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Editorial

COVID-19-associated mucormycosis: Looking for the culprit!



The Coronavirus Disease 2019 (COVID-19) pandemic continues to spread worldwide and has led, in its wake, to an increase in cases of opportunistic fungal infections, notably in critically ill patients treated with steroids [1]. Among those, COVID-19-associated pulmonary aspergillosis (CAPA) is the most frequent fungal superinfection and has been reported to affect up to one third of COVID-19 patients [1]. Although less frequent, mucormycosis was also observed in infected patients and might significantly increase morbidity and mortality [2,3]. Recently, thousands of COVID-19 associated mucormycosis (CAM) cases have been reported, almost all from India [3–5].

In this issue of the Journal, Jadaun et al. [6] report a case of a 47-year-old liver transplant (LT) recipient female, with a medical history of diabetes, admitted to the intensive care unit (ICU), five months after transplantation, with a critical COVID-19 treated with steroid therapy. After two weeks of ICU stay, she developed a rhino-cerebral mucormycosis that was rapidly diagnosed and intensively treated. Despite a double antifungal therapy (amphotericin B in association with posaconazole), a large surgical debridement, and tacrolimus and mycophenolate withholding, the patient died after a couple of days.

This case report emphasizes that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) would facilitate the development of mucormycosis particularly in organ transplant recipients [7]. Actually, multiple contributing factors to CAM have been identified including diabetes mellitus, obesity, use of corticosteroid, and the COVID-19 induced immune dysregulation (Fig); all factors observed

in this case report. The question raised here would be to specify the weight of each factor and the possibility of preventing them. In this regard, diabetes mellitus and steroids seem to require more attention from physicians [5]. The presence of diabetes mellitus among patients with COVID-19 varies from 9 to 17% [8] and COVID-19 might have further worsened their glucose profile (inflammation increase resistance to insulin and SARS-CoV-2 itself mediate pancreatic damages). Hyperglycemia leads to phagocyte dysfunction and would predispose to mucormycosis especially when ketoacidosis occurred [9]. Systemic steroids could further exaggerate the underlying glycemic control as well as impede the immune system; this should lead to a precise assessment of the use of high dose corticosteroid. Others factors are COVID-19 induced immune dysregulation, immune suppressive therapy, and traditional host factors for invasive mold diseases such as solid organ transplant, onco-hematological malignancy, and prolonged ICU stay [7,10]. The “endothelialitis” observed in severe SARS-CoV-2 infection could also explain the association between COVID-19 and mucormycosis, knowing that endothelial adhesion and penetration are critical early steps in mucormycosis [11,12]. Last but not least, the presence of high fungal spore burden in certain localities and communities may pose a threat during ongoing pandemic as it has been observed in India [7,10]. Indeed, the etiologic agent of mucormycosis is ubiquitous in nature and may be easily acquired especially via water used in oxygen humidifiers [13]. Also, construction of new hospital zones and restructuring the existing

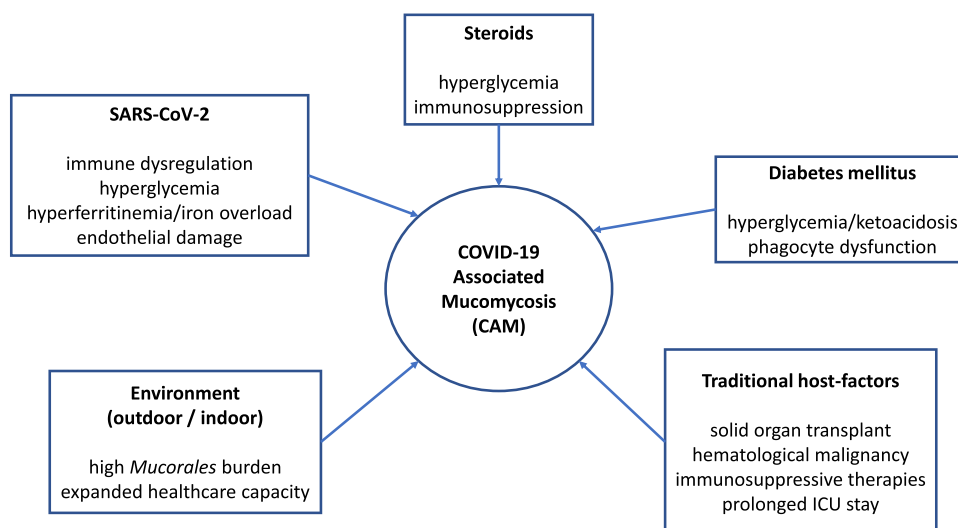


Fig. Risk factors of COVID-19 associated Mucormycosis (CAM).

wards to accommodate the large inflow of patients are common place in this pandemic and can potentially result in an outbreak [7,10]. Vulnerable populations, as the one reported in this case, exposed at high environmental burden of fungal spores would be at the highest risk.

The case reported by Jadaun et al. [6] also points the poor outcome of an invasive fungal infection in an immunocompromised critically ill with COVID-19 with special issues in diagnosis and management [1]. Of note, multi-disciplinary expert committees were formed to handle the task in an evidence-based format to enforce best practices of CAM management [14,15].

During ICU stay, clinical worsening of LT recipients with COVID-19 should prompt physicians to consider diagnoses of invasive fungal infections, especially in patients with recent transplantation, high dose and prolonged steroid therapy, immunosuppressive medicines, and diabetes. In any case, efforts to protect against the coronavirus and reduce intensive care admissions are mandatory in the whole population especially in LT recipients.

Romarc Larcher
Kada Klouche*

Department of Intensive Care Medicine Lapeyronie University
Hospital, Montpellier, France
PhyMedExp, INSERM U 1046, CNRS UMR 9214, University of
Montpellier, Montpellier, France

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