CASO CLÍNICO

A case of pulmonary alveolar proteinosis misdiagnosed as COVID-19 pneumonia

Un caso de proteinosis alveolar pulmonar mal diagnosticado como neumonía Covid-19

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Abstract

A 48-year-old female patient with complaints of shortness of breath and coughing had bilateral diffuse infiltration in her chest X-ray and diffuse ground-glass opacities in her chest computed tomography. Despite her polymerase chain reaction test being negative, she was treated 10 days for coronavirus disease 2019 (COVID-19) pneumonia due to her radiological images and clinical hypoxia. As there was no improvement in her symptoms, she was administered fiberoptic bronchoscopy and she was diagnosed with pulmonary alveolar proteinosis (PAP). PAP can be confused with COVID-19 pneumonia due to their similar clinical and radiological appearances.

Keywords: *Pulmonary alveolar proteinosis. Coronavirus disease 2019. Bronchoalveolar lavage.*

Resumen

Una paciente de 48 años con quejas de disnea y tos tenía infiltración difusa bilateral en la radiografía de tórax y opacidades difusas en vidrio deslustrado en la tomografía computarizada de tórax. A pesar de que su prueba de PCR fue negativa, fue tratada durante 10 días por neumonía COVID-19 debido a sus imágenes radiológicas e hipoxia clínica. Como no hubo mejoría en sus síntomas, se le administró fibrobroncoscopia y se le diagnosticó proteinosis alveolar pulmonar. La proteinosis alveolar pulmonar se puede confundir con la neumonía COVID-19 debido a su apariencia clínica y radiológica similar.

Palabras clave: *Proteinosis alveolar pulmonar. COVID-19. Lavado broncoalveolar.*

Introduction

With an unknown etiology, pulmonary alveolar proteinosis (PAP) is a rare disorder characterized by accumulation of large volumes of surfactants lipids and proteins in the alveolar and distal airways due to deficient macrophage activity[1]. Abnormal metabolism and clearance of surfactants occur, resulting in impaired gas exchange. The estimated prevalence of the disease is 1/100,000 and it is more common among males between 20 and 50 years of age. PAP forms include primary auto-immune (90-95%), secondary and congenital. Progressive exertional dyspnea and nonproductive cough are the most common symptoms in PAP. While spontaneous remission is seen in 10-50% of the PAP patients with good prognosis who have the primary type in

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particular, mortality may occur in approximately 10% of the patients mostly due to respiratory failure and infection[2,3].

A chest X-ray typically reveals bilateral diffuse infiltration areas in PAP. Computed tomography (CT) images show multifocal, patched, vaguely contoured infiltrations, and local consolidations with ground-glass opacities (GGOs) in both lungs. In addition to typical clinical and radiological signs, milky appearance and positive staining with periodic acid-Schiff (PAS) of the globules inside the materials from bronchoalveolar lavage or transbronchial biopsy help make the diagnosis[3]. The most common and effective method used in treatment is the whole lung lavage (WLL), in which material accumulated in the lungs is cleansed mechanically.

The coronavirus disease 2019 (COVID-19) is a pneumonia outbreak caused by a novel coronavirus and has been accepted as a pandemic by the World Health Organization. Although the reverse transcription-polymerase chain reaction (PCR) is the most widely used method in diagnosis, the low sensitivity of this method necessitates a chest CT scan in patients suspected of having COVID-19[4]. A chest CT has approximately 94% sensitivity and 37% specificity. Positive CT findings are not unusual in many PCR negative cases.

This case report presents and discusses, also referring to the literature data, a situation where PAP was confused with COVID-19 pneumonia due to its radiological images as well as the complications involved in WLL that was used to treat PAP.

Case report

A 48-year-old female patient presented to the emergency clinic with complaints of shortness of breath and cough that had started a year ago and increasingly worsened in the past 1 month. Since she had widespread infiltration in her chest X-ray and hypoxemia, she was administered a PCR test with a prediagnosis of COVID-19. Although her test turned out negative, she was bedded in the COVID clinic and administered medical treatment for 10 days as diffuse GGOs and infiltration and septal thickening in the interlobular/intralobular interstitium were found in her chest CT. Two more PCR tests applied during this time also turned out negative. With no improvement in her shortness of breath a week after her discharge, the patient was administered fiberoptic bronchoscopy (FOB) by the pulmonary diseases and was diagnosed with PAP as her bronchoalveolar lavage fluid was thick, opaque, and milky white coloration and PAS positive.

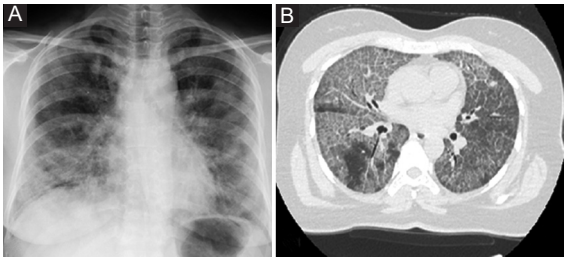

Figure 1. A: *Chest X-ray shows infiltrations in both basal zones.* **B:** *Chest computed tomography shows widespread ground-glass areas in the lungs on horizontal plane.*

In her physical examination to assess her for a lung lavage, dyspnea and cyanosis were found, and crepitant rales were heard in her both lungs but more in her left lung during auscultation. In her arterial blood gas at rest, pH was 7.38, $paCO_{2:}$ 38.2 mmHg, $paO_{2:}$ 71.3 mmHg, and $SO_{2:}$ 90.1%. Her pulmonary function testing showed restrictive ventilation and diffusion dysfunction. After infiltrations were detected in both basal zones in her chest X-ray, a chest CT was taken which showed widespread ground-glass areas tending to merge in both lungs (Fig. 1A and B).

With the intention of a right lung lavage, the patient was intubated under general anesthesia through a double-lumen endotracheal tube and given a right lateral decubitus position. The right bronchial system was aspirated by delivering 300 cc of warm 0.9% NaCl during each sequence. To ensure an effective cleansing, the patient's back was tapped with percussion during the aspiration. Since oxygen saturation dropped as a result of the lavage with 5000 cc, the procedure was discontinued and the patient was brought to the supine position. However, increased airway resistance, aeration difficulty and subcutaneous emphysema between the neck, and the left anterolateral hemithorax occurred. When it was found during auscultation that the left hemithorax did not participate in respiration, chest X-ray was taken, which showed pneumothorax on the left and subcutaneous emphysema, and a left tube thoracostomy was administered (Fig. 2A and B). The patient was taken to the intensive care unit intubated and when her clinical signs and oxygenation improved at the end of 24 h, she was extubated. After removing her chest tube 3 days later, she was discharged.

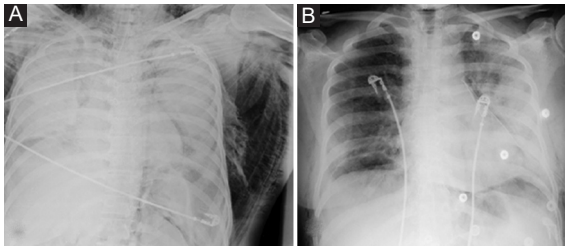

Figure 2. A: *Chest X-ray shows left pneumothorax and subcutaneous emphysema.* **B:** *Chest X-ray shows expanded left lung after tube thoracostomy.*

Figure 3. A: *The milky white coloration fluid taken by free drainage from double-lumen intubation tube is seems.* **B:** *During the procedure, the color of the lavage fluid turned from a milky appearance to a clear appearance.*

The patient was admitted again after 2 weeks to administer for the left lung lavage. This time, after double-lumen intubation, her right lung was ventilated, while she was in the supine position and 300 cc of warm 0.9% NaCl was delivered to her left bronchial system during each sequence without percussion; she was then put to the Trendelenburg position allowing self-drainage and the fluid was taken back (Fig. 3A). The cleansing involved 10,000 cc of isotonic in total. The color of the lavage fluid turned from a milky, densely particulated appearance to a clear appearance toward the end of the procedure (Fig. 3B). With no post-operative problems, the patient was discharged on the 2nd day.

The patient was invited again after a week to administer for right lung lavage. After double-lumen intubation, her left lung was ventilated, while she was in the supine position and 300 cc of warm 0.9% NaCl was delivered to her right bronchial system during each sequence without percussion; she was then put to the Trendelenburg position allowing self-drainage and the fluid was taken back. The cleansing involved 10,000 cc of isotonic in total. The color of the lavage fluid became clear toward the end of the procedure and apparent regression was found in her chest X-ray taken after the procedure. With no post-operative problems, the patient was discharged the next day. After a 6-months follow-up, the patient was found relieved of her clinical symptoms considerably with an improvement in her pulmonary function and regression in her CT findings.

Discussion

Due to this COVID-19 pandemic, many patients are being considered and treated these days as COVID-19 patients due to their positive radiologic images although their PCR results turned out negative. The typical chest CT findings of COVID-19 pneumonia are usually peripheral, bilateral GGOs, consolidations, interlobular/intralobular septal thickening (crazy-paving pattern), and subpleural linear opacities[4,5]. Some of these findings are similar to the radiologic imaging findings of many infectious and non-infectious diseases of the lungs. Although it is a rare condition, PAP's radiologic appearance and the severe dyspnea clinic can be confused with COVID-19 pneumonia. Similarly, the chest CT images of PAP also involve bilateral, diffuse GGOs, and consolidations as well as crazy-paving pattern. Failing to remember this radiological similarity may lead to patients' receiving wrong treatment for a long time with the assumption that they have COVID-19 pneumonia, and more importantly, serious delays in the diagnosis and treatment of PAP may occur. In our case, the patient was also misdiagnosed with COVID-19 due to bilateral widespread infiltration in her chest X-ray and widespread GGOs and crazy-paving pattern in her chest CT, and when it was seen that there was no clinical improvement despite the treatment, FOB was administered after a 10-day delay, and she was finally diagnosed with PAP.

The most effective treatment method in symptomatic PAP patients is the sequential WLL, where sterile 0.9% NaCl solution heated to 37°C is used in high volumes, approximately 12-15 L/single lung. Lavage is first applied to the lung affected most and if no complication develops, the same procedure is applied to the other lung after 3-7 days[3]. The intervention is performed under general anesthesia using a double-lumen intubation tube while ventilating a single lung. While ventilating the lung which will not be subject to lavage, the side to be administered lavage is delivered 300-500 ml of fluid each time until the lavage liquid becomes grossly clear. Then, the fluid delivered is

removed by way of manual chest percussions, gravity force, or aspiration. In the first lung lavage carried out in this patient, the intention was to detach the sticky material from the alveolar wall and discharge it with the fluid delivered also with the help of percussing the patient's back. However, because the patient was in the lateral decubitus position and the active percussion applied caused a shift in the double-lumen intubation tube, this resulted in an increase in the airway resistance and aeration difficulty in the patient who already had limited oxygenation due to single lung ventilation. The patient whose oxygen saturation rapidly declined was then brought to the supine position and the intubation tube was brought to the right position as soon as possible. Our efforts to improve oxygenation through high-pressure ventilation in the meanwhile caused pneumothorax to occur in the left lung. Although WLL is a procedure that is often completed without any problems, it may involve complications such as hypoxemia, pulmonary edema, hydropneumothorax, pneumonia, sepsis, bronchospasms, acute respiratory distress syndrome, and arrhythmia[3,6]. There are publications in the literature stating that WLL performed using percussion in the prone position is more effective[3]. In our case, the percussion performed in the lateral decubitus position caused displacement of the double-lumen intubation tube, which occurs quite often due to the movement it makes in the thorax and caused a problem in ventilating the lungs. The lavage we performed in the supine position and without percussion during the later sessions did not cause any position change in the intubation tube and no problem was experienced in the oxygenation of the patient.

Conclusion

PAP can be confused with COVID-19 pneumonia due to its radiologic images and severe dyspnea clinic. We also think that performing WLL used in PAP treatment in the supine position and without percussion is safer.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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