biopsy sample. FS reported the radiologic imagings. ZA and MRS started and adjusted the antifungal treatment. All authors read and approved the final manuscript.

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