Spontaneous pneumomediastinum in a COVID-19 patient after renal transplantation: a case report and literature review

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Case Report

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Abstract

**Background:** Spontaneous pneumomediastinum is a rare complication in COVID-19. Severe pneumonia complicated with pneumomediastinum after renal transplantation is rarely reported. Here we report a case of pneumomediastinum before invasive mechanical ventilation (IMV) in a COVID-19 patient with long-term immunosuppressive therapy after renal transplantation.

**Case presentation:** A 57-year-old man was admitted to our center with the main complaint of “fever and dyspnea for 5 days”. His past medical history was notable for renal transplantation and with long-term immunosuppressive and anti-rejection therapy. We made the diagnosis as COVID-19 pneumonia (severe type). We managed the patient with high flow nasal cannulae (HFNC), oral dexamethasone, broad-spectrum antibiotic, prophylactic anticoagulation, and anti-viral therapy with reduced dose of azvudine due to severe renal insufficiency. During hospitalization, the patient suffered from several times of aggravation of dyspnea. First bedside chest X-ray showed suspicious pneumomediastinum and subcutaneous emphysema, and the gas in the mediastinum gradually increased. The patient’s status deteriorated rapidly, we performed urgent trachea intubation and mechanical ventilation with low tidal volume lung-protective model and performed mediastinal decompression by suprasternal drainage. Despite our active rescue efforts, the patient still died of severe infection and multiple organ failure.

**Conclusions:** In conclusion, we are the first to report spontaneous pneumomediastinum in a renal transplant recipient with severe COVID-19 pneumonia. This case reminds us that pneumomediastinum is a severe complication and a poor prognostic factor of COVID-19 pneumonia, especially when it occurred without positive pressure ventilation and in immunocompromised patients.

Introduction

Spontaneous pneumomediastinum (SPM) is a rare complication in coronavirus disease 2019 (COVID-19). COVID-19 related SPM has been associated with a more severe course of the disease and a mortality rate of 28.5% versus non-COVID SPM, which has an estimated mortality rate of 5.6% [1]. Pneumomediastinum usually occurs in patients receiving positive pressure ventilation such as invasive mechanical ventilation(IMV), pneumomediastinum before IMV has very low incidence and high mortality[2]. Pneumomediastinum development was associated with the initial PiO2/FiO2 ratio (P/F ratio) and peak inspiratory pressure in patients receiving mechanical ventilation. Therefore, it was considered to be related to both the patient and barotrauma, and it is a poor prognostic factor for COVID-19[3]. However, severe pneumonia complicated with pneumomediastinum after renal transplantation is rarely reported. Here we report a case of pneumomediastinum with HFNC before IMV in a COVID-19 patient with long-term immunosuppressive therapy after renal transplantation.

Case presentation
A 57-year-old man was admitted to our center with the main complaint of “fever and dyspnea for 5 days”. He also had cough and diarrhea. His past medical history was notable for renal transplantation for 22 years and with long-term immunosuppressive and anti-rejection therapy (tacrolimus 1.5mg tid and mycophenolate mofetil 750mg bid). He also suffered from type 2 diabetes and hypertension. At admission, vital signs were at normal range. On physical examination, the patient was overweight (body mass index 27.78kg/m²), and moist rales could be heard in both lungs. He was also very anxious. The arterial blood gas analysis showed that PH was 7.36 (7.35-7.45), PCO₂ 21mmHg (35-45), PO₂ 65mmHg (80-100), Lactose 1.0mmol/L (0.5-1.8), FiO₂ 33%, P/F ratio 196mmH, implicating that the patient was hyperpneic. The serum creatinine level was 294umol/L (62-115), blood urea nitrogen 19.70mmol/L (2.3-7.8). Blood cell count showed that white blood cell was 5.35x10⁹/L (3.5-9.5), neutrophil rate 85.10% (40-75), lymphocyte rate 5.6% (20-50), hemoglobin 103g/L (130-175), C-reactive protein 9.8mg/L (0-5), ESR 60mm/h (0-20), PCT 0.16ng/ml (0-0.1). Coagulation function results showed that D-dimer level was 0.52ug/ml (0-5). The Chest computed tomography (CT) scan showed multiple ground-glass exudates mainly located in peripheral areas of both lungs (Figure 1), without pneumomediastinum or pneumothorax. COVID-19 nucleic acid test was positive.

We made the diagnosis as “COVID-19 pneumonia (severe type)”. Since the patient’s P/F ratio was lower than 200mmHg, as recommended, we managed the patient with HFNC, oral dexamethasone for 6mg qd, broad-spectrum antibiotic (sulprazone), prophylactic anticoagulation with low molecular weight heparin (LMWH) for 5000IU qd, and anti-viral therapy with reduced dose of azvudine (3mg qd) due to severe renal insufficiency. Considering that the patient was relatively stable at admission, we did not stop immunosuppressive and anti-rejection therapy in the first place. During hospitalization, the patient suffered from several times of aggravation of dyspnea and increased respiratory rate, and the symptoms could be relieved by increasing FiO₂. First bedside chest X-ray showed suspicious pneumomediastinum and subcutaneous emphysema, and the gas in the mediastinum and subcutaneous space gradually increased (Figure 2). After consulting with thoracic surgeon, we agreed to temporarily adopt conservative therapy because the patient was hemodynamically stable.

However, the patient’s status deteriorated rapidly, he became dysphoric, and P/F ratio gradually decreased to 80mmHg, we performed urgent trachea intubation and mechanical ventilation with low tidal volume lung-protective model. Nevertheless, the pneumomediastinum and subcutaneous emphysema still had obvious progress on high resolution chest CT scan (Figure 3), thus mediastinal decompression by suprasternal drainage was performed emergently to maintain hemodynamic stability and avoid cardiac tamponade. Despite our active rescue efforts including IMV, surgical mediastinal decompression and aggressive anti-infection therapy, the patient still died of severe COVID-19 pneumonia, secondary aspergillus infection and multiple organ failure.

**Discussion**

SPM is a special type of barotrauma. As reported, the mechanism of SPM was mainly Macklin effect, which is a pathophysiologic process initiated by alveolar basement membrane destruction, rupture,
interstitial emphysema, and dissecting air along the pulmonary vasculature into the mediastinum[4]. The lungs of patients with COVID-19 have significant interstitial involvement with edema, protein exudates, vascular congestion and inflammatory changes with low compliance and reduced elastance[5]. The pulmonary pathophysiology of COVID-19 is recognized to be attributed to a widespread inflammation and destruction of the alveolar–capillary unit[6], which makes the patient more prone to pulmonary barotrauma.

It is well known that SPM usually occurs in patients receiving positive pressure ventilation as IMV or non-invasive ventilation (NIV). In our case, the patient was receiving HFNC treatment when pneumomediastinum occurred. Since HFNC may generate a higher pressure (a positive end expiratory pressure of 3–5cmH₂O is produced at flows of 30–50L/min), it may potentially cause air leakage as well[7]. However, air leakage solely due to HFNC has been rarely reported. A few cases have reported that pediatric patients who received HFNC suffer from air leakage[8]. In adults, these adverse events have not been reported. Besides, a single center cohort study reported that HFNC is a safe and effective ventilatory approach for critical COVID-19 and has a positive role in associated complications such as pneumomediastinum and pneumothorax[9]. Therefore, we presume that the most probable cause for pneumomediastinum in our patient is diffuse alveolar damage due to COVID-19 pneumonia, not due to the use of HFNC. Besides, in this patient, anxiety caused hyperpnea, which could lead to increased alveolar pressure, we speculated that this may be one of the incentives of SPM. SPM solely related to HFNC may imply the severity of alveolar damage, and it might be a prognostic factor of high mortality in COVID-19 patients.

One specialty of our case is the patient is renal transplant recipient and receiving long-term immunosuppressive and anti-rejection therapy. The correlation between renal transplantation and pneumomediastinum is not fully clarified. There have been a few case reports of SPM after renal transplantation[10], pneumomediastinum usually has a benign course in these cases, the symptoms improve in about 2 days, and radiologic abnormalities resolve in about 4 days[11]. Presumably, when pneumomediastinum occurred in renal transplant recipients with COVID-19 pneumonia, the mortality might be higher than immunocompetent group. A large retrospective cohort study indicated that solid organ transplant recipients have higher rates of hospitalization and mortality from COVID-19 compared with the general population. Multivariate analysis results showed that older age, male gender, and higher body mass index were associated with increased mortality from COVID-19 in solid organ transplant recipients[12]. The reported mortalities of renal transplant recipients with COVID-19 were 19-50%[13]. In our case, the patient was male with higher body mass index, which implies poor prognosis.

Another important question in our case is whether to discontinue immunosuppressive therapy. The impact of immunosuppression on COVID-19 is still unclear[14-15]. In a report of 40 patients from Turkey with COVID-19, immunosuppression regimen on admission was associated with high mortality[16]. Reduction or withdrawal of calcineurin inhibitors, mycophenolate mofetil, mycophenolic acid, azathioprine, or mTOR-inhibitors was considered in most published articles. However, complete
withdrawal or significant reduction of immunosuppression could hypothetically exacerbate inflammation in the absence of anti-inflammatory agents. In contrast, continuation of immunosuppressive treatment could decrease the ability to mount an antibody response to COVID-19, especially in kidney transplant recipients[17]. Besides, it is also not clear if chronic immunosuppressive treatment of transplant recipients could decrease the severity of cytokine storm. Therefore, it is still not certain at what point during progression of clinical deterioration that immunosuppression should be minimized or discontinued. The NIH COVID-19 treatment guidelines recommend that decisions regarding stopping or reducing the doses of immunosuppressive drugs in patients with COVID-19 be made in consultation with the appropriate specialists; clinicians should consider factors such as underlying disease, the specific immunosuppressants, the potential for drug-drug interaction and the severity of COVID-19[18].

Furthermore, we found that bedside chest X-ray is not very sensitive in assessing the severity of pneumomediastinum. Once identified, all patients should undergo chest CT to confirm the diagnosis. Thus, in patients with suspected pneumomediastinum, despite the risk of transport, chest CT is still recommended to assess barotrauma and its extent, as well as to assess the degree and extent of pulmonary infiltration[19]. As we know, antiviral therapy is very essential in the treatment of COVID-19 patients. Azvudine is a thymus-homing anti-SARS-CoV-2 drug which is effective in treating COVID-19 patients[20]. In our center, we usually chose azvudine as our first-line antiviral therapy and have acquired good clinical outcomes. In this case, the patient had chronic renal insufficiency after renal transplantation, so we had to reduce the dose of azvudine, which may cause inadequate antiviral effect.

In conclusion, we are the first to report spontaneous pneumomediastinum in a renal transplant recipient with severe COVID-19 pneumonia. This case reminds us that pneumomediastinum is a severe complication and poor prognostic factor of COVID-19 pneumonia, especially when it occurred without positive pressure ventilation and in immunocompromised patients. Early recognition and assessment of pneumomediastinum using high resolution CT scan rather than X-ray, timely mediastinal drainage, early IMV with lung-protective model, discontinuation of immunosuppression regimen at proper time and sufficient anti-viral treatment may have great value in these immunocompromised patients, and might be helpful to reduce mortality.

**Abbreviations**

COVID-19: coronavirus disease 2019; SPM: spontaneous pneumomediastinum; IMV: invasive mechanical ventilation; NIV: non-invasive ventilation; P/F ratio: PiO$_2$/FiO$_2$ ratio; ECMO: extracorporeal membrane oxygenation; LMWH: low molecular weight heparin; HFNC: high flow nasal cannulae; CT: computed tomography

**Declarations**

**Ethics approval and consent to participate**
No ethical approval was required for this study was a case report.

Consent for publication

Consent for publication was obtained from the patient's wife according to our institutional consent form.

Availability of data and materials

The datasets used or analyzed during this case report are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflict of interests.

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None

Authors' contributions

Li Shaobo managed the patient during hospitalization. Sikong Yinhe collected the patient data and wrote the manuscript. Li Shaobo and Sikong Yinhe contributed equally to this manuscript. Ding Meiling and Li Jianjun made the diagnosis and supervised the whole clinical process. All authors reviewed and approved the final manuscript.

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References


**Figures**

**Figure 1**

High resolution chest CT scan at admission. Multiple ground-glass exudates mainly located in peripheral areas of both lungs.
Figure 2

Chest X-ray showing pneumomediastinum and COVID-19 pneumonia. First bedside chest X-ray showed pneumonia and suspicious pneumomediastinum and subcutaneous emphysema, and the gas in the mediastinum and subcutaneous space gradually increased.

Figure 3
Chest Computed tomography showing subcutaneous air leak and severe pneumomediastinum and diffuse parenchymal changes of severe COVID-19 in different layers.