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Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a pandemic since its onset at the end of 2019 [1]. COVID 19 is well known in affected individuals for causing several fatal complications. Among its rare complications are subcutaneous emphysema, pneumomediastinum and pneumothorax, with very few case reports has been published in the literature to date. We present four cases of reverse- transcriptase Polymerase chain reaction (RT-PCR) confirmed COVID-19 patients who developed these complications during their hospital course and its impact on their prognosis. Out of four patients, one patient died secondary to sepsis and multiple organ failure.

Keywords: Subcutaneous Emphysema; Covid-19; Pneumothorax; Pneumomediastinum

Introduction

Over the last few months, a number of COVID-19 cases with varying clinical features have presented to our tertiary care center. Among these, Subcutaneous Emphysema, Pneumomediastinum, and Pneumothorax were its few rare presentations. These complications are classically reported secondary to barotrauma in patients on invasive mechanical ventilation. Subcutaneous emphysema refers to the presence of air under the skin, most commonly secondary to pneumothorax and rarely secondary to pneumomediastinum. Pneumomediastinum, an uncommon, life-threatening condition, occurs due to alveolar rupture because of increased intrathoracic pressure, tracked by air dissection through the Broncho vascular sheath into the mediastinum [2]. Common predisposing factors associated with the development of these complications include male sex, thin lean built, respiratory infections, barotrauma, tracheobronchial injury, esophageal trauma and penetrating or non-penetrating injury to lungs and pleura. COVID-19 is well known for causing severe parenchymal damage in patients with acute respiratory distress syndrome (ARDS), putting a patient at potential risk of developing these complications.

Case Reports

Case 1

48-year-old gentleman, with a history of gastritis, presented to the Emergency department (ED) with complaints of fever and cough for the past two weeks and shortness of breath since last 2h hours. On arrival in ED, his oxygen saturation was 87% on room air, blood pressure was 98/50 mmhg, heart rate 102 beats per minute, respiratory rate 30 breath per minute and temperature 37.9°C. Laboratory workup demonstrated C-reactive protein (CRP) level of 62.7 mg/L (0 - 10 mg/L), Ferritin of 1446 ng/ml (22 - 322 ng/ml), D dimer of 0.2 mg/L FEU (< 0.5 mg/L FEU), LDH of 602 IU/L (120 - 246 IU/L). Procalcitonin (PCT) was within normal range 0.119 ng/ml (< 0.5 ng/mL).

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His X-ray Chest (CXR) was done, which showed inhomogeneous airspace shadowing in both mid and lower lung zones predominantly at the periphery (Figure 1a). Nasopharyngeal COVID-19 RT-PCR was sent, which came back positive. He received non-invasive ventilation support on the minimal setting, intravenous (IV) steroids, broad-spectrum antibiotics, and 40% Fraction of inhaled oxygen (FiO₂). He also received one dose of IV Tocilizumab. His oxygen requirement decreased to 28% and non-invasive ventilation was weaned off gradually. On day 5, his respiratory status deteriorated, and oxygen demand increased up to 60% FiO₂. CXR was done, which was suggestive of pneumomediastinum (Figure 1b). Chest computed tomography (CT) was done, which confirmed multiple air lucencies in the mediastinum extending along the right paratracheal border, superiorly up to the right side of neck, inferiorly it was seen along great vessels and the epicardium, representing pneumomediastinum (Figure 1c and 1d). Conservative management was chosen for its treatment with high flow oxygen. The subsequent CXR showed interval resolution of Pneumomediastinum. He was discharged on 2 Liters of oxygen with laboratory investigations showing a decrease in the level of CRP (0.81 mg/L), Ferritin (1323 ng/ml), and D Dimer (0.4 mg/L FEU).



Figure 1: A) CXR demonstrates bilateral airspace shadowing at arrival of patient. B) A Rim of air around cardiac borders can be seen suggestive of Pneumomediastinum. C) and D) Axial images showing presence of multiple air lucencies around great vessels of neck and around heart suggestive of Pneumomediastinum.

Case 2

Sixty-one years old male known case of Ulcerative Colitis on azathioprine got admitted to Gastroenterology with Jaundice for one week and fever for two days. On arrival, his blood pressure was 105/55 mmHg, heart rate 120 beats per minute, respiratory rate 24 breaths per minute, temperature 38.7°C and oxygen saturation 94% on 28% of FiO₂. Nasopharyngeal COVID RT-PCR on admission came out to be

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positive. In Complete blood cell counts, hemoglobin was 9.9 gm/dl (12.3 - 16.6 gm/dl), white cell count 2.8×10^9 /L ($4.8 - 11.3 \times 10^9$), and platelets 137×10^9 /L ($154 - 433 \times 10^9$). His liver functions tests (LFT) on admission showed total bilirubin of 13.3 mg/dl (0.1 - 1.2 mg/dl), direct bilirubin 11.0 mg/dl (0 - 0.2 mg/dl), Gamma-glutamyl transpeptidase (GGT) 238 IU/L (38 - 55 IU/L), Alanine transaminase (ALT) 186 IU/L (35 - 45 IU/L), Aspartate transaminase (AST) 150 IU/L (31 - 35 IU/L), Alkaline phosphatase (ALP) 214 IU/L (45 - 129). However, LFTs got gradually improved with supportive management after ruling out its common causes at this age. The patient was managed for severe COVID Pneumonia with possible cytokine storm syndrome and drug-induced Pancytopenia. He remained in the hospital for about one month, during which he developed worsening hypoxemia with increasing oxygen demand up to 50% FiO₂, despite non-invasive ventilation support and awake proning. Chest CT showed pneumomediastinum and Emphysematous changes, which were seen in both lungs predominantly involving diffuse ground glass (Figure 2c and 2d). The patient was managed conservatively with high flow oxygen through a face mask and did not require tube thoracostomy. No worsening of pneumomediastinum was observed in subsequent CXR (Figure 2a and 2b). In laboratory workup, the maximum levels of inflammatory markers detected were: Ferritin 2467 ng/ml, LDH 1197 IU/L, D Dimer 1.5 mg/l, PCT 2.2 ng/ml CRP 162 mg/l. He received IV broad-spectrum antibiotics and IV steroids for several days. On day 32, the patient's course got complicated with a sudden drop in the Glasgow coma score (GCS), hypotension, and bradycardia. He was started on vasopressors (norepinephrine and dobutamine), but the patient didn't show any improvement. He got pulseless at the last moment and Electrocardiograph (ECG) showed asystole and he passed away.



Figure 2: A) and B) CXR showing alveolar space shadowing in bilateral lung fields at time of admission and before discharges. C) and D) Axial images of CT showing pneumomediastinum along with emphysematous changes in lung parenchyma with ground glass haziness.

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Case 3

A 41-year-old male with a history of hepatitis C in the past presented in ED with complaints of fever, cough, and shortness of breath since the last six days. On arrival in ED, his Blood Pressure was 115/65 mmHg, heart rate 108 beats per minute, respiratory rate 26, oxygen saturation of 94% on 32% FiO₂ and temperature was 38.0°C. Initial laboratory workup showed raised inflammatory markers with a ferritin of 2390 ng/ml, PCT of 5.72 ng/ml, CRP of 338 mg/L, LDH of 1470 IU/L, and D-dimer of 9.1 mg/L FEU. In his Complete blood count, hemoglobin was 13.3 gm/dl, Leukocyte count 12.5 × 10°/L and Platelets counts 337 × 19°/L. First, CXR in ED showed bilateral interstitial and alveolar infiltrates, consistent with the diagnosis of pneumonia. COVID-19 nasopharyngeal RT-PCR was sent, which came out to be positive. The patient was given convalescent plasma and received non-invasive ventilation support for work of breathing. By day 4 of the hospital stay patient's oxygen requirement went up to 70% FiO₂ and repeat CXR showed subcutaneous emphysema in the neck, and suspicion of pneumomediastinum was raised (Figure 3a). The CT chest under appropriate lung window settings showed diffuse ground-glass haziness with septal thickening in bilateral lung fields (Figure 3c and 3d). There was evidence of pneumomediastinum with air tracking into the neck and a minimal right-sided pneumothorax along the right chest's medial border. Conservative management with high flow oxygen was opted. He was managed with IV steroids and IV antibiotics. His laboratory workup was remarkable for Leukocyte count 11.2 × 10°/L, CRP of 0.57 mg/L, D dimer of 3.3 mg/L FEU, Ferritin of 1663 mg/ml, PCT of 0.123 ng/ml, and LDH of 415 IU/L. On day 17, his CXR showed a complete resolution in subcutaneous emphysema and pneumomediastinum (Figure 3b) and later, he was discharged on 1 - 2 liters of oxygen via nasal prone.



Figure 3: A) Paratracheal air strips can be seen along with subcutaneous emphysema in neck region. B) CXR demonstrates resolution of subcutaneous emphysema before discharge. C) and D) Axial images of CT demonstrates presence of air in mediastinum.

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Case 4

56-year-old male, known case of ischemic heart disease, and hypertension presented to ED with shortness of breath, fever, and cough for three days. On arrival, his heart rate was 118 beats/minute, blood pressure 100/50 mmhg, respiratory rate 34 breaths/minute, temperature 38.3° C and oxygen saturation was 92% on 32% FiO₂. His COVID RT-PCR was sent, which came out positive, and his inflammatory markers were suggestive of cytokine storm syndrome. Initial laboratory workup showed Leukocyte count $24 \times 10^{\circ}$ /L, hemoglobin 11.3 mg/dl, platelets $117 \times 10^{\circ}$ /l, CRP 103 mg/L, Ferritin 2435 ng/ml, LDH 804 IU/L, and D dimers 12.3 mg/L FEU. He was started on systemic steroids, given two doses of tocilizumab and underwent plasma therapy. The patient remained initially on non-invasive support to decrease the work of breathing. On day 4, his respiratory status worsened, oxygen demand increased up to 60% FiO₂. Repeat CXR showed subcutaneous emphysema and pneumomediastinum (Figure 4a). A Chest CT scan was done, which confirmed extensive bilateral subcutaneous emphysema extending from the chest up to the neck and base of the skull (Figure 4c and 4d). The decision of conservative management with high flow oxygen support was made initially, but his condition deteriorated, and later, he also developed a right-sided pneumothorax (Figure 4b). A right-sided tube thoracostomy was done, and he was transferred on invasive mechanical ventilation due to impending respiratory failure. However, the patient's clinical course got complicated with sepsis and multiple organ failure despite being on broad-spectrum antibiotics, systemic steroids, and adequate ventilator settings. On the 20^{th} day of the hospital stay, the patient's family decided to shift the patient to another hospital setting, and they left against medical advice.



Figure 4: A) CXR showing subcutaneous emphysema and pneumomediastinum. B) A Pneumothorax can be appreciated on right side. C) and D) Axial images of CT demonstrates extensive subcutaneous emphysema and pneumomediastinum.

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Discussion

Patients with pneumomediastinum may present with acute shortness of breath, neck swelling, cough, hoarsens of voice and chest pain. Pneumothorax and subcutaneous emphysema are among some of the uncommon presentations [3]. Unlike Spontaneous pneumomediastinum, secondary pneumomediastinum generally has poor outcomes and may serve as an indicator of low prognostic factor. Several proposed mechanisms are described for this disease, but the exact etiology is still unknown [4,5].

Although in most cases, the development of these complications is usually secondary to barotrauma in patients in the intensive care unit (ICU) while being on a mechanical ventilator. However, in our cases, none of these patients underwent mechanical ventilator before developing such complications. Only one patient got intubated and remained on a mechanical ventilator, and that too after developing respiratory failure due to extensive emphysema, pneumothorax, and pneumomediastinum. COVID-19 associated pneumomediastinum, subcutaneous emphysema, and pneumothorax have also been demonstrated in various patients in recent case reports and case series [6-9]. In most of these cases, patients developed these complications without being on an invasive mechanical ventilator, although in some instances, non-invasive ventilation was used initially.

Non-invasive ventilation (NIV) is an essential tool used in most hospital settings for acute respiratory failure (ARF). The use of NIV has been reported previously to be effective in the treatment of SARS-related ARF without having significant infection risks to health care workers [10]. It may also increase the pressure in the respiratory tract causing the pressure gradient between alveoli and surrounding tissues, which may lead further into the development pneumomediastinum, and subcutaneous emphysema secondary to rupture of alveoli and the formation of interstitial emphysema. Thus, the use of NIV with high-pressure settings can further aggravate respiratory dysfunction. Literature shows 5% to 15% of barotrauma incidence secondary to NIV use in different patients [11-13]. However, its continuous use in these complications is still controversial.

An acute rise in oxygen demand and worsening of clinical condition in patients with COVID-19 should always raise a suspicion of underlying pneumomediastinum and pneumothorax. X-Ray findings like air in the subcutaneous tissue and the paratracheal strip of aeration might also help detect these complications. There are no clear guidelines until now for the management of these complications in COVID-19 patients. In our cases, we managed most of these patients conservatively, abutting any intervention causing a further increase in morbidity in already diseased lungs except in the fourth case, which required tube thoracostomy as he developed pneumothorax.

Conclusion

Upon reviewing these cases, we concluded that all patients with COVID-19 should be vigilantly monitored and examined. Early signs of these complications can easily be missed clinically and should always be confirmed with CT chest. Moreover, non-invasive ventilation with high-pressure settings could be the predisposing factor for these morbidities; hence, therefore, it must be individualized according to the patient's lung status, with minimum pressure setting. However, more studies are needed to further assess the correlation between COVID-19 and non-invasive ventilation.

Declaration of Interests

We declare no competing interests.

Authors' Contributions

All the authors have made substantial contribution.

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Bibliography

- Spinelli A and Pellino G. "COVID-19 pandemic: perspectives on an unfolding crisis". *The British Journal of Surgery* 107.7 (2020): 785-787.
- 2. Macklin CC. "Transport of air along sheaths of pulmonic blood vessels from alveoli to mediastinum: clinical implications". Archives of Internal Medicine 64.5 (1939): 913-926.
- Iyer VN., et al. "Spontaneous pneumomediastinum: analysis of 62 consecutive adult patients". In Mayo Clinic Proceedings 84.5 (2009): 417-421.
- 4. Macia I., et al. "Spontaneous pneumomediastinum: 41 cases". European Journal of Cardio-Thoracic Surgery 31.6 (2007): 1110-1114.
- 5. Maunder RJ., *et al.* "Subcutaneous and mediastinal emphysema: pathophysiology, diagnosis, and management". *Archives of Internal Medicine* 1144.7 (1984): 1447-1453.
- 6. Sun R., *et al.* "Mediastinal emphysema, giant bulla, and pneumothorax developed during the course of COVID-19 pneumonia". *Korean Journal of Radiology* 21.5 (2020): 541-544.
- 7. Zhou C., et al. "COVID-19 with spontaneous pneumomediastinum". The Lancet Infectious Diseases 20.4 (2020): 510.
- Wegner U., et al. "Spontaneous Pneumomediastinum Associated With SARS-CoV-2: Infrequent Complication of the Novel Disease". Cureus 12.7 (2020): e9189.
- 9. Mohan V and Tauseen RA. "Spontaneous pneumomediastinum in COVID-19". BMJ Case Reports 13.5 (2020): e236519.
- 10. Yam LY., et al. "SARS: ventilatory and intensive care". Respirology 8.1 (2003): S31-S35.
- 11. Ruggeri P and Girbino G. "Fatal pneumomediastinum associated with use of non-invasive mechanical ventilation". *Respirology Case Reports* 2.4 (2014): 126-128.
- Fuchs H., et al. "The cause of acute respiratory failure predicts the outcome of non-invasive ventilation in immunocompromised children". Klinische Pädiatrie 227.6-7 (2015): 322-328.
- Liu XQ., et al. "Management of critical severe acute respiratory syndrome". Chinese Journal of Tuberculosis and Respiratory Diseases 26 (2003): 329-333.

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