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LETTER

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No time for pending confirmation of invasive fungal disease in critically ill COVID-19 patients—think empirical treatment

Anne-Lise Bienvenu^{1,2*} , Nathalie Bleyzac¹, Jean-Christophe Richard³ and Gilles Leboucher¹

To the Editor,

In a recent study, Wang et al. [1] reported invasive pulmonary aspergillosis in patients with coronavirus disease 2019 (COVID-19), thus claiming for an early intervention with bronchoscopy and the importance of obtaining evidence of fungal microbiology in patients with severe/critical COVID-19. We fully agree on this point considering that invasive fungal infections (IFI), mostly invasive pulmonary aspergillosis, are increasingly reported in COVID-19 patients admitted in intensive care units (ICU); coronavirus-associated pulmonary aspergillosis (CAPA) was demonstrated to affect up to 30% of ventilated patients with COVID-19 [2]. Nevertheless, few issues should be addressed.

First, CAPA diagnosis is challenging. Questions remain if COVID-19 patients have a true invasive aspergillosis or are just colonized with *Aspergillus* in regards with serum galactomannan negativity [3]. Nevertheless, an independent association between CAPA and 30-day mortality was recently demonstrated using a multivariate logistic regression model among intubated patients [2], although a causal link remains to date unproven.

Second, the use of corticosteroids or anti-IL6 antibody in addition to standard of care is proposed for critically ill patients with COVID-19. But corticosteroids are well-known risk factors for IFI and identified as a negative outcome predictor of invasive aspergillosis [4], whereas

IFI were reported in patients treated with anti-IL6 antibody [5]. Thus, it is expected that incidence of IFI may increase with the more extensive use of corticosteroids or other immunomodulating therapies, and this, mostly in patients with risk factors for CAPA such as older age, initial antibiotic usage of beta-lactamase inhibitor combination, and chronic obstructive pulmonary disease (COPD) [1].

In this context, it is urgent to consider the opportunity of empirical use of antifungals without waiting for the final evidence of fungal microbiology, in case of a clinical suspicion of IFI. This is especially true for critically ill COVID-19 patients receiving immunomodulating therapies. Certainly, it will be most of the time an off-label use of antifungals in ICU patients, but what a prize to win under the emergency conditions of COVID-19 pandemic. Antifungal stewardship programs should support the implementation of such strategies, including the discontinuation of antifungals with negative mycological results and the impact assessment of antifungal use in terms of efficacy, safety, drug interactions, and resistance emergence.

Abbreviations

CAPA: Coronavirus-associated pulmonary aspergillosis; COVID-19: Coronavirus disease 2019; ICU: Intensive care units; IFI: Invasive fungal infections; COPD: Chronic obstructive pulmonary disease

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Authors' contributions

ALB has contributed to the conception of the manuscript and wrote the first draft. NB, JCR, and GL were major contributors in writing the manuscript. All authors read and approved the final manuscript.

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