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COVID-19 associated with concomitant mucormycosis and aspergillosis



Dear Editor,

In addition to SARS-CoV-2 itself, secondary infection with other fungus can develop in patients with COVID-19, especially for severe or critically ill patients.^{1,2} However, concomitant pulmonary mucormycosis and aspergillosis was extremely rarely for COVID-19 patient.³ Herein, we reported an unusual case of critical COVID-19 developed concomitant pulmonary mucormycosis and aspergillosis.

A 70-year-old man presented with fever, cough with sputum and dyspnea for four days. His nasopharyngeal swab polymerase chain reaction test was positive for SARS-CoV-2. Chest radiography showed diffuse increase infiltrations. Emergent endotracheal intubation was done for acute hypoxemic respiratory failure and dexamethasone 6 mg daily and tocilizumab 600 mg once were given. Empirical antibiotic with ceftaroline and levofloxacin were added for covering co-infections. On Day 7, the culture from endotracheal aspirate yielded *Candida albicans* and *Aspergillus* spp. and the aspergillus galactomannan antigen from non-bronchoscopic lavage (NBL) showed 11.018. Voriconazole and anidulafungin were added. However, a large pneumatocele was observed over left upper lobe (Fig. 1A, arrow) in the follow-up of radiography. Thus, antifungal agent was switched to liposomal amphotericin B with dose of 400 mg per day (5 mg/kg/day) on Day 13. On Day 30, he had sudden onset of dyspnea and desaturation and chest radiography disclosed left pneumothorax. Thoracostomy was conducted for drainage and turbid pleural fluid with exudative characteristics was sent for microbiological investigation. Because no clinical improvement was observed, isavuconazole (200 mg once daily followed by 200 mg every 8 h for two days) was added on Day 32, and increased liposomal amphotericin B dose to 800 mg per day (10 mg/kg/day).

Mold isolates recovered from endotracheal aspiration and pleural fluid were sent for identification by morphological characteristics and sequence analysis of the internal transcribed spacer (ITS) region and additional calmodulin gene for *Aspergillus* spp. The former yielded *Aspergillus terreus*, and the latter Mucorales (*Cunninghamella bertholletiae*, Fig. 1B). Unfortunately, the clinical condition still deteriorated and finally he died on Day 43.

This is the first case of COVID-19 associated with concomitant pulmonary mucormycosis and aspergillosis in Taiwan. The diagnosis of mucormycosis in the present cases was based on the isolation of *C. bertholletiae* which was identified by initial morphological characteristics and confirmed by further ITS sequencing from the sterile specimen. Thus, the present case could be diagnosed as COVID-19 associated proven mucormycosis and probable aspergillosis.^{4,5}

Both invasive pulmonary aspergillosis and mucormycosis share similar risk factors, including use of corticosteroid, underlying immunocompromised status (hematological malignancy, organ transplant, using immunosuppressant or chemotherapy) and neutropenia.^{4,5} Additionally, diabetes mellitus, especially for uncontrolled diabetes with ketoacidosis was the most common risk factor of mucormycosis.⁴ The present case had only COPD, but he did not have underlying immunodeficiency or diabetes mellitus. However, he received prolonged corticosteroid for managing his severe COVID-19. Only three issues – corticosteroid, tocilizumab and COVID-19 could be the precipitating factors causing the development of concomitant pulmonary mucormycosis and aspergillosis in this patient.

In conclusion, this report is to highlight the need for a high clinical suspicion for coinfection with mucormycosis and aspergillosis in critical COVID-19 patients.

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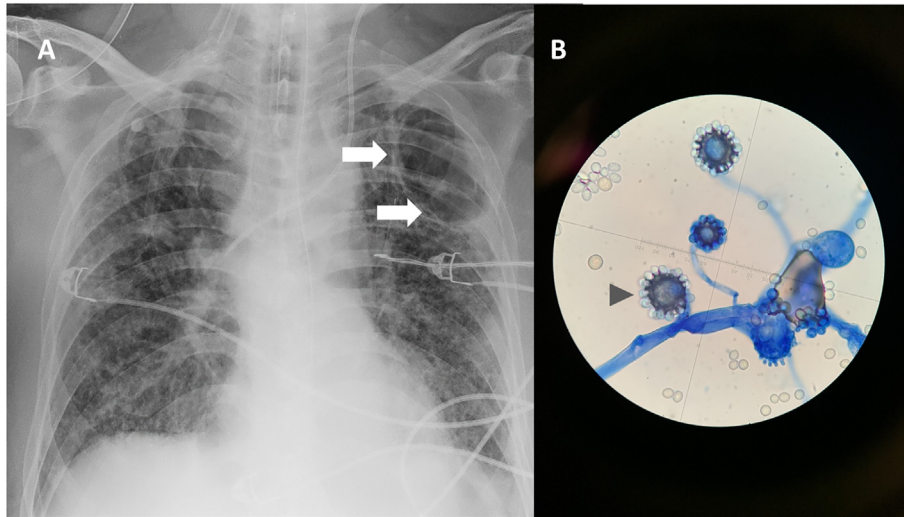


Figure 1. (A) Chest radiography showed a large pneumatocele (arrow) was observed over left upper lobe (B) Pleural fluid culture grew *Cunninghamella bertholletiae*, demonstrating characteristic single-spored sporangia (arrow head) (lactophenol cotton blue stain, 1000x magnification).

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