

A 67-Year-Old Man with a History of COVID-19 Infection, Cough, and Hemoptysis

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WHAT IS YOUR DIAGNOSIS?

A 67-year-old man with a history of COVID-19 infection was admitted to our hospital due to cough and hemoptysis. The patient was hospitalized with a COVID-19 diagnosis (positive PCR assay) 50 days ago in another hospital and had been treated with remdesivir and high dose steroid (methylprednisolone 500mg for three days followed by dexamethasone) after which he developed hyperglycemia and the creatinine level was increased. After improving from COVID-19, the patient has developed a productive cough, which has been exacerbated recently. During the last two weeks, the patient has become febrile. He had an episode of massive hemoptysis five days before. The patient had a history of hypertension and ischemic heart disease but he was not diabetic. On physical examination, the patient was ill with stable vital signs. On pulmonary examination crackles were heard on the right lung. Other physical exams were unremarkable. Laboratory tests are summarized in Table 1. Abdominopelvic sonography was normal. In echocardiography, the patient had an ejection fraction (EF)=40%. Figure 1 shows chest computed tomography (CT) on the first day of the second admission.

Table 1. Laboratory tests

Analysis	Result	Normal range	Analysis	Result	Normal range
WBC ^a , × 10 ⁹ /L	8.2	4-11	Aspartate aminotransferase, IU/L	28	5-40
Neutrophil, %	86.7		Alanine aminotransferase, IU/L	44	5-40
Lymphocyte, %	7.4		Lactate dehydrogenase, IU/L	591	Up to 530
Monocyte, %	5.8		D-Dimer, ng/dL	1853	Up to 500
Eosinophil, %	0				
Basophil, %	0.1		Prothrombin time, sec	13.4	11-14
Hemoglobin, g/dL	9.4	13-16	Partial thromboplastin time, sec	30	25-38
Platelet, × 10 ⁹ /L	180	150-450	International normalized ratio	1.05	
Erythrocyte sedimentation rate, mm/hr	30	0-30			
C-reactive protein, mg/L	25	Up to 10	COVID PCR	Negative	
Urea, mg/dL	65	18-55	Human immune deficiency virus antibody	Non reactive	
Creatinine, mg/dL	1.5	0.7-1.4			
Sodium, mEq/L	126	135-145			
Potassium, mEq/L	4.7	3.5-5.0			

^aWhite blood cells

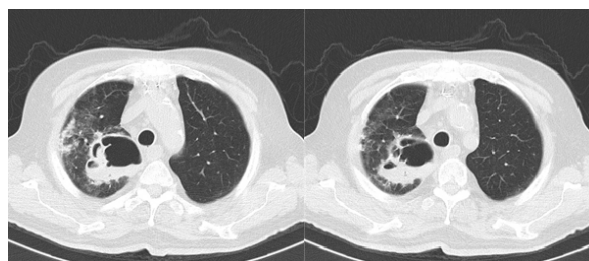


Figure 1. Patient's chest CT scan

Answer

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Klebsiella Pneumonia and Pulmonary Aspergillosis

Chest CT showed ground-glass opacities and a cavitary lesion in the upper lobe of the right lung. Sputum smear was negative for acid-fast bacilli (AFB). Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) was isolated from sputum. Also, the sputum smear revealed yeast and pseudo mycelium, and sputum PCR for *Aspergillus* and *Candida Albicans* was positive. In blood culture *Klebsiella pneumoniae* was grown. Antibiogram confirmed CRKP. *Klebsiella pneumoniae* and *Candida* species were isolated from bronchoalveolar lavage (BAL). Serum and BAL galactomannan were 0.9 and 4, respectively .

Bacterial and fungal superinfections have a significant negative effect on the COVID-19 course (1, 2). *Klebsiella pneumoniae*, a gram-negative bacillus, a normal flora of the intestine, skin and oral cavity, majorly involves immunocompromised patients (3). As reported, *Klebsiella spp.* is the etiology of 15 percent of hospital-acquired bacterial coinfections in COVID-19 patients (1). According to recent studies, there has been an increase in the Carbapenem-resistant Enterobacteriaceae (CRE) during the COVID-19 era (4). The similarity of COVID-19 presentations to community-acquired bacterial pneumonia, lack of a definite COVID-19 treatment, and complication of COVID-19 with bacterial and fungal pathogens have pushed clinicians towards widespread use of empirical antimicrobial therapies. As a result, more than 50% of hospitalized COVID-19 patients are treated with IV antibiotics, leading to an increased rate of antibiotic resistance (4, 5).

COVID-19, like influenza, by developing acute respiratory distress syndrome (ARDS), prone patients to Aspergillosis (6). Regarding prevalence, survival rate, and time to diagnosis following intensive care unit (ICU) admission, COVID-19-associated pulmonary Aspergillosis (CAPA) is similar to Influenza-associated pulmonary Aspergillosis (IAPA). CAPA is mainly diagnosed by testing galactomannan level and culture of BAL fluid obtained by bronchoscopy (6). Although bronchoscopy is rarely performed for COVID-19 patients, and the absence of a standard definition for *Aspergillus* has made it difficult to comment on its actual emergence rate in patients with COVID-19 ARDS, recent studies have reported increased incidence of CAPA (2, 5, 6).

Primary viral infections predispose to secondary infections by weakening immune responses (7). Also, the diminished number of lymphocytes and the hyper inflammation state caused by COVID-19 make way for the emergence of *Aspergillus* (6). Lung injury and developing ARDS are other factors can induce superinfections by bacteria and *Aspergillus* (6, 8). COVID-19 anti-inflammatory therapies with corticosteroids and immune modulators such as steroids and probably tocilizumab underline the dysregulated immune responses during the course of illness (2, 8).

Primarily, our patient was empirically treated with piperacillin/tazobactam and caspofungin. Due to life-threatening massive hemoptysis, surgical intervention was considered but the risk of surgery was estimated very high and thoracotomy was not performed. As an alternative, bronchial artery angioembolization was done. After isolation of CRKP, we replaced piperacillin/tazobactam with high dose meropenem and polymyxin E (colistin) for three weeks. Caspofungin was changed to voriconazole and continued for two months. The patient's symptoms improved dramatically and cavitary lesion regressed after two months. Hemoptysis was not repeated (Figure2).



Figure 2. Chest CT of patient two months after treatment initiation

In conclusion, when confronting post-COVID-19 patients we have to consider superinfections with bacteria and opportunistic fungi. We recommend improving antimicrobial stewardship programs and appropriate use of immune modulators and antibiotics in the course of COVID-19.

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