MUCORMYCOSIS AND COVID-19 PANDEMIC: AN ADDITIONAL CHALLENGE

MUCORMICOSE E PANDEMIA DE COVID-19: UM DESAFIO ADICIONAL

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DOI - 10.5935/2236-5117.2021v58a62

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Declarations of interest: none to disclaim.

Dear Editor,

We have read some articles recently published in international Journals with comments on misdiagnoses involving viral, bacterial, fungal or parasitic infections in the COVID-19 pandemic.^{1,2} Switzerland specialists in Internal Medicine, Pneumology, and Radiology reviewed data at admission of 344 patients (210 abnormal chest CT-scans and 172 positive swabs for SARS-CoV-2). 38 had additional work-up and were included, 20 were females, and the average age was 66 years. Alternative diagnoses (near 20%) were 22 bacterial pneumonias, pulmonary embolism, acute heart failure, chronic obstructive pulmonary disease exacerbation, and 3 no respiratory-related conditions. Other identified infectious agents included *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Mycoplasma pneumoniae*, *Legionella pneumophila*, Adenovirus, Human coronavirus OC43, and *Pneumocystis jirovecii*. The hospital mortality rate was elevated (10.8%).¹ The authors emphasized the role of differential hypotheses in sceneries of pandemics because the earliest correct diagnosis and adequate management of concomitant conditions affect the outcomes.¹ In this setting, one must highlight the recent article by Pasero *et al.* about challenges related to the coexistence of SARS-CoV-2 and necrotizing pulmonary mucormycosis in a 66-year-old male.² Predisposing factor to pneumonia with cavity

was the significant lymphopenia due to COVID-19. His symptoms started one week before admission, he utilized a schedule of hydroxychloroquine plus lopinavir and ritonavir for 10 days, and further also underwent mechanical ventilation at ICU. CT-scans revealed opacification and thickening with sclerosis of the left maxillary sinus, in addition to cavitary lesions in the lingular segment of the left lung. Microbiological study of bronchial aspirate revealed the diagnosis of *Rhizopus spp.* and the patient underwent liposomal amphotericin B [L-AmB], posteriorly shifted to isavuconazole, but he died at day 62 after the ICU admission.² The authors called attention to opportunistic mycoses to be also investigated in cases of COVID-19, and antimicrobial therapy including antifungal agents when consistent data suggest mucormycosis.²

Mucormycosis is an uncommon infection by Mucorales, with a severe invasive course in people with hematological malignancy, solid organ or stem cell transplant, and diabetes mellitus.^{2,7} This opportunistic infection has an angioinvasive property causing tissue necrosis and thrombosis; and species of the *Rhizopus*, *Mucor*, and *Lichtheimia* (*Absidia*) genera are more often involved.³ Pulmonary mucormycosis due to the inhalation of spores can cause pneumonia with lung necrosis and cavity, and may spread to mediastinum and heart or to distant sites by hematogenous route.^{2,7}

Jeurkar *et al.* reported a 64-year-old woman with an acute myeloid leukemia [AML] and allogeneic transplant who had angioinvasive mucormycosis and central nervous system infarction.⁴ Pulmonary infection was the most probable primary source of the severe disseminated condition. The authors stressed the exceeding unusual occurrence of mucormycosis-related intracerebral swelling, and possibility of unsuspected or underreported mucormycosis in transplanted patients.⁴ Qi *et al.* reviewed clinical data, treatment, and prognosis of 7 patients with diagnosis of mucormycosis; 4 were males, and median age was 36 (19-79) years.⁵ Predisposing conditions were AML (2), acute B lymphoblastic leukemia, T-cell lymphoma, chronic myelocytic leukemia in blastic phase, myeloproliferative neoplasm, and severe aplastic anemia after the transplantation. Clinical forms were pulmonary in 4 patients, disseminated, rhino-orbital-cerebral, and cutaneous. The utilized antifungal drugs

were amphotericin B, L-AmB, and posaconazole; and 4 patients had surgical treatment (3 radical debridements) but the mortality was elevated (57%). The authors emphasized early diagnosis, control of the base disease and the immunosuppressive status, prompt effective antifungal treatment, and radical surgical debridement improving the survival rate.⁵ Ribeiro *et al.* reported a 38-year-old woman with AML, neutropenia, and invasive mucormycosis.⁶ Three months before admission she had febrile leucopenia and underwent vancomycin plus cefepime further changed by meropenem and L-AmB. Chest CT detected pleural effusion and bilateral interstitial infiltrate and bronchoalveolar lavage detected *Candida spp.*, while blood cultures were positive for *Candida zeylanoides* treated by caspofungin and voriconazole. CT of control showed pulmonary nodules and a voluminous splenomegaly with scattered hypoattenuated lesions. Splenectomy and biopsy of hepatic lesions established the final diagnosis of mucormycosis. The management was successful including L-AmB, deferasirox, and hyperbaric oxygen therapy. The authors highlighted classical features of this rare condition and the usual treatment challenges.⁶ Shao *et al.* reported a 56-year-old female with AML and pulmonary mucormycosis complicated by lung infarction.⁷ She had productive cough, and chest CT showed widened pulmonary artery, thick-walled cavity in the left upper lobe, consolidation in the left lower lobe, and left pleural effusion. Bronchial biopsy revealed the diagnosis of mucormycosis, treated by L-AmB and posaconazole. She further had hemoptysis and imaging studies revealed a large pulmonary embolism and a bronchopleural fistula. Soon after pneumonectomy the AML relapsed and she died three months later. The authors emphasized the early diagnosis, control of risk factors, antifungal drugs, and wide surgical excision to decrease mortality (96% in disseminated and 76% in lung mucormycosis).⁷ COVID-19 and mucormycosis share a propensity to thromboembolisms and pulmonary infarctions, phenomenon that increases the possibility of under diagnosis and misdiagnosis in dual infections.^{1,3}

ABSTRACT

The authors comment international articles recently published about the possibility of misdiagnoses involving viral, bacterial, fungal or parasitic infections in the COVID-19 pandemic. The awareness about differential diagnosis during pandemics is highlighted because the earliest correct diagnosis and adequate management of concomitant conditions affect the outcomes. Additional comments are related to mucormycosis and COVID-19 dual infections.

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