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Culture-negative pleural empyema after Coronavirus disease-19 resolution – A case report

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ABSTRACT

Even after more than a year, novel Coronavirus disease-19 (COVID-19) clinical presentation and complications are still being reported. We present a 75-year-old patient with culture-negative pleural empyema a month after COVID-19 resolution without re-infection. We hypothesize that culture-negative empyema can be present in patients with immune defect, e.g., elderly or diabetic patients, and prior antibiotic exposure. Empyema after COVID-19 resolution may be related to delayed inflammation improvement in chronic disease, which resulted in the patient's more vulnerability to secondary infection.

1. Introduction

More than a year after first case in Wuhan, China, the number of Coronavirus disease-19 (COVID-19) patients is still very high; more than two million died and there is still no cure. Vaccines may help lower new-severe cases but only few treatments can be given for patients already contracted with the disease. Patients with heart disease, diabetes, and hypertension have worse prognosis in COVID-19 compared to their age-gender counterparts without the same predicaments [1]. The risk increases exponentially with the presence of COVID-related complications [2].

Complications after COVID-19 resolutions are common but usually persist from the onset of the infection. We report a unique case in which an elderly patient with metabolic and cardiac comorbidities suffered from new onset empyema after a time we considered COVID-19 had been resolved.

2. Case illustrations

A 75-year-old male, heavy smoker with a history of COVID-19 infection, coronary artery disease (CAD), heart failure with mid-range ejection fraction, diabetes, hypertension, and deep vein thrombosis was admitted to our emergency room for worsening dyspnea. He had no fever, chest pain, nor cough.

Diagnosed with COVID-19 infection two months ago, he had been hospitalized for 1.5 months because of severity of the disease. For his infection, we treated him with hydroxychloroquine, lopinavir/ritonavir, un-fractioned heparin, and quinolones. During that time, he slowly improved until the reverse transcription-polymerase chain reaction (RT-PCR) for COVID-19 was tested negative twice. There was no residual dyspnea or other symptoms at discharge; his chest x-ray at discharge showed no pleural effusion (Fig. 1).

About a week after, he experienced progressive dyspnea that got worse with left lateral decubitus position. Physical examination revealed heart rate of 125 bpm, respiratory rate of 28 breaths/min, oxygen saturation of 88% under non-rebreathing oxygen mask at 15 L/min, and muffled breath sound on right lung. Blood tests showed leukocytosis (29,870/μL), neutrophilia (89%), and increased level creatinine (2.68 mg/dL). His RT-PCR for COVID-19 was still negative.

Chest X-ray showed right pleural effusion (Fig. 2). However, thorax ultrasound showed that the effusion was highly echogenic and subsequent thoracocentesis only resulted in 5 cc yellow milky pus. Chest tube was immediately inserted and there was initial purulent material of 1600 mL on the first day (Fig. 3). We started him on meropenem adjusted dose and heparin. Pleural fluid analysis showed purulent fluid with positive Rivalta test, pH of 7.2, 2561 polymorphonuclear cells/μL, 1549 mononuclear cells/μL, protein level of 3.0 g/dL (fluid-serum ratio = 0.64), glucose level of 56 mg/dL, and lactate dehydrogenase level of 792 U/L (fluid-serum ratio = 2.9). There were negative results on pleural fluid culture and acid-fast staining. He had been already tested

Abbreviations: CAD, coronary artery disease; COVID-19, Coronavirus disease-19.

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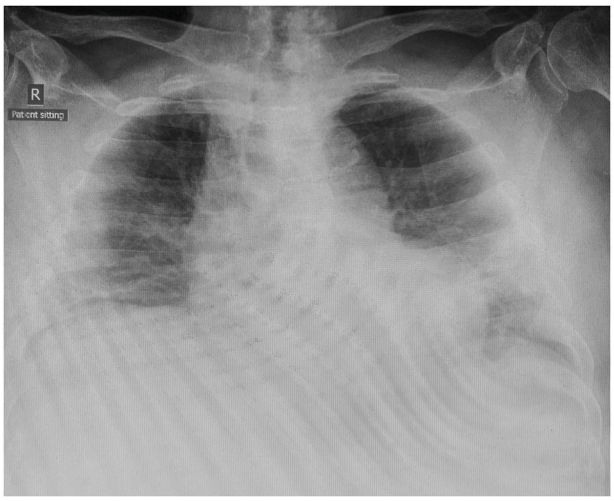

Fig. 1. Patient chest X-ray at the end of COVID-19 hospitalization.

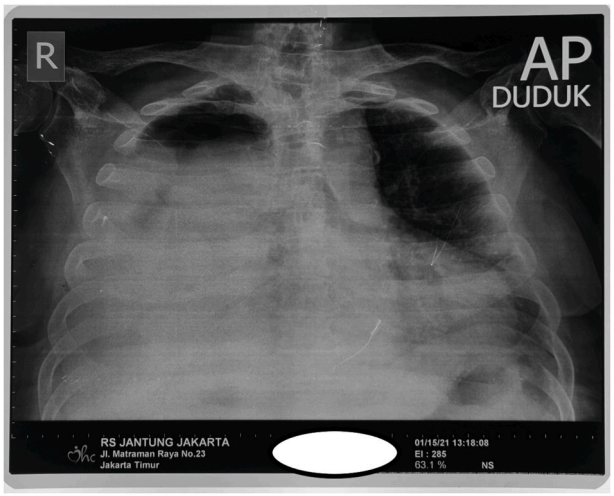

Fig. 2. Patient chest X-ray on admission showed massive right pleural effusion.

negative for human immunodeficiency virus (HIV) in previous hospitalization.

After the procedure, we observed a progressive clinical and radiological improvement (Fig. 4a, b, 4c) that allowed discharge. Chest tube was removed on 10th day and he was discharged after the latest x-ray showed significant progress (Fig. 5). The patient visited outpatient clinic in good conditions without any further complication.

3. Discussions

Empyema is purulent pleural fluid caused by infection. It usually arises from parapneumonic effusion from bacterial infection – causing pleural inflammation – that evolves into a full-blown pleural infection [3]. In COVID-19 setting, the incidence of COVID-related pleural effusion is highly varied across numerous observational studies. Those aged 60 years old or above and with severe diseases are the main risk factors [4]. Unilateral exudative effusion with high LDH and fluid-serum LDH ratio is predominant in such patients [3–6].

Also a common finding in COVID-19, culture-negative empyema is usually associated with autoimmune patients, immunocompromised host, and or prior antibiotic exposure [4,7,8]. Our patient, an elderly man with many comorbidities, was clearly one of such patients. He had also been hospitalized earlier for quinolones; hence non-growth pleural fluid culture was highly probable. In this case, if readily available,

Fig. 3. Initial purulent material from chest tube insertion, about 1,600ml.

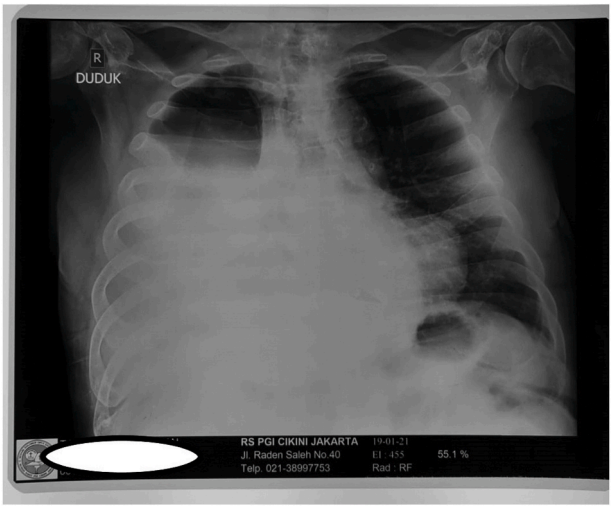

Fig. 4a. Patient chest X-ray just before chest tube insertion.

bacterial PCR would have been useful to confirm bacterial presence [5].

To this date, within our knowledge there has been no report about delayed empyema after COVID-19 resolution. Therefore, we are proposing our take in the pathophysiology process. In CAD and or diabetic patients, the worsening chronic low-grade inflammation, due to hosts' inability to fully resolve the acute inflammation in severe COVID-19, will propagate over time. As a result, the inflammation level in CAD and or diabetic patients may exhibit slower declining curve than in non-CAD or non-diabetic patients [9,10]. The delayed exacerbated immune response, along the persistent higher level of inflammation, plays important role in delayed COVID-related complications, including cardiovascular event and pulmonary infection [9]. The still-vulnerable lungs of the hosts are becoming more prone to secondary bacterial infection. The late superimposed bacterial infection, in turn, will precipitate empyema that is often found to be sterile due to previous antibiotics exposure, similar to our patient's history.This event is highly comparable to findings in human immunodeficiency virus

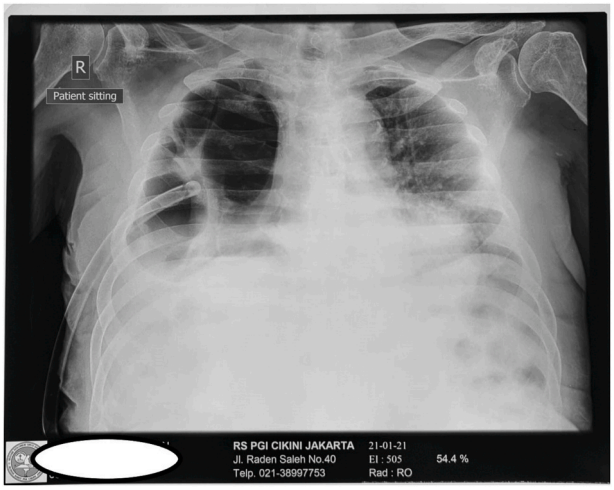

Fig. 4b. Patient chest X-ray on the 3rd day of chest tube.

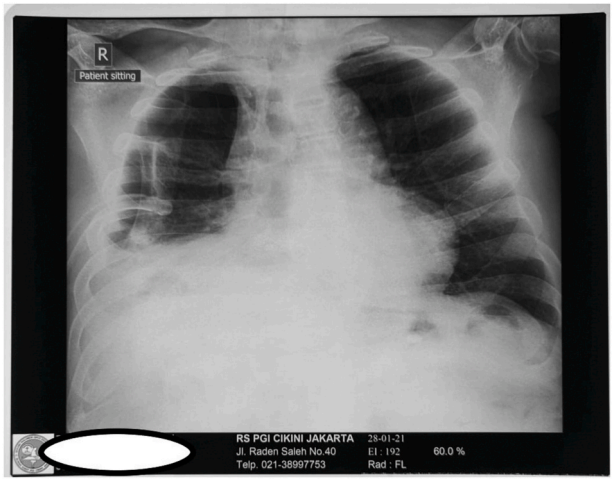

Fig. 4c. Patient chest X-ray on the 10th day of chest tube (before removal).

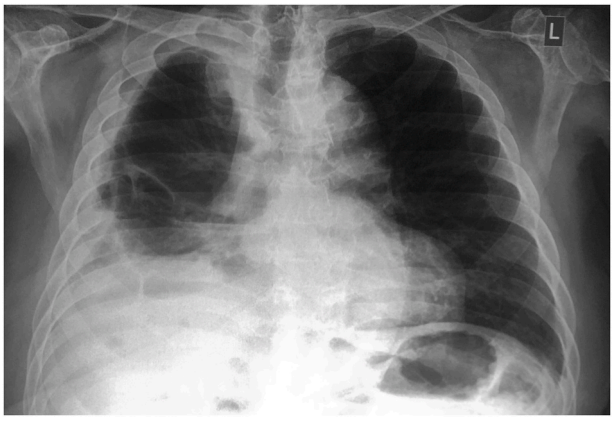

Fig. 5. Chest X-ray before patient was discharged.

(HIV)-positive patients, in whom empyema developed secondary to community-acquired pneumonia [11].

4. Conclusions

- Delayed complications after COVID-19 resolution are closely related to worsening chronic inflammatory state of some patients making them more prone to late secondary bacterial infection.
- Patients with such a condition, including those with CAD, diabetes, and or autoimmune patients are to be thoroughly monitored for delayed complications.
- Thoracic empyema as COVID-related complication can be sterile but prompt treatment with empirical antibiotics and chest tube are still essential.

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Declaration of competing interest

The authors declare no conflicts of interest.

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