CLINICAL VIGNETTE

Cavitary Lung Disease as a Late Complication of COVID-19 Infection

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Case Report

A 65-year-old female was seen for outpatient follow up one month after hospitalization for COVID-19 pneumonia and acute hypoxemic respiratory failure. She presented with fever, cough, loss of taste and smell with initial arterial oxygen saturation of 62% as measured by pulse oximetry. Chest radiograph revealed bilateral patchy ground glass infiltrates. Pertinent laboratories on admission revealed C reactive protein (CRP) of 9.23 mg /dl (normal < 0.49), D Dimer 607 ng/ml (normal <230), LDH 856 units/L (normal<250).

The patient was supported by high flow nasal cannula (HFNC). Infectious Disease and Pulmonary consultations were obtained. The patient was treated with solumedrol IV 40 mg every 12 hours, remdesivir and tocilizumab.

She slowly improved with decreasing oxygen requirements and was discharged after 12 days with supplemental oxygen at 2 liters nasal cannula.

The patient completed a tapering course of prednisone 10 days after discharge. Symptomatically she complained of persistent cough productive of lesser amounts of yellow sputum with an occasional streak of blood. She denied any fever, chills, night sweats or chest pain, but reported occasional wheezing. She had been prescribed a budesonide/formoterol inhaler but had not been using it consistently.

Past medical history revealed hypothyroidism and remote smoking, stopping 40 years ago. There was no history of diabetes.

On physical examination the patient was afebrile. She appeared comfortable and in no distress with oxygen saturation 100% on 2 liters nasal cannula. Auscultation of the lungs revealed mild expiratory wheezing and scattered rhonchi. There was no peripheral edema.

Laboratory data included normal WBC and differential. CRP was normal at 0.5 mg/dl. Sedimentation rate was elevated at 91 mm/hr. D Dimer 690 ng/ml.

The patient was prescribed a five-day course of azithromycin. Her bronchospasm was treated with 5 days of prednisone 20 mg once daily and she restarted budesonide/formoterol inhaler.

Follow up visit 2 weeks later found the patient feeling much better off supplemental oxygen with minimal cough and resolution of wheezes. Repeat sedimentation rate had normalized to 19 mm/hr. She was continued on her maintenance inhaler.

One month later, ten weeks after hospital discharge, the patient developed hemoptysis of bright red blood of approximately 5cc without associated symptoms. She denied fever, night sweat, chest pain or dyspnea. Following the initial episode, she continued to expectorate streaks of blood.

Physical examination was unremarkable. Chest radiograph revealed a small cavitary lesion in the left upper lobe (Figure 1). The bibasilar ground glass infiltrates seen during initial hospitalization had resolved (Figure 2).

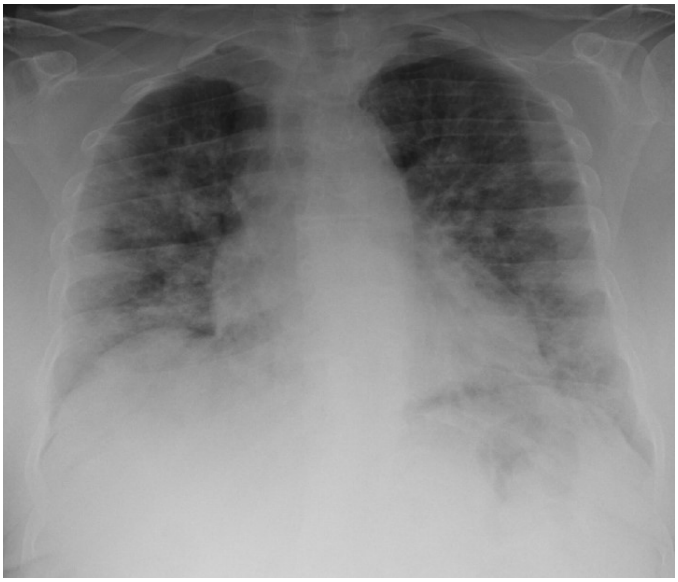

Figure 1

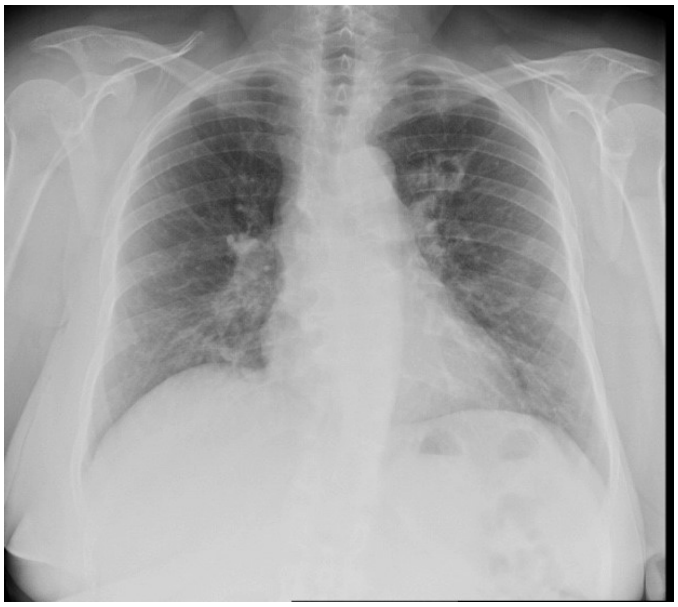

Figure 2

Laboratory data revealed negative serologies including MTB QuantiFERON Gold and coccidiomycosis. Sputum cultures revealed normal flora. AFB and fungal smears were negative with negative culture to date. (1,3)-Beta-D-Glucan was positive at 163 pg. l (>80 pg./ml abnormal). Patient was referred for Infectious Disease consultation.

Discussion

Radiographic abnormalities in patients with COVID-19 pneumonia have been well documented.[1] Most often noted are peripheral ground glass opacities followed by areas of consolidation with air bronchograms.[2] Computerized tomography reveals additional findings of interlobular septal thickening and "crazy paving" pattern.[2]

Development of pulmonary cavitation in COVID-19 pneumonia is rare. In one retrospective study of 689 patients hospitalized with pneumonia diagnosed with COVID-19 only 1.7% were found to have evidence of cavitation.[3] Patients that were admitted to the intensive care unit for acute hypoxemic respiratory failure had a higher percentage of 11%.[3]

Risk factors for development of cavitation mirror those associated with contracting COVID-19, including diabetes mellitus, hypertension, and chronic lung disease.[4]

A cavity has been defined as a gas-filled area within a zone of consolidation or within a mass or nodule, produced by elimination of a necrotic tissue of the lesion via the bronchial tree. Radiographically it is defined as a lucency within a zone of pulmonary consolidation, a mass, or a nodule.[5] Cavitation in viral pneumonia is uncommon,[6] including SARS-CoV and MERS-CoV.[7]

Bacterial, mycobacterial, and invasive fungal infections are associated with lung cavitation, with or without history of immunosuppressive agents. Mycobacterial and fungal infections are often diagnosed late in the clinical course of cases of COVID-19.[8]

Hypothetical causes are felt to be multifactorial, including bacterial superinfection, opportunistic fungal and mycobacterial infections in the face of immunosuppressive/corticosteroid therapy and thrombosis with infarction. Corticosteroids, despite suppressing the immune system, have been shown to improve survivability.[9]

Immunosuppressant drugs used in severe cases of COVID-19 pneumonia have been implicated in development of cavitary lung disease. In a series of 12 patients that developed cavitary disease, all had received tocilizumab.[3] Tocilizumab, a human recombinant antibody directed against interleukin-6 receptors is given to COVID-19 patients with laboratory evidence of "cytokine storm", as this has been shown to improve survival.[10]

Patients with COVID-19 are associated with a prothrombotic state.[11] COVID-19 binds to receptors of Angiotensin converting enzyme II on alveolar epithelial cells. It is postulated that increased levels of angiotensin II promote vasoconstriction and a prothrombotic state.[12] In a small autopsy series of 12 patients that expired secondary to COVID-19 with cavitary disease, all had tissue necrosis associated with occlusive thrombosis of the supplying pulmonary artery.[13]

Summary

Cavitary lung disease in patients with COVID-19 is rare but with significant frequency in patients admitted to the intensive care unit. Postulated etiologies include superimposed infection and increased risk of opportunistic infections with immunosuppressive drugs such as corticosteroids and tocilizumab. Mechanisms of a prothrombotic state causing occlusion of a supplying pulmonary artery with infarction and necrosis of dependent lung parenchyma have been proposed.

Our patient developed hemoptysis and evidence of cavitation 10 weeks after hospital discharge. She received both corticosteroids and tocilizumab. Cultures remain negative to date. Due to her elevated (1,3)-Beta-D-Glucan, the patient is still being evaluated for invasive fungal infection.

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