Case report

Pneumothorax as an Ominous Side Effect in COVID-19 Patients under Mechanical Ventilation: Report of Seven Patients

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Abstract

Today, due to the pandemic of novel coronavirus 2019 (COVID-19), extensive information over all parts of the world is spreading rapidly. We present seven cases of COVID-19 patients with pneumothorax as one of the ominous side effects of the disease and a strong predictor of death which is a new challenge in controlling the transmission and distribution of the disease.

Keywords: COVID-19, Pneumothorax, Chest tube; COVID-19; Novel coronavirus

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Introduction

In a short period, health care providers and the general population have been severely challenged by another emerging virus. The COVID-19 pandemic is an unprecedented global crisis, as COVID-19 spreads quickly from Europe and Asia to the rest of the world; hospitals are rapidly becoming hot zones for treatment and transmission of the disease in settings with rising community transmission (1). The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death (2, 3). Initial reports suggest that COVID-19 cases associated with severe disease that requires intensive care are approximately 5% of proven infections (4). Among patients who require hospitalization, the mortality rate maybe 5% to 15%, and for those who become critically ill, there is currently a wide mortality range, from 22% to 62% (5). The principal feature of patients with severe disease is the development of acute respiratory distress syndrome (ARDS); a syndrome characterized by acute onset of hypoxemic respiratory failure with bilateral infiltration of lungs (6).

The pathological result of SARS and COVID-19 is diffuse alveolar damage with fibrin rich hyaline membranes and a few multinucleated giant cells (7). SARS-CoV-2 preferentially infect type II alveolar cells compared to type I (8). It propagates within type II cells and then a large number of viral particles are released, and the cells undergo apoptosis and die. Therefore, this disease may lead to more severe scarring and fibrosis than other forms of ARDS.

For management, evidence-based treatment guidelines for ARDS should be followed, including conservative fluid strategies for patients without shock

following initial resuscitation, empirical early antibiotics for suspected bacterial co-infection until a specific diagnosis is made, lung-protective ventilation, prone positioning, and consideration of extracorporeal membrane oxygenation for refractory hypoxemia (9). In this study, bilateral pneumothorax is introduced as another challenge in the critical care of these patients and possibly a deadly predictive side effect.

Case Report

We represent seven cases of bilateral pneumothorax in the intensive care unit (ICU) admitted COVID-19 patients. The SARS-CoV-2 infection was confirmed by a positive polymerase chain reaction (PCR) testing result of a nasopharyngeal sample and lung computed tomography (CT) in all cases (Figure 1). Patients were admitted to the ICU of Imam Hossein Medical Center in Tehran from March 10 to April 6, 2020, due to severe respiratory failure. They were all tracheal intubated and underwent respiratory support with ventilators and mechanical respiration. The mean time of intubation was 78 hours. The ventilators settings were adjusted by the ICU specialist as follows: Assisted Control Ventilation (ACV) mode, respiratory rate (RR) = 20-30 per minute, positive end-expiratory pressure (PEEP) = 8-18 cmH_2O, tidal volume (TV)=5-6 cc/Kg, Fraction of inspired oxygen (FiO2) = 90-100%, I/E 1-2. Concomitant diseases included diabetes in 4 patients (57.14%), hypertension in 2 patients (28.57%), and chronic kidney disease in one patient (14.28%). Five patients received vasopressors (71%). The mean age was 61.71 ± 14.15 (range: 45-77) years and 6 (85%) patients were male. All patients suddenly experienced a drop in blood pressure, hypoxia, and extensive bilateral subcutaneous emphysema during their ICU stay. Bilateral chest tubes were immediately installed for all patients and connected to regular chest bottles. Blood oxygen levels and airway pressures improved immediately after chest tube insertion but all patients died 3-48 hours (mean time 15 hours) after chest tube insertion due to worsened respiratory failure and cardiac arrest. A chest x-ray was taken after the chest tubes were inserted (Figure 2).

Discussion

The widespread distribution of COVID-19 disease is a major global concern. The molecular and cellular basis of the disease is under research. Several groups of scientists in China have discovered that SARS-CoV-2 requires angiotensin-converting enzyme 2 (ACE2) as a

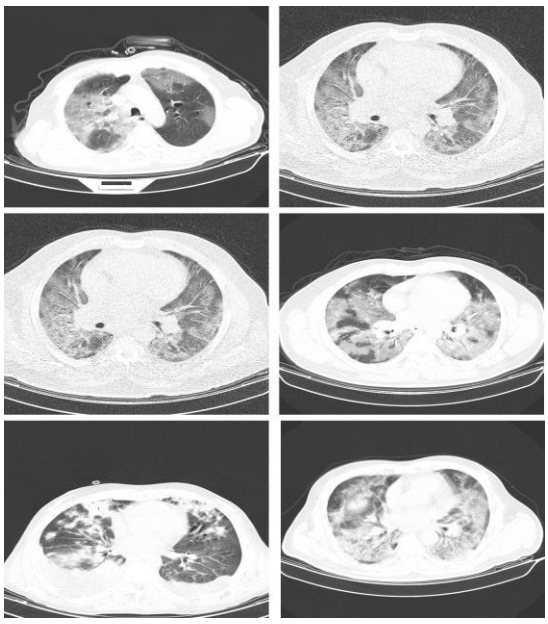

Figure 1. Chest CT scan of patients at ICU admission.

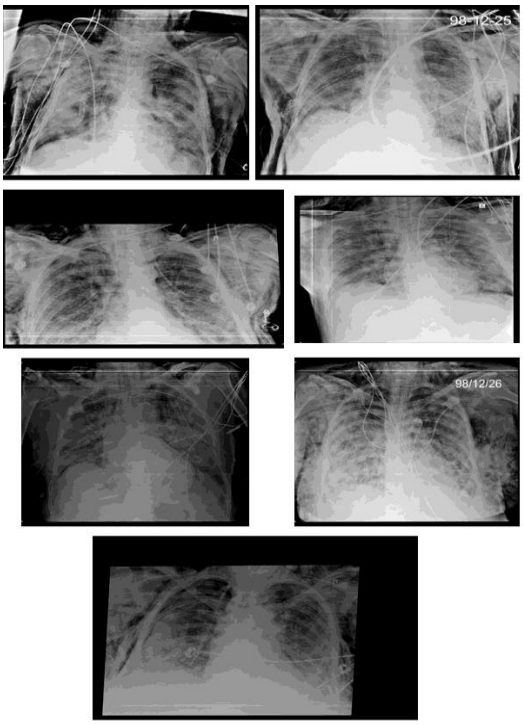

Figure 2. Chest X ray of patients after chest tube insertion.

receptor to enter cells (10). The entry of SARS-CoV into cells was initially identified to be accomplished by direct membrane fusion between the virus and plasma membrane (11). Entering the cells, the viral RNA genome is released into the cytoplasm and is translated into two polyproteins and structural proteins, after which the viral genome begins to replicate (12). The newly formed envelope glycoproteins are inserted into the membrane of the endoplasmic reticulum or Golgi, and the nucleocapsid is formed by the combination of genomic RNA and nucleocapsid protein. Then, viral particles germinate into the endoplasmic Reticulum-Golgi intermediate compartment (ERGIC). At last, the vesicles containing the virus particles fuse with the plasma membrane to release the virus (13).

In particular, older age, d-dimer levels greater than 1 μg/mL, and higher sequential organ failure assessment scores (SOFA) on admission were associated with higher odds of in-hospital deaths. Elevated levels of blood IL-6, high-sensitivity cardiac troponin I, and lactate dehydrogenase, and lymphopenia were more commonly seen in severe COVID-19 cases (2). Our patients had a high rate of ARDS and a high risk of death, similar to published data from China. In another study, the risk factors for death included age over 60 and underlying diseases such as heart disease and chronic respiratory disease, and renal failure (14). As a result, complete evaluation such as echocardiography in critically ill cases is recommended (15).

Pneumothorax in mechanical ventilated covid-19 patients can be related to the cellular aspect of the disease. The virus enters the airways and reaches the gas exchange units of the lung and infects alveolar type II cells. Both SARS-CoV and influenza preferentially infect type II cells compared to type I (8). The infected alveolar units tend to be peripheral and subpleural (16). The pathological result of COVID-19 is diffuse alveolar damage with fibrin rich hyaline membranes and a few multinucleated giant cells (7). The ultimate result is likely a self-replicating pulmonary toxin as the released viral particles infect type II cells in adjacent units. The aberrant wound healing may lead to more severe scarring and fibrosis than other forms of ARDS. The ARDS lung is stiff because of alveolar and interstitial edema and physiologically small. During mechanical ventilation, PEEP inflates and recruits some of the collapsed regions, but also overinflates the

normal regions. The lung regions subjected to high-pressure overinflation may develop alveolar rupture resulting in pneumothorax (17).

In our study, all patients died, and it seems that pneumothorax could be one of the strong predictors of death in these patients. As a result, being vigilant for the symptoms of barotrauma is inevitable. Moreover, attention to Plateau pressure (P_{plat}) and airway pressure ($_{Paw}$) during mechanical ventilation will be crucial in such cases.

In our experience, we connected the patients' chest tubes to a regular chest bottle and established a normal drainage system. Depending on how the disease spreads, droplets from the drainage system can contaminate the environment. We have not studied this issue and it is suggested that this issue could be the subject of future research to control the spread of this virus in the mentioned conditions.

Conclusion

According to the findings of this study, pneumothorax in patients with COVID-19 disease who are under mechanical ventilation is a potential mortality predictor. Attention to Pplat and Paw and the symptoms of pneumothorax in tracheal intubated COVID-19 cases are crucial.

Acknowledgment

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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