Pneumothorax Following COVID-19: Based on Autopsy Findings

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Research

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Abstract

Background  More and more studies showed pneumothorax is a complication of the 2019 novel coronavirus disease (COVID-19). But no autopsy findings of pneumothorax in COVID-19 decedent were reported, and direct relations between pneumothorax and lung pathology in these decedents were not discussed so far.

Methods  A 62-year-old man with COVID-19 presenting with persistent hypoxemia and suddenly dead, who was treated by mechanical ventilation in the intensive care unit (ICU) for 5 days. A systemic autopsy examination of COVID-19 decedent, including histopathology study, was conducted and the medical record, chest computerized tomography (CT) image were reviewed by forensic pathologists and clinicians.

Results  Severe pneumothorax, diffuse alveolar damage and airway obstruction were observed. Pneumothorax should be one of the causes of death.

Conclusion  Pneumothorax, due to SARS-CoV-2 infection, is a fatal complication of COVID-19. Regular examination of chest CT or X-ray and airway management are important to clinical treatment.

Introduction

Since its first description in Wuhan, Hubei Province, China, in December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a pandemic of the world, and the World Health Organization (WHO) officially declared it as a global health emergency on January 30, 2020. COVID-19 can cause a wide clinical spectrum from asymptomatic infection, mild respiratory cold-like illness, to severe pneumonia and multi-organ failure(1). Besides, more and more studies showed pneumothorax is a fatal complication of COVID-19, with or without medical intervention, like ventilator assistance and endotracheal intubation, especially at the late stage of infection with unmarkable prodrome(2–6). But there were only reviews of clinical data and histopathological observations without findings of pneumothorax, lacking of direct pathologic findings based on autopsy and pathological examination in these patients(7–10). Here we reported a patient with COVID-19 and severe pneumothorax who dead suddenly in the Intensive Care Unit (ICU), in order to provide insights into the disease characteristics, clarify the causes of pneumothorax and improve the treatment measures in these patients.

Case Presentation

A 62-year-old man who lived in Wuhan with developed intermittent fever (temperature up to 39 °C) 16 days ago, accompanied by chills, palpitations, mild symptoms of chest tightness and panting, was admitted to hospital on 6th Feb 2020. The patient was in good health before, without diabetes, hypertension, cardiovascular disease and history of smoking. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid test was positive in the laboratory. Prehospital thoracic computerized tomography scan (22th Jan) showed ground-glass opacities in the upper lobe of right lung
(Fig. 1A). On admission, his body temperature (T) was 36.7 °C, with heart rate (HR) 93 per min, breathing rate 20 per min, blood pressure (BP) 106/62mmHg and consciousness to alert and oriented. His laboratory test results reflected leukocytosis with neurophilia, lymphopenia and thrombocytopenia, elevated procalcitonin (PCT, 1.52ng/ml, normal: < 0.5ng/ml), and ferritin (> 2000ng/ml, normal: 21.8-274.6ng/ml), with normal D-dimer level. Chest computed tomography (CT) (7th/14th Feb) showed bilateral ground-glass options and consolidation (Fig. 1B/C). SpO2 was 98% with 5L/min of supplemental oxygen. He was treated with supplemental oxygen at 5L/min and antiviral medications of Ribavirin, immunoglobulin and Moxifloxacin. 10 days later, without high body temperature and worsening cough, severe chest tightness and dyspnea happened suddenly with oxygen saturation 61%, and 63% after high-flow nasal cannula oxygen therapy (100% concentration, flow rate 50 L/min). Intubation and mechanical ventilation were used (volume control model FiO2 65%, positive end-expiratory pressure 12 cmH2O) in ICU, HR 102 per min, breathing rate 25 per min, BP 112/62mmHg, oxygen saturation 85%-97%. Laboratory test results revealed elevated PCT (6.02ng/ml, normal: <0.5ng/ml) and D-dimer level (15.94ug/mL, normal: 0-1.5ug/mL). Bedside X-ray (18th Feb) showed diffuse bilateral airspace opacities (Fig. 1D). His medications were modified to sulperazone, arbidol, low molecular weight heparin (LMWH) and XueBiJing. Then he died 5 days later suddenly without daily chest image check.

Methods

A complete autopsy was performed by forensic pathologists 3 hours after his death. Histopathological examination was performed by several pathologists with more than ten years of experience. Internal conditions of the body were observed and photographed. After lungs and other major organs were removed, the gross visual observations of the surface and section of the organs were recorded. Then 10% formalin solution was used for fixation for 3 days, followed by tissue sampling, paraffin embedding, section preparation and stained by routine hematoxylin and eosin (H&E) staining. Also the clinical records were reviewed.

Results

Autopsy findings were cyanosis of lips and fingernails, pale toenails. There was no effusion in the abdominal cavity. Severe pneumothorax was seen on the left, and the left diaphragm protruded into the abdominal cavity, reaching 6 centimeters below the costal margin at the midline of the clavicle (Fig. 2A). There was a little effusion on both sides of the thoracic cavity. The surface of the lungs was variegated, with carbon deposits and flake bleeding at the edge of the left lung. The left lung was severe atelectatic (Fig. 2B), weighs 410 g, and a collapsed multiple pulmonary bullae (8×6 cm2) on dorsal upper lobe was seen (Fig. 2C), containing a small amount of liquid. The right lung weighs 640g, with patchy hemorrhage on the surface, formation of pulmonary bullae on the dorsal side, congestion on the cut surface (Fig. 2D). The findings showed severe pulmonary fibrosis, hyperplasia of residual alveolar epithelial cells in alveolar wall, hyaline membrane formation, emphysema, and inflammation and destruction of the pulmonary capsule (Fig. 3A/B), also thrombus formation in pulmonary arterioles was found. In the
airway, changes mainly involved the mucosa and muscle layer of bronchioles and terminal bronchioles, including thickening of the basement membrane, hyperplasia of epithelial cells in bronchioles and terminal bronchioles. The bronchioles were filled with red blood cells, inflammatory cells, cellulose, eosinophilic staining flocculent, even sputum bolt formation in the whole lumen (Fig. 3C/D). With the condition of persistent hypoxemia and sudden death, the causes of his death were determined to be pneumothorax, DAD, ARDS following COVID-19.

Discussion

Novel coronavirus pneumonia 2019 (COVID-2019) caused by SARS-CoV-2 has a worldwide outbreak since it first emerged in December 2019, Wuhan city, China, and World Health Organization increased the coronavirus risk to 'very high'. It showed that most patients had organ function damage, including 35 (67%) with acute respiratory distress syndrome (ARDS) (1). The major clinical manifestations were fever, chills, cough, shortness of breath, generalized, myalgia, malaise, drowsiness, diarrhea, confusion, dyspnea, and pneumonia1. Chest CT was suggested as an important tool for SARS-CoV-2 infection diagnosis, especially in a patient with a history of close contact with SARS-CoV-2-infected patients, and ground glass lung opacification was found in these SARS-CoV-2 patients(11, 12). As so far, there was less information about autopsy and pathological findings of the deceased with pneumothorax due to COVID-2019. Like Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) infection, pathology findings of COVID-2019 were mainly about abundant pulmonary edema and hemorrhage, desquamated bronchial and alveolar epithelial cells, also extensive pulmonary interstitial fibrosis, and alveolar emphysema and obstruction of bronchioles and terminal bronchioles with exfoliated mucosal epithelial cells and inflammatory necrotic material, even mucus plug(9). CT scan showed patchy ground-glass shadows, which progressed rapidly, and pneumothorax was found in some patients. In clinical observational study on critical ill patients with COVID-2019, there were survivors developing pneumothorax, but lack of further information of pathology(1). As so far, there were limited autopsy reports about COVID-2019, showing the causes of death in these patients were pulmonary embolism, DAD, acute bacterial bronchopneumonia likely caused by aspiration(13, 14). To our knowledge, it was the first pathological report of pneumothorax in deceased patients. Pneumothorax may result in increased pressure in the pleural space, collapsing major blood vessels that return blood to the heart, even life-threatening. In our case, in gross examination, there was pulmonary bullae at the upper lobe of the left lung, the diaphragm moves downwards reaching 6 cm below the costal margin, showing severe pneumothorax. The cut surfaces of the lung displayed adhesion of mucus lumen, obstruction of the small airway. In histopathological examination, interstitial mononuclear inflammatory infiltrates dominated by lymphocytes and severe pulmonary fibrosis were seen in lung. Besides, the obstruction of bronchioles, terminal bronchi and alveolar cavity was prominent, containing mucus, edema fluid, desquamated epithelial cells, and inflammatory cells. This observation brings us a hint that pneumothorax could be one of the causes of death. Being reported, the virus homology was over 79% between novel coronavirus pneumonia and SARS(15). Several studies showed the pathological changes of COVID-19 were similar to SARS patients(9). Clinical details were reported that 6 cases (1.7%) of
spontaneous pneumothorax occurred among 356 SARS patients in two Hong Kong hospitals. It showed the concentrations of peripheral leukocytes and serum lactate dehydrogenase in patients with SARS and pneumothorax were greater than in other patients with SARS in Hong Kong, which supported the clinical perception that pneumothorax was associated with more severe disease(16). But in our autopsy cases, there was no significant elevation in peripheral leukocytes (11.72 ~ 17.79×10^9/L, normal: 3.5 ~ 9.5×10^9/L) and serum lactate dehydrogenase (385 ~ 522 U/L, normal: 120 ~ 150 U/L) than other 8 deceased.

Combined with the results of pathological studies, we hypothesized that the occurrence of pneumothorax with COVID-2019 might be caused by the following reasons: first, diffuse alveolar damage (DAD), and obstruction of ventilation function in small airway, resulting in focal emphysema and rupture of pneumothorax. The second is the severity of the interstitial inflammatory response and diffuse fibrosis can lead to pulmonary contracture, air can permeate through the pleura to the chest, causing pneumothorax; the third is the injury of the pleura of the lung caused by inflammatory reaction, which can cause the rupture of the pleura. In addition, low compliance due to various lung diseases such as ARDS is associated with a high incidence of pneumothorax related to mechanical ventilation(17). It should be noted whether the use of positive pressure ventilator mode to assist breathing will aggravate or promote the occurrence of pneumothorax, and daily chest x-ray or CT scan can be used to evaluate the indications and treatment options for ventilator using, even there are some restrictive conditions (18).

In this case, the common causes of persistent hypoxemia are DAD, airway obstruction with inflammatory mucus, and severe pneumothorax, which was overlooked because hypoxemia is generally believed to be caused by DAD following COVID-2019. Also, sputum aspiration by using prone position ventilation, phlegm aspiration by fiberoptic bronchoscope and mucus dissolution with mucolytic agents to keep airway unobstructed should be used in clinical practice, especially in ICU.

In summary, we investigated the pathological characteristics of a patient who died from COVID-2019 with severe pneumothorax suddenly, aiming to facilitate understanding of the pathogenesis of COVID-19 and improve clinical strategies against the disease.

**Conclusion**

Pneumothorax, due to SARS-CoV-2 infection, is a fatal complication of COVID-19. Regular examination of chest CT or X-ray and airway management are important to clinical treatment.

**Declarations**

**Declaration of interests:** The authors declare no competing interests.

**Ethics approval and consent to participate**
The autopsy study was approved by the ethics committee of Jinyintan Hospital, Wuhan, China. A formal consent was obtained from the next of kin prior to the decedent.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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Authors’ contributions

RW, LL and QL contributed to the conception of the study and wrote manuscript, RW, RC, LL, PL performed autopsy, SX did H&E staining, RW, YW, GQ, RC, QL and LL analyzed H&E staining and reviewed clinical records.

All authors read and approved the final manuscript.

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures
Figure 1

A. Prehospital chest CT obtained on 22th Jan 2020, showing ground-glass opacities in upper lobe of right lung (arrowhead); B/C. Chest CT obtained on 7th/14th Feb 2020, showing bilateral ground-glass opacities and consolidations (arrowhead); D. X-ray obtained on 18th Feb 2020, showing diffuse bilateral airspace opacities.

Figure 2

A. the left diaphragm protruded into the abdominal cavity (arrowhead); B. The left lung was severe atelectatic; C. Collapsed multiple pulmonary bullae (8×6 cm2) on dorsal upper lobe (arrowhead); D. Cut face of lung for gross examination.

Figure 3
A/B. pathology founding of emphysema, inflammation, fibrosis in lungs; C/D. Bronchiolar obstruction with inflammatory cells, cellulose and eosinophilic staining flocculent (arrowhead).