A case of COVID-19 complicated by Klebsiella pneumoniae, Cytomegalovirus, Aspergillus and Zygomycete infections

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Abstract

Co-infection between SARS-CoV-2 and other pathogens have become a serious threat. There are reports of fungal, bacterial and viral co-infections with SARS-COV-2. Herein, we report the unusual case of concomitant aspergillosis, mucormycosis, cytomegalovirus pneumonia and also klebsiella pneumoniae empyema as the complication of COVID-19 infection.

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Abstract

Co-infection between SARS-CoV-2 and other pathogens have become a serious threat. There are reports of fungal, bacterial and viral co-infections with SARS-COV-2. Herein, we report the unusual case of concomitant aspergillosis, mucormycosis, cytomegalovirus pneumonia and also *klebsiella pneumoniae* empyema as the complication of COVID-19 infection.

Keywords: CMV, *Klebsiella pneumoniae* , mixed infection, SARS-COV-2, mucormycosis, aspergillosis

Key messages:

Secondary infections or co-infections are identified between SARS-CoV-2 and other pathogens. This entity have become another serious threat in the treatment of patients with COVID-19 infection which should not be neglected.

Introduction

Secondary infections or co-infections are commonly identified in severe influenza and also other severe respiratory viral infections with high mortality and morbidity rate [1]. Co-infection between SARS-CoV-2 and other pathogens have become another serious threat in the treatment of patients which should not be neglected [2]. These co-pathogens are including bacteria, such as *Streptococcus pneumoniae* and*Staphylococcus aureus,* fungal pathogens including*Aspergillus* or *Mucorales* species and also viruses such as influenza, and rhinovirus/enterovirus [3]. Herein we report the first case of concomitant aspergillosis, mucormycosis, cytomegalovirus (CMV) pneumonia and also *klebsiella pneumoniae* empyema as the complication of COVID-19 infection who had a favorable clinical outcome.

Case presentation

A 68-year-old diabetic man was presented to the emergency department with a five days history of fever (38.7 °C), dry cough, and dyspnea (SpO2 was 90% - room air). He was on oral hypoglycemic agent (metformin 500 mg every 12 hours) for several years. Laboratory studies showed elevated C reactive protein

(120 mg/dl), and RT-PCR confirmed SARS-COV-2 diagnosis. High-resolution chest CT scan obtained at admission was consistent with COVID-19 pneumonia. The patient received remdesivir and dexamethasone and was discharged after 9 days with improvement of signs and symptoms. After 12 days the patient was re-admitted because of severe dyspnea and fever. Chest CT scan revealed left sided pleural effusion and the chest tube was inserted and discharged after seven days with improvement of dyspnea. After 10 days the patient was referred to our center for the first time, because of malaise, fever, chills and purulent discharge at previous chest tube excite site.

At admission the patient was febrile and the vital signs were as following: PR: 110 beats/min, RR: 25 breath/min T: 38.5 and BP: 120/90 mmHg. The initial laboratory data were as following: white blood cell count (WBC): 4900/mm^3 (neutrophils: 83%, lymphocytes: 8%), hemoglobin (Hb): 10.2 gr/dl, platelets (PLT): 250,000/mm^3, blood sugar: 187 and creatinine: 1.1 mg/dl. Also COVID-19 PCR was reported positive. Pleural fluid was sent for analysis, bacterial and fungal smear and culture. Blood cultures were negative. The pleural fluid analysis were as following: turbid appearance, white blood cell >500,000, polymorphonuclear 90%, lactate dehydrogenase (LDH) 26,448 U/L, sugar <10 mg/dl, protein 2.9 gr/dl, albumin 1.9 gr/dl. Serum LDH level, total protein and albumin were 523 U/L, 5.1 gr/dl and 3.2 gr/dl respectively, indicative of empyema and chest tube was inserted.

Imipenem 500 mg every 6 hours and vancomycin 1 gr every 12 hours were started as empiric treatment. The result of culture was reported*klebsiella pneumoniae* which was sensitive to meropenem and also imipenem. The vancomycin was discontinued and imipenem with amikacin was continued. The patient presented extensive subcutaneous emphysema in both sides and left chest tube was inserted (Figure 1). After several days the left sided chest tube was came out. According to the right sided empyema and no significant improvement, the patient underwent right thoracotomy with decortication. In addition, right upper lobe and right lower lobe wedge resection, hilar lymph node biopsy and partial pleural peel resection was performed. After the operation, the whole lung was expanded and an anterior and posterior chest tube was implanted for the patient.

In histopathology right upper lobe wedge resection, revealed severe suppurative necroinflammatory process associated with presence of a few partially degenerated fungal hyphae (both wide and irregular). Right lower lobe wedge resection showed extensive severe suppurative necroinflammatory process associated with presence of numerous fungal hyphae (both wide and irregular). Also vessel wall infiltrated by several fungal hyphae including both thin and broad fungal hyphae and calcium oxalate crystals accompanied by fungal hyphae was indicative of aspergillosis (Figure 2).

Hilar lymph node, biopsy revealed fibro-inflammatory process including foci of anthracotic pigment deposition. Fibro-adipose tissue showed bland looking gland like structures, patchy lymphocytic infiltration and presence of few large cells with cytopathology suggestive of CMV infection. Immunohistochemistry (IHC) was performed and confirmed the diagnosis of CMV pneumonia (Figure 3).

According to the invasive fungal infection with both *Aspergillus*and *Mucoraceae* species and also with the diagnosis of CMV disease, the liposomal amphotericin B, 5 mg/kg/day and intravenous gancyclovir 5 mg/kg every 12 hours were initiated. Also the imipenem with amikacin was continued for *Klebsiella pneumoniae* empyema. The patient signs and symptoms were improved and was afebrile. After discontinuation of amphotericin B and intravenous gancyclovir course, posaconazole oral suspension 200 mg every 6 hours and valgancyclovir 900 mg every 12 hours was started. The patient was discharged after one month with favorable clinical outcome.

Discussion

The possibility of SARS-CoV-2 co-infections with bacterial, fungal and also viral pathogens should not be neglected. Fungal co-infections among hospitalized patients with COVID-19 is a challenging issue. Few recent studies revealed cases of COVID-19 infection involving more than one species of aspergillus or concomitant two different fungal infections. Costache et al. reported a case of COVID-19 associated pulmonary aspergillosis with both *Aspergillus fumigatus* and*Aspergillus flavus* with favorable outcome [2]. Johnson et al.

reported a case of combined probable pulmonary aspergillosis and possible mucormycosis in a diabetic male with COVID-19 in the ICU who treated with liposomal amphotericin B [3].

Critical illness is an important risk factor for CMV reactivation due to immunosuppression. Although co-infections with CMV are frequent in the critically ill patients, but the impact on COVID-19 patients is unclear. Moniz et al. presented five case reports of CMV reactivation in COVID-19 patients admitted to the ICU with respiratory failure [4]. It has been well described that critical or severe illness can induce immune suppression. The most common laboratory finding in patients with COVID-19 is lymphopenia, which correlate to diseases severity. Recent findings revealed that disease severity is dominated by the decline in cell-mediated immunity especially the decrease in T cell counts [5]. On the other hand, number of iatrogenic factors including the usage of corticosteroids in the treatment of severe COVID-19 may predispose the patients to other infection [6]. In addition to ICU admission and mechanical ventilation, other entities including transfusions, sepsis, corticosteroids and acute respiratory distress syndrome have also been found to be associated with the risk of CMV reactivation [7].

In a minority of patients, bacterial and fungal co-infections can complicate the course of COVID-19 infection. In a retrospective study, the second most common respiratory pathogen detected from patients with COVID-19 was *Klebsiella pneumoniae* [8, 9]. Montrucchio et al. reported patients with COVID-19 related acute respiratory distress syndrome who developed invasive infections due to carbapenemase-producing Klebsiella pneumoniae [10]. In our patient, the culture of empyema and visceral pleural peel, confirmed the superimposed of *Klebsiella pneumoniae* infection on COVID-19.

Tissue invasion by a filamentous fungus through histopathological examination of biopsy, provides a diagnosis of proven invasive fungal infections and positive culture of *Aspergillus* from the specimen is required to make a proven diagnosis of invasive aspergillosis [11]. In our case, right upper lobe wedge resection and right lower lobe wedge resection revealed wide and irregular fungal hyphae indicative of mucormycosis. Also vessel wall infiltrated by several thin and also broad fungal hyphae. Calcium oxalate crystals accompanied by fungal hyphae was indicative of aspergillosis. Definitive diagnosis of CMV pneumonia is determined based on lung tissue samples by histopathologic testing and immunohistochemical analysis [12]. According to the data, our case is consistent with the proven CMV pneumonia.

According to the histopathology and IHC, our patient had pulmonary aspergillosis, mucormycosis, and CMV disease with *Klebsiella pneumoniae* infection. The combined risk factors including diabetes mellitus, recent corticosteroid treatment and also COVID-19 per se, contributed to concomitant infections in our patient which is a unique report.

Conclusion

Secondary infections or co-infections are identified between SARS-CoV-2 and other pathogens. This entity have become another serious threat in the treatment of patients with COVID-19 infection which should not be neglected.

Author contributions

P.T; M.PT; A.H; Z.A; A.M; M.R and M.MD acquired data, analyzed and interpreted the data. A.H wrote the first draft of the manuscript. All authors have read and approved the final manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

Ethical statement:

This research was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and written informed consent was obtained from the patient.

Data availability statement:

Data sharing is not applicable to this case report type article as no new data were created or analyzed in this study.

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Figure legends

Figure 1. Multiple thick wall cavitary lesions in right upper lobe and ground glass opacities with complicated pneumothorax, pneumomediastinum and subcutaneous emphysema.

Figure 2 (A), Suppurative necrosis including several fungal hyphae, (B), vessel wall infiltrated by several fungal hyphae including both thin and broad fungal hyphae, (C), calcium oxalate crystals accompanied by fungal hyphae indicative of aspergillosis.

Figure 3 (A), Endothelial cells with cytoplasmic change of CMV, (B), IHC with CMV antibody confirming CMV cytopathic change.

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zygomycete-infections