Case Report

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Successful treatment of pulmonary mucormycosis (*Lichtheimia spp.*) in a post-partum patient with COVID-19 ARDS requiring extra-corporeal membrane oxygenation using salvage therapy

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Abstract

Case Summary: A 31-year-old female presented to a regional hospital at 27 weeks pregnant and was found to have COVID-19 ARDS. She underwent intubation and caesarian section for worsening hypoxia and non-reassuring fetal heart tones. Hypoxemia was refractory to proning requiring ECMO and transfer to a tertiary care center. Admission chest radiography showed a new right lower lobe cavitating lesion with computed tomography scan revealing a large multi-loculated cavity in the right lung and extensive bilateral ground-glass opacities. The patient was started on amphotericin and posaconazole, with final respiratory cultures growing Lichtheimia spp. Source control was discussed via possible open thoracostomy, but medical management alone was continued. Total ECMO support was 3 weeks. At the time of discharge to acute rehab, 1 month of amphotericin and posaconazole had been completed, with continuation of posaconazole. At last update, she had been discharged from rehab and was back home with her infant. Conclusion: Pulmonary mucormycosis, even in the non-ECLS population, carries a high mortality. Treatment in pulmonary disease with surgery improves mortality but is not always feasible. Salvage therapy with extended course antifungal medications may be an option for those not amendable

Keywords

extra-corporeal life support, infectious disease, mucormycosis, critical care, pulmonary

Introduction

Fungal co-infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been described in the literature.[1] Mortality in mucormycosis can be as high as 47%; with pulmonary involvement, it approaches 87%.[2] Here we report a case of successful medical treatment of pulmonary mucormycosis in a post-partum patient on VV-ECMO for COVID-19 ARDS.

Case report

A 31-year-old female with quiescent inflammatory bowel disease (not on current treatment) presented to a regional hospital at 27 weeks pregnant (G4P4) with worsening dyspnea for 1 week. Chest radiograph revealed diffuse infiltrates. She was diagnosed with SARS-COV-2-associated (COVID-19) pneumonia

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initially amenable to low-flow O_2 therapy, and consequently committed to remdesivir, dexamethasone (tocilizumab was deferred due to thrombocytopenia[3]), and broad-spectrum antibiotics. She underwent elective intubation and caesarian section on hospital day 5 for worsening hypoxia and non-reassuring fetal heart tones, developing bilateral pneumothoraces requiring chest tube placement (28 Fr) with persistent air leak. Prone positioning and inhaled nitric oxide were trialed briefly for progressive hypoxemia and respiratory acidemia (P/F < 150, PCO2 of 130 mmHg with pH of 7.02) without success necessitating emergent V-V ECMO via right internal jugular 16 Fr (reinfusion cannula) and right femoral 25 Fr (drainage cannula). She was transferred to our center for ECMO management on day 13 post diagnosis at referring facility.

Upon arrival, the patient had extensive subcutaneous emphysema, pneumomediastinum, and bilateral pneumothoraces with air leak. Bronchoscopy with BAL was performed on day 17, revealing a low cycle threshold value (<20 in our institution) for SARS-CoV-2, and she received an extended course of remdesvir (total 10 days). Admission chest radiograph revealed a new right lower lobe cavitating lesion and computed tomography scan revealed a large multi-loculated cavity in the right lung with multifocal peri-bronchial consolidations and bilateral ground-glass opacities (Figure 1). Infectious work revealed a negative aspergillus galactomannan serum, with prior bronchoalveolar lavage (BAL) resulted positive with respiratory cultures growing *Lichtheimia* spp. on hospital day 20, suggestive of pulmonary mucormycosis. Head CT and otolaryngologic evaluation ruled out

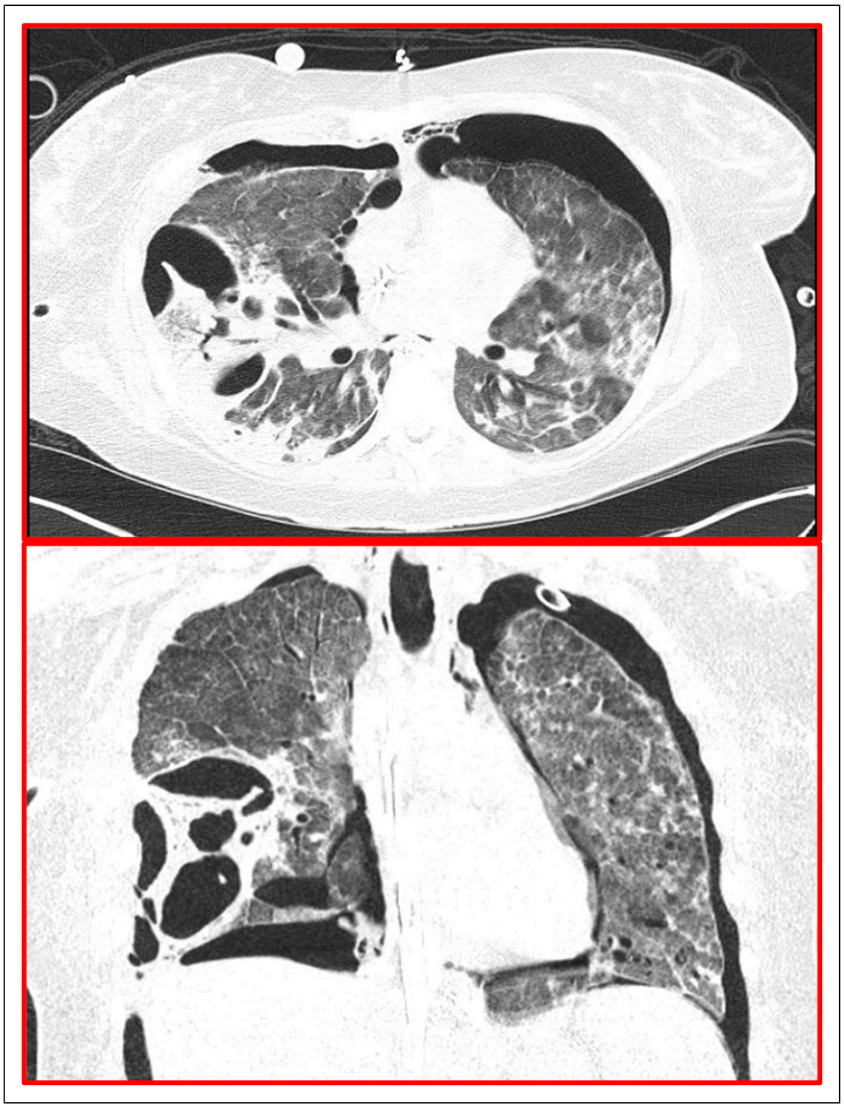

Figure 1. Computed tomography scan of the chest with axial (top), and coronal (bottom) images showing a large multi-loculated cavity in the right lung with multifocal peri-bronchial consolidations and extensive bilateral ground-glass opacities.

rhino-cerebral involvement. The patient was started on amphotericin and Posaconazole. Source control via open thoracostomy was discussed, but given improvement on medical therapy alone, invasive surgical intervention was deferred. Patient underwent a tracheostomy on hospital day 27. On hospital day 28, she underwent bilateral segmental ballooning for grade 4 air leak in an effort to identify potential targets for one-way endobronchial valves day without success. Repeat BAL with cultures was done on day 33, which showed same fungal spp.

ECMO support was gradually decreased and was supplanted by higher inflation pressures on MV as the lung injury resolved, with ventilatory weaning on day 29. The patient was managed solely on ECMO to allow the suspected bronchopleural fistulas to heal, with resolution of air leaks on hospital day 38 and separation from ECMO on hospital day 36 after 25 days.

The patient was transferred to the regular nursing unit on hospital day 38 and underwent tracheostomy de-cannulation on hospital day 42. She was discharged on hospital day 49 to an acute rehabilitation center. She has been maintained on 4 months of therapy (posaconazole), with follow up CT at 2 months post discharge with significant improvement in parenchymal lung disease but with a middle lobe ball-like lesion inside a cavity, partially surrounded by a radiolucent sign (Monod's Sign), compatible with mycetoma. At her 4-months outpatient post hospital discharge follow up, her pulmonary function testing showed normal spirometry, normal total lung capacity, mildly reduced diffusion capacity, with a six-minute walk test that was mildly reduced. At her last Infectious Disease appointment, planned maintenance posaconazole will continue likely at least for 1 year, with serial CTs every 4 months to monitor resolution. Her most recent CT at 8 months post discharge continues to show improvement.

Discussion

Mucormycosis is a fungal infection caused by members of the order Mucorales, (including the family Lichtheimiaceae, which infected our patient).[4] It occurs largely in immunocompromised patients with hematological malignancies and solid organ transplant recipients, but can be seen in patients with diabetes mellitus, iron overload and deferoxamine use.[5] In observational studies, corticosteroid use has also been implicated in increased susceptibility via multiple mechanisms.[6] Furthermore, viral pneumonias are often followed by secondary respiratory infections, including fungal.[7] In our patient, identified risk factors included corticosteroid use and COVID-19 infection. Of note, there was no history of gestational diabetes.

While fungal infections in the ICU are not uncommon, in the ECMO population, Mucorales as a cause of infection is rarely reported.[8] Our literature search showed only 4 cases of mucormycosis on ECMO (renal,[9] intestinal,[10] cutaneous,[11] and disseminated[12]).

Diagnosis is histopathologic, with broad, non-septate hyphae branching at right angles seen on biopsy.[4] Supportive cultures should be present as well. Importantly, serologic tests, namely galactomannan and 1-3-β-D-glucan, are *not* positive in mucormycosis, as Mucorales do not synthesize these cell wall components.[13]

Treatment revolves around correction of underlying pre-existing conditions, source control via surgical resection, and antimycotic therapy.[14] Surgical expertise should be sought, as this has been shown to improve mortality, particularly in pulmonary infection. With pulmonary disease, possible surgical interventions can range from wedge resection to pneumectomy.[15,16]

Amphotericin B and isavuconazole are considered first-line treatment, while posaconazole has variable species-dependent in vitro activity against Mucorales and is used for salvage therapy.[17] A common clinical practice is combination therapy, usually amphotericin B with a newer triazole, such as posaconazole or isavuconazole.[14] BAL cultures in our patient demonstrated sensitivity to amphotericin B, posaconazole and isavuconazole (with resistance to voriconazole), hence salvage therapy with posaconazole was used after discharge. Although ECMO is known to affect the pharmacokinetics of multiple medications, it does not appear to affect posconazole and amphotericin based on case reports.[18,19] To our knowledge, this was the first successful case of medically managed mucormycosis in a post-partum COVID-19 patient requiring ECMO.

Conclusion

Pulmonary mucormycosis carries a high mortality. Treatment in pulmonary disease with surgery improves mortality but is not always feasible. Salvage therapy with extended course antifungal medications may be an option for those not amendable. ECMO support is feasible and can be considered.

Declaration of conflicting interests

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Informed Consent

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