Pulmonary Complications of Coronavirus Disease 2019 (COVID-19)

A case report

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Abstract

Rapid evolution of pulmonary complications associated with severe COVID-19 pneumonia often pose a management challenge to clinicians especially in the critical care setting. Serial chest imaging enable clinicians to better monitor disease progression and identify potential complications early which may decrease the mortality and morbidity associated with COVID-19. We report a case of severe COVID-19 pneumonia in a 69-year-old man that presented to University Malaya Medical Centre in March 2020 with multiple pulmonary complications including lung cavitation, bronchopleural fistula, pneumothorax, pneumomediastinum, subcutaneous emphysema and acute pulmonary embolism which we highlight through serial chest radiographs (CXR) and computed tomography (CT). The patient unfortunately succumbed to his disease one month after admission. COVID-19 patients may develop pulmonary complications due to a combination of direct viral lung damage, hypoxemia and high stress ventilation. Awareness of COVID-19 complications can prompt early diagnosis and timely management to reduce morbidity and mortality.

Keywords: COVID-19 case report, lung cavitation, bronchopleural fistula, pneumothorax, pneumomediastinum
Introduction
Coronavirus disease 2019 (COVID-19) emerged from Wuhan, Hubei Province, China in December 2019 and has rapidly spread worldwide. Most affected patients have mild symptoms with good prognosis. However, WHO-China Joint Mission on Coronavirus Disease 2019 reported severe and critical diseases in 13.8% and 6.1% of patients respectively. 1 Pneumonia is a common complication of COVID-19 infection, whilst acute respiratory distress syndrome (ARDS) is the most severe sequela. Presence of pleural effusion, lung cavitation and lymphadenopathy are associated with severe disease and often carry poorer prognosis. 2 Many studies have reported common COVID-19 chest manifestation on CXR and CT, however, studies that described chest complications on imaging are limited. Herein, we report a case of severe COVID-19 pneumonia, which progresses to multiple pulmonary complications including acute pulmonary embolism, pneumothorax, pneumomediastinum, extensive subcutaneous emphysema and ruptured lung cysts causing bronchopleural fistula. This case report aims to raise awareness of potential complications, spectrum of respiratory manifestations and sequelae of COVID-19 infection.

Case report
A 69-year-old male with underlying diabetes mellitus and hypertension presented to the emergency department with a 6-day history of high-grade fever and occasional dry cough on the 21 March 2020. He had recently attended a mass gathering, however there was no known history of close contact with a confirmed or probable COVID-19 case. Clinical examination revealed elevated body temperature of 38.5 °C and bibasal lung crepitations on auscultation. Laboratory blood tests revealed normal neutrophil count of 6.5 x10⁹/L (normal range: 2.0-7.0 x10⁹/L), borderline lymphocyte count of 1.14 x 10⁹/L (normal range: 1.0-3.0x10⁹/L), raised C-reactive protein of 137.6 mg/L (normal range: <5.0) with high serum ferritin of 2268 ug/L (normal range: 22.0-322.0). The rest of the blood investigations were normal. Screening tests for respiratory pathogens i.e. influenza A, influenza B, respiratory syncytial virus, legionella, mycoplasma pneumonia, and chlamydia pneumonia were negative. SARS-CoV-2 was detected in the patient’s oropharyngeal and nasopharyngeal swab specimen through real-time reverse-transcription–polymerase chain- reaction (RT-PCR) assay.

The CXR at presentation showed classic peripheral consolidations in both lower zones. At day 3 of hospitalization (9 days after the onset of fever), the patient developed worsening
dyspnoea despite escalation of oxygen support to venturi mask. He was then transferred to the intensive care unit (ICU) and was put on high flow nasal cannula (HFNC) non-invasive ventilatory support. No clinical improvement was seen despite optimum HFNC setting (fraction of inspired Oxygen 0.6, Flow 60 L/min). Patient was started on empirical intravenous ceftriaxone, azithromycin, hydroxychloroquine, lopinavir/ritonavir and subcutaneous enoxaparin prophylaxis dose based on the best evidence at that point of time during the early phase of COVID-19 in our country.

He remained tachypnoeic with respiratory rate of >30/min and oxygen saturation of 88-92% with partial pressure oxygen (PaO₂) of 51mmHg on arterial blood gas analysis. The patient eventually required intubation and mechanical ventilation after 6 hours. High-resolution CT (HRCT) chest was done on the next day (day 10 of illness) which revealed ground-glass opacities (GGO) with consolidations and crazy-paving patterns in both lung fields, predominantly in a subpleural distribution with about 50% of total lung involvement. There was also gravity-dependent lung atelectasis in posterior lung bases bilaterally. No cystic lung lesions were noted in this initial CT. In view of worsening respiratory distress, the patient required mechanical ventilation with positive end-expiratory pressure (PEEP) averaging 10-14 cmH2O.

On day 18 of illness and approximately one week after commencement of mechanical ventilation, patient developed worsening oxygenation and extensive subcutaneous emphysema at the neck, chest and abdomen region. Immediate CXR and abdominal radiograph (AXR) showed left pneumothorax, pneumomediastinum as well as extensive subcutaneous emphysema as mentioned (Figure 1A, B). Positive D-dimer was also detected at the same time. An urgent CT pulmonary angiography (CTPA) which was performed on the same day showed filling defect consistent with emboli in the right main pulmonary artery extending to the segmental arteries of the right middle and lower lobes as well as in the segmental branches of the left lower lobe pulmonary artery (Figure 1E, F). Left pneumothorax, pneumomediastinum, extensive subcutaneous emphysema and extraperitoneal emphysema extending from the pneumomediastinum were also observed. No parenchymal or subpleural cysts were present. There were also worsening dependent consolidations in both lung fields (Figure 1C, D). Subsequently, a chest tube was inserted for the left pneumothorax
and subcutaneous enoxaparin was upgraded to treatment dose in view of the pulmonary embolism diagnosis.

The patient was continued on mechanical ventilation due to difficult weaning. Possible development of superimposed bacterial infection could have contributed to the worsening respiratory status of the patient. Antibiotic treatment was escalated to intravenous meropenem and vancomycin on day 21 of illness, and intravenous hydrocortisone 50mg 6-hourly was initiated for septic shock. This was followed by addition of intravenous trimethoprim/sulfamethoxazole as stenotrophomonas maltophilia was yielded based on the positive respiratory and blood culture results. CXR done on day 24 of illness demonstrated a new well-defined cystic lesion at the right lower zone (Figure 2A). There was no pneumothorax in the right chest. The left pneumothorax and subcutaneous emphysema has improved. A follow-up CTPA showed residual right pulmonary artery emboli (Figure 2B) and a large cyst in the consolidated right middle lobe communicating with a segmental bronchus (Figure 2C). There were also multiple subpleural cysts, some communicating with each other in the right middle and lower lobes (Figure 2D). At the time, we postulated that these cysts were likely secondary to underlying severe COVID-19 lung changes. However, complication secondary to pulmonary infarct cannot be excluded. The next day, the patient developed right tension pneumothorax secondary to rupture of the lung cysts and an emergency right chest tube insertion was done (Figure 3A, B). Unfortunately, despite insertion of double chest tubes over the right lung, the pneumothorax persisted. Subsequently, blood pleurodesis was carried out but no clinical improvement was noted.

Throughout the ICU stay, the patient required multiple cycles of prone positioning as rescue therapy to improve oxygenation. He also developed multi-organ failure requiring vasopressors and continuous renal replacement therapy. On day 24 of hospitalization (Day 30 of illness), a fourth CT was performed in view of worsening clinical condition and difficult ventilation. The CT depicted extensive bilateral consolidation, loculated right hydropneumothorax with a fluid filled cyst and communication between the pulmonary cyst with pleural space and segmental bronchi causing a bronchopleural fistula (Figure 3C, D). Despite maximal organ support and medical treatment, the patient’s clinical condition deteriorated and he eventually succumbed on day 31 of illness.
Figure 4 summarizes the timeline for major chest imaging findings of the pulmonary complications according to days of illness and hospitalization.

Informed consent was obtained from the patient’s family member.

Discussion
Chest imaging is indicated in COVID-19 patients for establishing a baseline for the patient’s pulmonary condition, identification of cardiopulmonary comorbidities and for monitoring disease progression. In the event of clinical deterioration, imaging assessment helps to diagnose disease progression and acute cardiopulmonary complications such as pulmonary embolism, superimposed bacterial infection, heart failure or less commonly, complications such as pneumothorax and pneumomediastinum.

Typical chest findings in COVID-19 patients show bilateral lung involvement with patchy or asymmetric diffuse air space opacities, predominantly in a peripheral, posterior distribution and mainly in the lower lobes. In later stages of the disease, CT may show increased GGO, dispersed consolidation, reticular opacities, crazy-paving, bronchiectasis, pleural thickening, septal thickening and involvement of subpleural region. As the disease progresses, atypical CT features such as pleural effusion, cystic changes, pericardial effusion, nodules, and lymphadenopathy may be present. Besides, complications such as pulmonary embolism, pneumothorax, pneumomediastinum and cavitation or cysts in COVID-19 patients have emerged which further elucidate the complexity in managing such patients.

COVID-19 pneumonia is described as a unique disease despite fulfilling most of the Berlin definition of ARDS. The pathophysiology of this disease is attributed by hyperimmune reaction of the host which results in massive vascular endothelial injury and alveolar epithelial cell damage. In our case study, the patient had no history of smoking or underlying lung pathology. The initial viral infection may impose structural damage to alveoli, particularly at the subpleural regions where ‘stress and strain’ insult is the greatest. This could possibly result in pneumatoceles or cysts in the subpleural areas of consolidation, as in our case. The development of lung cavitation is uncommon in COVID-19 and could occur secondary to direct lung damage caused by the virus, stress imposed by the mechanical ventilation or may also result from secondary bacterial or fungal infection. Possibility of secondary infection must be ruled out in the wake of development of lung
cavitation in COVID-19 and appropriately managed to improve the patient outcome. The high stresses generated during mechanical ventilation can cause barotrauma leading to bronchial or alveolar rupture, which is evidenced by air leak detected as pneumothorax, pneumomediastinum and subcutaneous emphysema on imaging.\textsuperscript{4, 5, 9}

In addition, our patient developed acute pulmonary embolism during the course of the illness, which further exacerbated the ventilation/perfusion imbalances. Klok et al. reported that pulmonary embolism is the most common thrombotic complication encountered in patients with COVID-19.\textsuperscript{10} 16-31\% of pulmonary embolism are complicated by pulmonary infarction\textsuperscript{11, 12} and cavitation complicates 4-7\% of pulmonary infarctions.\textsuperscript{13} Infarcts with cavities are commonly single, right sided and after 2 weeks, is associated with a large area of consolidation.\textsuperscript{14} Severe COVID-19 pneumonia is susceptible to both venous and arterial thromboembolism due to deranged coagulation, excessive inflammation, hypoxia and prolonged immobilization. In addition, an increased D-dimer concentration at the time of admission is significantly associated with mortality.\textsuperscript{10, 15} Hence, judicious use of anticoagulant therapy is prudent in patients with COVID-19 pneumonia in the absence of bleeding risk.

**Conclusion**
In conclusion, our case highlights the imaging findings of multiple pulmonary complications in a patient with severe COVID-19 pneumonia. Widespread lung damage, hypoxemia and high-stress ventilation may lead to severe manifestations as seen in our patient. Prompt recognition of these complications, cautious ventilation strategy and timely intervention targeted at the complications should be the direction of care for such patients to reduce morbidity and mortality.

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Figure 1. (A) CXR on day 18 of illness showing left pneumothorax, in the form of deep sulcus sign in the left hemithorax (black arrowheads), pneumomediastinum (black solid arrows). There was also subcutaneous emphysema in both chest and neck region (black-frame arrow) (B) AXR demonstrating subcutaneous emphysema involving lower abdominal subcutaneous tissue (black-frame arrow). There were also curvilinear lucencies at the upper abdomen suggestive of pneumomediastinum extending to extra-peritoneal space (black arrowhead). (C, D) CTPA in coronal and sagittal lung window showing left pneumothorax (white arrowheads), pneumomediastinum (black solid arrows), subcutaneous emphysema (black-frame arrows) and extra-peritoneal emphysema (black arrowhead). Bilateral multifocal peripheral subpleural GGO (white solid arrows) and dependent consolidations were seen. (E, F) Axial and coronal view CTPA in mediastinal window showing filling
defects (white line arrows) in the right main pulmonary artery extending into the segmental branches of right middle and lower lobes as well as involving the segmental branch of the left lower lobe.

Figure 2. (A) CXR on day 24 of illness showing a new well-defined cyst (black solid arrows) at right lower zone and resolving left pneumothorax, pneumomediastinum and subcutaneous emphysema. (B) Axial view follow-up CTPA in mediastinal window demonstrating residual thrombus in the right pulmonary artery (arrowhead). (C) Coronal view CTPA in lung window showing a large cyst in a consolidated right middle lobe with communication with adjacent segmental bronchi (black line arrow). (D) Axial view of same scan showing communication
between the cysts (white solid arrow). There were other several smaller non-communicating subpleural cysts in right middle and lower lobes (not shown).

Figure 3. (A) CXR on day 25 of illness demonstrating right tension pneumothorax. (B) Post chest tube insertion showed improving right pneumothorax with several right lower zone cysts (white arrows) as seen in previous CT. (C, D) Coronal and axial view HRCT chest in lung window depict smaller right middle lobe cysts (black arrows) and loculated right hydropneumothorax (black arrowhead). There was direct communication between the one of the cysts with the pleural space/pneumothorax suggesting a ruptured cyst causing bronchopleural fistula (white arrow line).
Figure 4: Timeline of Major Imaging Findings According to Day of Illness and Day of Hospitalization from March 21 to April 14, 2020.

| Day of Illness | Day of Hospitalization |
|---------------|------------------------|
| 7             | 1                      |
| 8             | 2                      |
| 9             | 3                      |
| 1             | 1                      |
| 2             | 2                      |
| 3             | 3                      |
| 4             | 1                      |
| 5             | 2                      |
| 6             | 3                      |
| 7             | 1                      |
| 8             | 2                      |
| 1             | 1                      |
| 2             | 2                      |
| 3             | 3                      |
| 4             | 1                      |
| 5             | 2                      |
| 6             | 3                      |
| 7             | 1                      |
| 8             | 2                      |
| 9             | 3                      |

**Major Imaging Findings**

**CXR**
- Bilateral peripheral consolidations at lower zones.
- Multifocal peripheral GGO, consolidations with 50% of total lung involvement.
- New left pneumothorax, pneumomediastinum, extensive subcutaneous emphysema.
- New right lower zone cysts.
- New right middle and lower lobe cysts with bronchial communication, residual PE, worsening lung consolidations and dependent atelectasis.
- Right tension pneumothorax secondary to ruptured cysts, resolved left pneumothorax.
- Right hydro-pneumothorax, ruptured cyst and bronchopleural fistula, extensive multifocal consolidations.

**HRCT**
- Ground-glass opacification.
- Abdominal X-ray.
- Computed Tomography Pulmonary Angiography.
- Pulmonary embolism.
- Real-time reverse transcription-polymerase chain reaction.

**RT-PCR swab for SARS-CoV-2**
- Ct Value

25.44 22.11 25.68 29.67 31.33 35.53

CXR: Chest X-ray; HRCT: High Resolution Computed Tomography; GGO: Ground-glass opacification; AXR: Abdominal X-ray; CTPA: Computed Tomography Pulmonary Angiography; PE: pulmonary embolism; RT-PCR: Real-time reverse transcription-polymerase chain reaction; Ct value: cycle threshold value.