
COVID-19 Associated Fatality from Invasive Rhino-Sinusitis in an Immunocompetent Patient

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Abstract

Background: COVID 19 infections have been associated with invasive fungal infections in immunocompromised patients and those given immunomodulating medications to help treat COVID 19. These fungal infections have a high mortality and often require emergent and extensive surgical debridement. We present a case of an immunocompetent young female patient that did not receive any interventions for her COVID 19 infection and had resolution of her respiratory symptoms, but eventually succumbed to mucor rhinosinusitis.

Case Presentation: In this case report, we describe a 41-year-old unvaccinated female with recent COVID 19 infection. The patient was initially monitored in the outpatient setting but developed invasive fungal rhinosinusitis, which led to a precipitous clinical decline despite multiple surgical debridements, eventually resulting in death within days.

Conclusions: The patient in this report had no treatment for COVID 19 that might have caused iatrogenic immunomodulation. It is the authors' contention that the patient's COVID-19 infection contributed to mucosal sloughing, which, in conjunction with diabetic status, facilitated fungal angioinvasion that progressed into invasive fungal sinusitis.

Keywords: COVID-19; Mucor; Rhizopus; Invasive rhinosinusitis; Diabetic complications

Introduction

Invasive fungal sinusitis associated with COVID-19 has been reported in India and Egypt and has been associated with high mortality [4,5]. Poorly controlled diabetes and use of corticosteroids among COVID-19 patients appears to increase rates of mucormycosis. Optimizing glucose control and judicious use of corticosteroids in patients with COVID 19 is therefore mandatory [4].

Other studies have looked at COVID-19 and associated invasive fungal sinusitis [5] but none, to our knowledge, has demonstrated a case where the patient did not receive any immunosuppressive or other treatments for COVID-19 and had symptom resolution prior to symptoms of invasive fungal sinusitis.

This case report highlights one of the deadliest complications occurring after recent COVID-19 infection with resolution of symptoms. The patient in this report had no history of immunosuppressive medications or corticosteroid use. She did not receive monoclonal antibodies or other dedicated treatments for COVID 19. It is the authors' contention that the patient's initial COVID-19 infection contributed to mucosal sloughing, which, in conjunction with her uncontrolled diabetes, facilitated fungal angioinvasion that progressed into invasive fungal sinusitis. Therefore, the continued diligence of providers to quickly recognize this condition is imperative so patients can undergo timely interventions.

Case Presentation

This report details the case of an unvaccinated 41-year-old female with poorly controlled diabetes mellitus and multiple admissions for diabetic ketoacidosis. Her previous medical history included anemia, asthma, recurrent pancreatitis with pancreatic necrosis, and familial hypertriglyceridemia. The patient reported Coronavirus disease 2019 (COVID-19) exposure 13 days prior to admission and tested positive one week prior to admission. She experienced mild symptoms and was instructed by an urgent care evaluation at another facility to complete home quarantine and was not given further treatments. Her mild respiratory symptoms resolved prior to the events of her hospital stay discussed in this report.

Three days prior to admission to our facility, the patient experienced nausea and vomiting and had signs of diabetic ketoacidosis and was then admitted to an outside hospital. She developed hematemesis and was transferred to our facility for GI evaluation. After undergoing esophagogastroduodenoscopy (EGD), she developed right-sided facial droop. A stroke code was called, and magnetic resonance imaging (MRI) demonstrated no intracranial abnormalities; however, it did suggest abnormal hyperintensity in the right ethmoid sinus. A follow-up computed tomography (CT) scan demonstrated complete opacification of the ethmoid air cells with mucosal thickening concerning for invasive sinusitis (Figures 1 and 2).

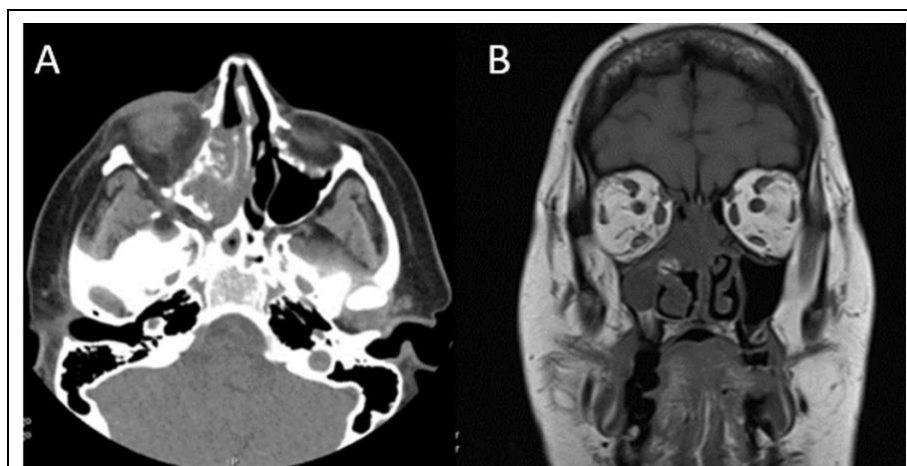


Figure 1: Initial Imaging: (A): Axial and coronal; (B): Magnetic Resonance Imaging (MRI) slice demonstrating opacification of ethmoid air cells, which, in the context of poorly controlled diabetes, was concerning for fungal angioinvasion.

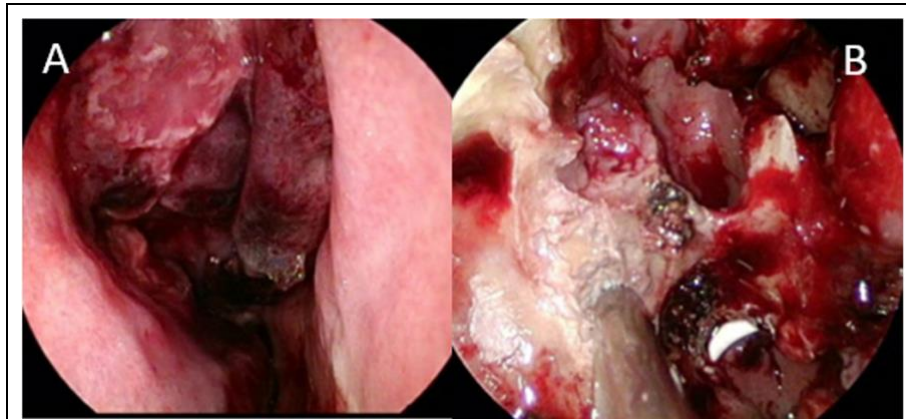


Figure 2: First Debridement: Endoscopic images from first debridement of ethmoid sinus on day of admission. Extensive necrosis and was visualized with extension into nasopharyngeal mucosa. Cultures of scrapings returned positive for methicillin-resistant staphylococcus aureus and rhizopus species.

Amphotericin B was immediately administered along with antibiotics and the ENT service was consulted to evaluate for surgical intervention. She underwent right functional endoscopic debridement on the day of her admission. Findings were remarkable for extensive necrosis with extension into the mucosa of the nasopharynx, (Figure 3 and 4). Culture of scrapings from the necrotic tissue was found to contain *Rhizopus* species and methicillin-resistant *Staphylococcus aureus* (MRSA). Pathology of the specimen showed invasive fungal sinusitis with angioinvasion and infiltration of fungus into the mucosa and underlying bone.

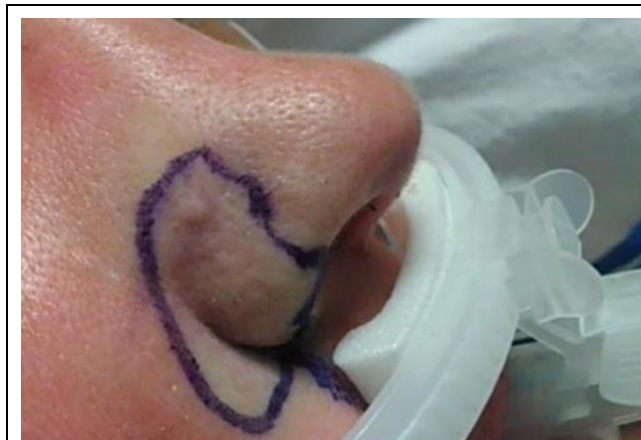


Figure 3: Progressive tissue devitalization: Examination on day three after admission demonstrated progression of devitalized tissue which extended to the skin surrounding the right nares, requiring debridement.



Figure 4: Facial debridement: On day three, the patient's tissue necrosis continued to progress. This image, taken intraoperatively with an endoscopic camera, demonstrates the extent of nonviable tissue removed at after repeated debridement.

The patient remained intubated postoperatively. On the second day of her admission, the patient's hyperglycemia resolved; however, she was found to have a right mydriatic ("blown") pupil. A follow-up head CT scan was again found to be negative for intracranial abnormalities. The patient underwent repeat debridement on day two of her admission, with findings remarkable for progressive necrosis, purulence, and duskiness of the mucosa. On day three, a further repeated debridement demonstrated rapid progression of the necrosis which extended to the surface of the nares (Figure 5) that required facial debridement (Figure 6). On day four, her right eye was deemed to be nonviable after further progression demonstrated on CT scan.

After this rapid progression, surgical options were deemed to be limited to extensive midface resection with orbital excision as the disease had reached the base of the skull with penetration not excluded. It was felt that disease free margins would be difficult to obtain even with aggressive resection. After discussion between the family and medical team the decision was made to pursue comfort care measures only with pain management; the patient expired shortly after extubation on day five of admission.

Discussion

The majority of acute invasive fungal rhino-sinusitis cases involve patients with immunosuppression. Presenting symptoms typically include facial swelling (64.5%), fever (62.9%), nasal congestion (52.2%), ophthalmoplegia (50.9%), facial pain (46.8%), and headache (46.3%). The natural history of the disease ranges from days to weeks and progresses from fungal angioinvasion to resultant tissue infarction and subsequent necrosis. Acute, fulminant sinus infections are usually caused by *Aspergillus*, *Fusarium*, and *Mucorales* [1]. While clinically significant mucor infections primarily affect the upper respiratory system, there have been reports of other significant clinical manifestations including gastric infestations resulting in life-threatening GI bleeds [2].

Diagnostic methods include CT scan, usually sensitive for detecting bony erosions, and MRI, which is more sensitive for soft tissue (e.g. brain, eye) involvement. Orbital involvement can also occur and results in proptosis and fixation of the globe. Confirmation of the disease process and fungal causative agent requires endoscopic biopsy with fungal cultures.

Amphotericin B is used as an empiric antifungal against the possibility of mucormycosis. If mucormycosis is excluded (presence of septate hyphae, unbranched sporangiophore consistent with *Rhizopus* present), transition to voriconazole is usually made. Surgical debridement is an independent prognostic factor for survival, likely due to the decreased fungal burden, removal of avascular necrotic tissue, and increased ability to monitor for remaining disease. Surgical goals include resection of all involved mucosa and bone, as far as the dura mater and periorbital area. Resection to healthy/bleeding tissue is required, including resection of all involved bone. Frozen sections may be useful to guide resection margins. Transdural and intracranial extension portends a poor prognosis. Due to the aggressiveness of the disease process and high mortality rate, this should be considered a surgical emergency. Mortality hovers around 50% [3].

Authors Contributions

Roche Conor: Writing, Researching, Editing paper

Floyd Edward Rand: Researching, Editing paper

Nagpal Avish: Consulting physician, Editing paper

Zreik Khaled: Principal investigator, Editing paper

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