






## PAP with COVID-19 Radiology - Differential Diagnosis Discussion

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Diffuse interstitial lung diseases (DILD) are a heterogeneous group of diseases in which thoracic computerized tomography (CT) is an important diagnostic tool. Fibrotic or inflammatory processes yield some highly specific radiological findings. Although some of them were seen in several diseases and identified as a “pattern,” a few of them might be helpful to recall a specific diagnosis. Crazy paving was one of those patterns, and it is a characteristic of pulmonary alveolar proteinosis (PAP). However, recently, it has appeared in the list of typical radiological findings for coronavirus disease 2019 (COVID-19), a novel viral pneumonia. In this pandemic, these kinds of interactions might cause difficulty in clinical decision and misfortune for patients.

We will discuss the difficulty of differential diagnosis during the pandemic in light of a patient who was followed-up for PAP in our center, diagnosed with COVID-19 upon application to another hospital with respiratory complaints during the pandemic, and quarantined and started on COVID-19 treatment.

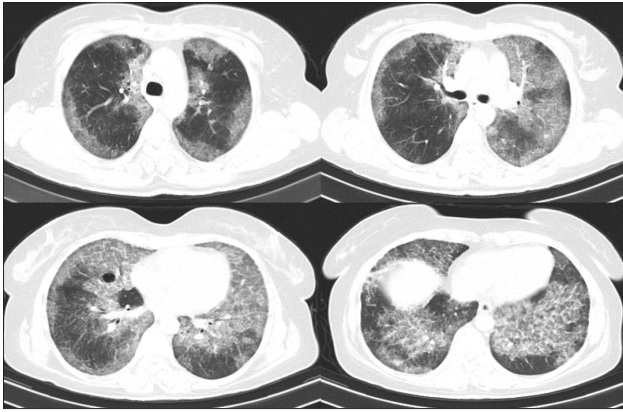
A 42-year-old female patient, diagnosed with PAP in another center, came to our clinic for total lung lavage (TLL) 1 year ago. The main symptom was exercise dyspnea. After TLL, her dyspnea decreased, and no oxygen treatment was needed for almost 10 months. Radiological progress was also observed in the patient with an increase in dyspnea. TLL was indicated with an appointment on March 17, 2020. However, she was unable to attend because of the COVID-19 pandemic because the first case of COVID-19 in our clinic was diagnosed on March 13, 2020. The functioning of health institutions has been reshaped in our country, and because TLL was determined as an “elective procedure,” the appointment had to be postponed. The patient had to apply to the hospital in the city where she was living owing to an increase in dyspnea and cough. She was hospitalized with a preliminary diagnosis of COVID-19 pneumonia because of bilateral ground-glass opacities on CT. The reverse transcriptase polymerase chain reaction test was performed 3 times consecutively and yielded a negative result. She was considered as a “possible case for COVID-19” and treated in another institution. Although she told that the radiological findings had lasted for 1 year in her CT, she had to complete the obligatory procedure of treatment and then 14-day isolation with her family. When she contacted us, we planned immediate TLL under high-protection measures as emergency situations. TLL was performed consecutively on both the lungs with 1-week interval. Oxygen saturation was increased from 84% to 93% in room air before discharge.

PAP is one of the rare DILDs characterized by accumulation of surfactant in the alveoli. Clinically, dyspnea and hypoxemia and radiologically crazy paving pattern are typical. The diagnosis of PAP is usually made by bronchoalveolar lavage, which has a milky appearance, and amorphous material that stains periodic acid-Schiff-positive is typical in cytological examination. The main treatment for PAP is TLL. As in our case, TLL decision was made because of respiratory distress and worsening of pulmonary function tests. In our case, the symptoms and radiological findings improved after first TLL in accordance with the literature [1].

The viral pneumonias, such as COVID-19, may show similar CT findings to those of interstitial lung disease (ILD). As a result of COVID-19 pulmonary inflammation, alveolar edema; fibrin, hyaline membrane, and cell infiltrations; and associated interstitial changes are observed [2]. In thoracic CT, bilateral, especially subpleural, patchy ground-glass areas, crazy paving pattern, organizing pneumonia-like infiltrations, such as reverse halo signs or ground glass with extensive subpleural consolidations, and air bronchograms are typical findings for different stages of the disease [3].

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**Figure 1.** The crazy paving pattern and ground-glass opacities which is bilateral, peripherally located in the upper lobes, more common in the lower lobes, including expanding vascular structures, are seen in the Thorax CT



**Figure 2.** Total Lung Lavage procedure under high protection measures in negative pressure operation room



**Figure 3.** Fluids collected by Total Lung Lavage from right lung; showing the difference between the color of two bottles placed in front and the higher level of sedimentation in first bottle (\*)

Delay in the differential diagnosis of these 2 diseases with completely different treatments may result in failure to isolate a COVID-19 case or to treat an ILD case properly to prevent progression or even mortality. In this case, COVID-19 had been considered with respiratory distress and radiological findings, and the treatment followed by quarantine was indicated because of the pandemic conditions. In this process, the patient's respiratory distress increased, and she required continuous oxygen therapy. In the differential diagnosis of these 2 groups of diseases, detailed questioning of clinical symptoms, evaluation of medical history, laboratory parameters, and evaluation of the patients' previous radiology would be helpful. Besides dyspnea, cough and myalgia are the common symptoms in COVID-19 [4]. Symptoms are acute in COVID-19; ILD is mostly chronic. Although shortness of breath and cough are common, fever is rare [5]. Laboratory parameters, especially acute phase reactants owing to inflammation, may have a moderate pitch or may be completely normal in ILD. For COVID-19, lymphopenia and increase in acute phase reactants are common laboratory findings [5].

The similarities between ILD, especially PAP, and COVID-19 may complicate the diagnostic approach and radiological diagnosis. Although delays are important in diagnosis and correct treatment, the most important attempt should be questioning the patient carefully and making decisions according to the symptoms, duration of symptoms, medical history, previous tests, and response to treatment.

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