Tokai J Exp Clin Med., Vol. 47, No. 4, pp. 162-164, 2022

Autopsy Case Report of Severe COVID-19 Pneumonia at a General Municipal Hospital

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(Received January 19, 2022; Accepted July 13, 2022)

We present the autopsy procedure and findings of severe coronavirus disease 2019 (COVID-19) pneumonia in an 85-year-old man. The patient required intubation immediately after admission for severe COVID-19 pneumonia. He had severe hypoxia that did not improve despite treatment with remdesivir, corticosteroids, and appropriate mechanical ventilation. On day 13, the patient developed sudden hypercapnia. His renal dysfunction subsequently worsened and became associated with hyperkalemia, and he passed away on day 15. An autopsy was performed to clarify the cause of the hypercapnic hypoxia. None of the medical personnel involved in the autopsy developed symptoms of COVID-19. Histologic examination showed various stages of diffuse alveolar damage throughout the lungs, with intra-alveolar hemorrhage in the upper zones. Microscopic examination of the kidneys revealed acute tubular necrosis. There was no significant systemic thrombosis. The autopsy findings were consistent with those typical of COVID-19.

Key words: COVID-19, SARS-CoV-2, pneumonia, autopsy, personal protective equipment

INTRODUCTION

Although therapeutic agents and vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are being developed, coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 infection has significantly impacted the health of millions of people worldwide [1]. COVID-19 has greater transmission potential than the various viruses that have caused pandemics in the past and results in multiple organ failure, especially affecting the lungs, leading to a high mortality rate [2]. Although the mechanisms related to the severity of COVID-19 have been reported [3], several unresolved issues remain. Therefore, to better understand the mechanisms of COVID-19, there is a need to evaluate the pathological findings. Although pathological autopsy guidelines with appropriate precautions for COVID-19 have been reported [4, 5], there are few reports from Japan. We have performed several COVID-19 autopsies at our institution and have not observed any cases of SARS-CoV-2 infection among the healthcare workers involved in the autopsies. Herein, we report the first autopsy case of COVID-19 performed at our institution under guidelines to prevent infection.

CASE

An 85-year-old man with a history of hypertension and dyslipidemia presented to our hospital with a 4-day history of fever (> 37.5°C). He had not been vaccinated against SARS-CoV-2. Upon arrival at hospital, he had no specific complaints and had a body temperature of 38.4°C, blood pressure of 96/40 mmHg, pulse rate of 94 beats/min, and respiratory rate of 24 breaths/min. Pulse oximetry revealed an oxygen saturation (SpO_2) of 91% on 10−15 L/min of oxygen via a non-rebreathing face mask with a reservoir bag. Laboratory data showed a normal white blood cell count, low platelet count (5.5×10^4/ml), mildly elevated concentration of fibrin degradation products (FDP) (16.4 μg/ml), extremely high lactate dehydrogenase concentration (977 IU/l), and elevated C-reactive protein concentration (15.21 mg/dl). Blood gas analysis showed severe hypoxemia, with a pH of 7.49, PaO_2 of 56.6 mmHg, $PaCO_2$ of 30.7 mmHg, and HCO_3^- of 23.2 mmol/l. Chest radiography and computed tomography showed extensive ground-glass opacity and consolidation in the lungs, except for a part of the left upper lobe (Fig. 1a, 1b). The treating clinician decided to intubate with the patient's consent, as there was prolonged "silent" hypoxemia even under high-flow oxygen therapy.

The acute hypoxic respiratory failure was consistent with acute respiratory distress syndrome (ARDS) in

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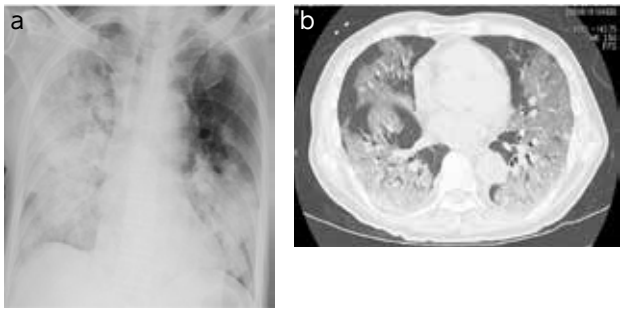

Fig. 1 Chest radiography and computed tomography images at admission.
The radiograph (a) and computed tomography image (b) show extensive ground-glass opacity and consolidation.

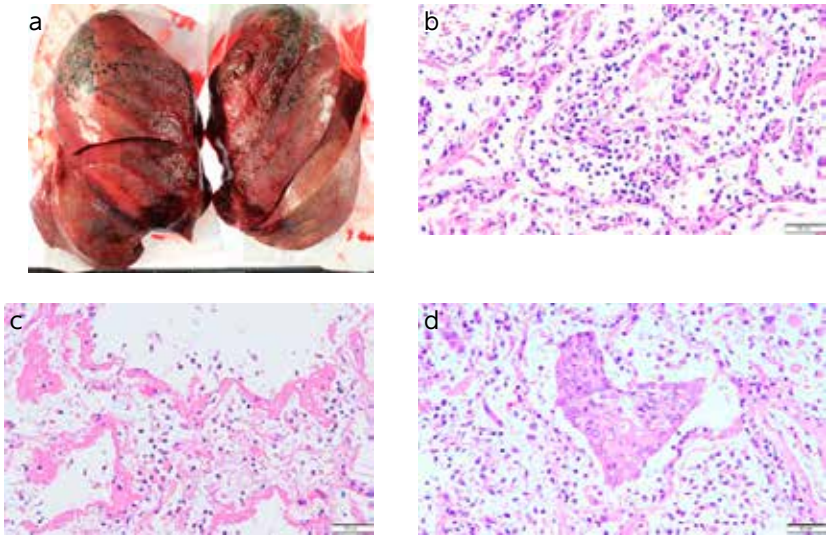

Fig. 2 Gross and microscopic autopsy findings in the lungs.
Gross examination shows (a) heavy, red, and edematous lungs. Histological examination reveals (b) diffuse alveolar damage in the acute stage, (c) hyaline membranes, and (d) squamous metaplasia of the alveolar epithelium.

accordance with the Berlin definition, and was classified as severe [6]. The initial mechanical ventilation settings were based on several guidelines, with the low tidal volume set at 8 ml/kg of the predicted body weight, positive end-expiratory pressure (PEEP) level of 10 cmH_2O, and driving pressure of ≤ 15 cmH_2O; however, his SpO_2 level was still low at < 90%, and he required 100% oxygen immediately. SARS-CoV-2 screening was performed using nasopharyngeal swabs, and the infection was confirmed 24 hours later by real-time reverse-transcription polymerase chain reaction. After admission, the patient received remdesivir and dexamethasone for 10 days as antiviral therapy and was given continuous intravenous unfractionated heparin as anticoagulant therapy under activated partial thromboplastin time monitoring. During treatment, the PaO_2/FiO_2 ratio remained < 100 despite the ventilator settings being adapted in accordance with the results of regular blood gas analyses. On day 5, his platelet counts increased to 10.9×10^4 /ml, FDP level was 5.4 μg/ml, and antithrombin activity was 100%. We did not detect major bleeding during the subsequent clinical course. However, on day 13, we identified hypercapnic hypoxemia (pH 7.276, PO_2 54 mmHg, PCO_2 57.4 mmHg, HCO_3^- 26.7 mmol/l) despite the absence of worsening pneumonia or pulmonary congestion on plain radiography. This respiratory failure did not improve even after adjusting the respiratory settings (e.g., PEEP, respiratory rate, tidal volume, plateau pressure), and the airway pressure gradually increased. The patient required inotropic agents to maintain his blood pressure; however, he developed hyperkalemia and bradycardia that resulted in worsening renal function. The patient passed away on the 15th day after admission.

An autopsy was performed to clarify the cause of the hypercapnic hypoxemia. With the consent of the patient's family, the autopsy was performed at 19 hours postmortem with a minimum number of participants in a room equipped for autopsies. During the autopsy, the staff practiced thorough hand hygiene and used personal protective equipment (PPE) including N95 masks, face shields, disposable gowns, gloves, disposable scrub caps, and rubber shoes. None of the healthcare workers involved in this autopsy developed symptoms of SARS-CoV-2 infection or COVID-19.

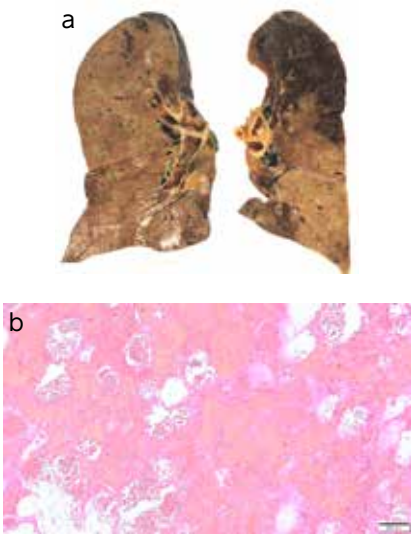

Fig. 3 Extensive intra-alveolar hemorrhage in the upper lobe of the left lung.
In the upper lobe of the left lung, there is (a) intra-alveolar hemorrhage on gross examination, and (b) extensive accumulation of red blood cells in the intra-alveolar space.

Upon pathological examination, the lungs were red and edematous with bilateral pleural effusions on gross examination (Fig. 2a). The right and left lungs weighed 1,280 g and 1,595 g, respectively. Histologic examination of the lungs showed various stages of diffuse alveolar damage (DAD), a pathological hallmark of ARDS (Fig. 2b). Hyaline membranes (which mainly characterize the exudative phase of DAD), intra-alveolar histiocyte infiltration, and degeneration and desquamation of epithelial cells were observed, mainly in the alveolar compartment in the middle to lower zone of the lungs (Fig. 2c). Squamous metaplasia of the alveolar epithelium (which characterizes the second or proliferative phase of DAD) was also seen (Fig. 2d). Moreover, intra-alveolar fibrinous exudates and alveolar inflammatory cell infiltration (characteristic of the second or proliferative phase of DAD) were noted in the subpleural area of the upper zone of the lungs. Intra-alveolar hemorrhage was also observed in the upper zone (Fig. 3a, 3b). No gross abnormalities were observed in the kidneys. Microscopic examination revealed acute tubular necrosis, but no primary glomerulonephritis. Systemically, no significant thrombosis was observed. The pathologist determined that the histological findings in this case were consistent with COVID-19.

DISCUSSION

We described the first autopsy case of COVID-19 at our institution, which is a general municipal hospital. We decided to perform the autopsy mainly to clarify the mechanism of hypercapnic hypoxemia during the clinical course. This type of hypoxemia has been observed in several cases of COVID-19 and is reportedly associated with a poor prognosis [7]. Hypercapnic hypoxemia has been reported to be accompanied by increased dead space ventilation, including pneumonia, pulmonary congestion, and alveolar hemorrhage, but this condition is not yet fully understood [8]. Although we identified alveolar hemorrhage on autopsy, there were no specific radiographic findings suggestive of alveolar hemorrhage on day 13.

Understanding the pathogenesis of novel infectious diseases is valuable in the development of effective therapeutics agents and vaccines. In particular, the distribution of pathogens in organs is important in elucidating the relationship between the disease and the causative organism [9, 10]. While pathological studies of COVID-19 have been conducted worldwide, such studies are relatively rare in Japan. According to a survey conducted in Japan between April 2020 and January 2021, although 197 of the responding institutions accredited by and registered with the Japanese Society of Pathology accepted patients with COVID-19, only 10 institutions had autopsied a patient with COVID-19 [11]; this is presumed to be because of concerns about the risk of infection while conducting autopsies. We emphasize that stringent safety precautions were employed throughout the autopsy described in the present report. The autopsy procedure was performed by a limited number of participants using full PPE. Since this initial case, we have performed several autopsies of individuals with COVID-19 using similar techniques and have found no evidence of infection in the healthcare workers involved. We believe that this report may encourage the performance of autopsies in institutions concerned about the risk of infection during autopsies involving COVID-19.

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