Letter to Editor

Candidiasis in COVID-19 Patients

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Dear Editor-in-Chief

Based on previous studies, some comorbidities influence the morbidity and mortality of COVID-19 disease[1]. Among these factors, opportunistic fungal infections could have a major impact on the mortality of COVID-19 patients[2]. Two reasons are assumed to play important roles in compromising the immune system[8] of patients during the early stages of COVID-19 disease. The first one is a significant decrease of different cell components, essentially microphages, neutrophils, and lymphocytes. The second one is the downregulation of tight junction proteins and the integrity and barrier function of the epithelium of many body organs, such as lung, intestine, and brain impairs[3]. The immune response varies based on the anatomical site of infection and the fungal species. However, defects in cell-mediated immunity and breakdown of mucosa or integument are the main etiology of fungal infections[4]. In addition, severe COVID-19 patients have a higher risk of other infections due to invasive ventilation as well as usage of immunosuppressive medications and especially antibiotics[2].

Fungal infection of the central nervous system (CNS) is rare; however, it is associated with a poorer prognosis and a higher morbidity rate, compared to other infections of CNS[5]. The severity of CNS fungal infections mainly depends on the host immune status and virulence of the fungal strain. These infections have become remarkably common during recent years, especially in immunocompromised hosts[6]. The common route of fungal infection is through inhalation of aerosolized fungi which causes infection in the lungs. Generally, in immunocompromised patients, infection through this route spreads to other organs and results in hematogenous dissemination that could affect CNS[5,6]. In immunocompromised patients, the common agents causing CNS fungal infections are species from *Candida*, *Aspergillus*, and *Cryptococcus* genera[6].

During the COVID-19 pandemic, the incidence of fungal infections has increased significantly. It is noteworthy that the most common agents responsible for these fungal infections are from *Aspergillus* and *Candida* genera[7]. *Candida* species are the most isolated fungi responsible for invasive infection of extrapulmonary sites in COVID-19 patients[2, 7, 8]. Due to the haematological dissemination of *Candida* species, they commonly form abscesses in different areas of the brain. Consequently, meningoencephalitis occurs in the early stages, and by the progress of the infection, the late stages result in cerebral infarction and major complications[5].

Table 1: Studies that reported extrapulmonary candidiasis in COVID-19 patients.

Study	Country	Site of infection	Mortality	Common species
Salehi *et al.*[2]	Iran	Oropharyngeal candidiasis	NM	*C. albicans*
Agrifoglio *et al.*[9]	Spain	Disseminated candidiasis	40%	*C. albicans*
Seitz *et al.*[10]	Germany	Disseminated candidiasis	0% *	*C. glabrata*
Cataldo *et al.*[11]	Italy	Disseminated candidiasis	NM	*C. parapsilosis*
Hughes *et al.*[12]	United Kingdom	Disseminated candidiasis	NM	*C. albicans*
Pemán *et al.*[13]	Spain	Disseminated candidiasis	11%	*C. albicans*
Antinori *et al.*[14]	Italy	Disseminated candidiasis	NM	*C. parapsilosis* *C. tropicalis*
		Endocarditis		*C. albicans*
		Endophthalmitis		*C. albicans*
Rawson *et al.*[15]	United Kingdom	Disseminated candidiasis	NM	*C. albicans*

NM: not mentioned
*: case report study

As mentioned above, in addition to the direct effects of COVID-19 on the immune system, different medical procedures could predispose COVID-19 patients to opportunistic fungal infections in different sites, such as CNS[6]. Due to different clinical manifestations of COVID-19, fungal co-infections were not identified in many cases. Moreover, due to inadequate sampling and empirical therapy for these infections, the clinicians face many challenges during the treatment of COVID-19 and fungal co-infections[7,16]. Overall, the fungal infections of CNS are rare; however, they are one of the major concerns due to the higher chance of occurrence in such vulnerable patients. Therefore, an early diagnosis and usage of proper medical procedures are essential for the prevention of the dissemination of fungal infections and the reduction of their high mortality rates.

Keywords: COVID-19, Candidiasis, CNS fungal infections

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