Invasive pulmonary aspergillosis in a COVID-19 recovered patient: unravelling an infective sequelae of the SARS-CoV-2 virus

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Dear Editor,

A 55-year-old, non-smoker, morbidly obese (BMI>35) woman with no other co-morbidities or pre-existing lung disease presented to the emergency room with complaints of high-grade fever, cough with minimal sputum, progressive breathlessness, streaky haemoptysis, and anorexia for the past 5 days. She was admitted to intensive care unit (ICU) for severe COVID-19 pneumonia three months back and had successfully recovered after 24 days of hospitalization. She had received broad-spectrum intravenous antibiotics, antivirals (initially favipiravir then switched to remdesivir), corticosteroids (dexamethasone 6 mg I.V OD), anticoagulation (low molecular weight heparin) and other supportive treatment for COVID-19 pneumonia. After recovery, her medications were discontinued and she was discharged to home on short-term oxygen therapy for residual dyspnoea and hypoxemia (PaO2-53.5 on room air). However, she had multiple hospitalizations for worsening dyspnoea and had received pulse corticosteroid therapy in the next 2 months. On present admission, there was tachycardia, tachypnoea, severe respiratory distress and reduced peripheral oxygen saturation (SpO2-74%) on room air. Arterial blood gas revealed acute respiratory alkalosis and hypoxemic respiratory failure. On chest auscultation, bilateral basal inspiratory crepitations were heard. In view of worsening hypoxemia, she was intubated and put on controlled mechanical ventilation. Chest radiograph showed bilateral fine interstitial shadows and haziness in the lower lung fields. Reverse transcriptase-polymerase chain reaction (RT-PCR) of nasopharyngeal swab was negative for COVID-19 and endotracheal aspirate for microbiological cultures were non-contributory. High resolution computerized tomography (HRCT) of the thorax disclosed bilateral mid and lower zone ground glass opacities with superimposed septal thickening, consolidation in left lower lobe and discrete pulmonary nodules (Figure 1). Bronchoscopy and bronchoalveolar lavage (BAL) were performed to rule out infectious cause. BAL cytology and microbiology was negative for tuberculosis and bacterial infections. However, BAL fluid fungal stain revealed acute angled branching septate hyphae with narrow base and fungal culture grew Aspergillus fumigatus. Serum and BAL galactomannan (GM) levels were significantly raised with GM index of 1.2 and 4.7 of serum and BAL fluid respectively. She was labelled as a case of COVID-19 associated invasive pulmonary aspergillosis (CAPA) and initiated on intravenous voriconazole therapy. There was a dramatic response to antifungal therapy and she was successfully weaned off from mechanical ventilation after 10 days. Finally, after 21 days of hospitalization, she was discharged on antifungals in a hemodynamically stable condition with advice to follow up in OPD and a repeat CT thorax planned after 6-8 weeks of voriconazole therapy.

Pulmonary aspergillosis encompasses a plethora of clinical syndromes predominantly caused by the ubiquitous mould A. fumigatus, depending on the host immune response and pulmonary structural abnormalities [1]. IPA, a severe form of aspergillosis, usually occurs in immunodeficiency states but also has been found to occur in critically-ill immunocompetent patients [2]. Influenza infection can independently predispose to IPA referred to as influenza associated pulmonary aspergillosis (IAPA), occurring in severe influenza related pneumonia and acute respiratory distress syndrome [3]. COVID-19 pneumonia shares similar clinical features with influenza infection and akin to IAPA, “COVID-19 associated pulmonary aspergillosis” (CAPA) have been reported recently in hospitalized patients with severe COVID-19 in the ICUs [4-7] (Table 1). Various mechanisms which have been proposed to predispose to CAPA include exuber-
Table 1. Demographic and clinical characteristics of CAPA patients and their outcomes.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age in years and sex</th>
<th>Co-morbidities</th>
<th>EORTC/MSG risk factors</th>
<th>Microbiological diagnosis of CAPA</th>
<th>Antifungal treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prates et al. [4]</td>
<td>70, M</td>
<td>COPD, DM, OSA</td>
<td>Absent</td>
<td>ETA culture</td>
<td>Voriconazole</td>
<td>Death</td>
</tr>
<tr>
<td>Helleberg et al.  [5]</td>
<td>2 patients 63, F 53, F</td>
<td>HTN, BA</td>
<td>Absent</td>
<td>ETA culture, BAL and serum GM</td>
<td>Voriconazole</td>
<td>Death-2</td>
</tr>
<tr>
<td>Arkel et al. [6]</td>
<td>6 patients Median age-64, all were males</td>
<td>DM, BA, COPD Cardiomyopathy</td>
<td>absent</td>
<td>BAL culture and BAL GM-3 ETA culture-2 Sputum culture-1</td>
<td>Voriconazole and Anidulafungin-5 Liposomal AMB-1</td>
<td>Death-4 Recovery-2</td>
</tr>
<tr>
<td>Rutsaert et al. [7]</td>
<td>7 patients Median age-66, all were males</td>
<td>DM, HTN, OSA, Obesity, hyperlipidaemia, HIV, CKD, AML, IPA, Pemphigus</td>
<td>Present in 2 cases</td>
<td>Histology-4 BAL-1 ETA culture-1</td>
<td>Voriconazole-4 Isavuconazole- 2</td>
<td>Recovery-3 Death-4</td>
</tr>
<tr>
<td>Present case</td>
<td>55, F</td>
<td>Obesity</td>
<td>Absent</td>
<td>BAL culture, BAL and serum GM</td>
<td>Voriconazole</td>
<td>Recovery</td>
</tr>
</tbody>
</table>

DM, diabetes mellitus; HTN, hypertension; OSA, obstructive sleep apnoea; AML, acute myeloid leukaemia; HIV, human immuno deficiency virus; BA, bronchial asthma; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; EORTC/MSG, European organisation for research and treatment of cancer and mycosis study group; AMB, amphotericin B; ETA, endotracheal aspirate.

Figure 1. HRCT thorax axial reformatted images at the level of inferior pulmonary vein shows patchy ground glass opacities (yellow asterix) in bilateral lung fields and a left lower lobe consolidation (red arrow) and a few ill-defined centrilobular nodules.

References


