Clinical Communication

Unusual complications of spontaneous pneumomediastinum and subcutaneous emphysema in patients with SARS-CoV-2 infection: A case report

INTRODUCTION

Coronavirus disease of 2019 (COVID-19) pneumonia caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus was first reported in Wuhan in December of 2019. Its rapid worldwide spread resulted in an unprecedented pandemic. The virus mainly affects the lungs and commonly causes symptoms of fever, cough and shortness of breath. Around 5% of patients require intensive care unit (ICU) admission with severe acute respiratory distress syndrome (ARDS). The classical computed tomography (CT) thorax description is that of ground glass opacifications (GGO) which are bilateral and arranged peripherally affecting the lower lobes.[1]

Being trained in providing both invasive and non-invasive mechanical ventilation, anaesthesiologists played a crucial role in multidisciplinary intensive care management in this pandemic.[2-4] Our ICU, as a designated centre for patients with severe COVID-19, received 612 patients from June 2020 to February 2021, most of whom required some form of invasive ventilation. Herein, we report four patients who developed spontaneous pneumomediastinum (SPM) and subcutaneous emphysema (SCE) in the absence of invasive mechanical ventilation. Although, there are several reports of pneumomediastinum and SCE in mechanically ventilated patients, these are uncommon in non-intubated patients.[5]

CASE REPORT

We noted the demographic characteristics, clinical course and final outcome of our patients [Table 1]. All the patients received medications for COVID-19 according to our institute protocol and choice of oxygen therapy and other supportive medications were at the discretion of the attending ICU consultant anaesthesiologist. The normal values for the blood investigations mentioned in Table 1 are as follows: blood urea 20-40 mg/dl; creatinine 0.8-1.2 mg/dl; White blood cell (WBC) count 4000-11000 cells/ml3; ferritin 20-250 ng/ml; C-Reactive protein (CRP) <0.3 mg/dl; D-dimer <0.4 μg/ml; lactate dehydrogenase (LDH) 140-280 U/L.

DISCUSSION

Severe COVID-19 disease may cause shortness of breath, loss of appetite, confusion, persistent pain or pressure in the chest along with fever leading to severe acute respiratory syndrome (SARS), especially in patients with comorbidities. Presence of extra-alveolar air in the mediastinum without obvious sources of mediastinal air (perforation of hollow organs, trauma, gas producing infections etc.) is defined as SPM and it has been reported in SARS virus infections, influenza, Pneumocystis jirovecii pneumonia.[6]

Our hospital was one of the two main ICUs admitting severe COVID pneumonia patients in our city. Of all the 612 patients admitted with severe ARDS with COVID pneumonia since June 2020, only three patients developed SCE [Figure 1]. In this case report, out of four patients, two had both SPM and SCE (case 1 and 4), one each had isolated SPM (case 2) and isolated SCE (case 3). None of our patients developed pneumothorax. We have come across only few cases reporting the association of SPM and COVID-19 in our literature search.[7]

The postulated mechanism underlying SPM in COVID-19 is that SARS-CoV-2 causes diffuse alveolar membrane damage by disruption of the alveolar membrane integrity. Any increase in the alveolar pressure or any decrease in the interstitial pressure causes an increase in the pressure gradient between the alveoli and the interstitium. This may lead to alveolar rupture resulting in accumulation of air in the interstitium. This air may dissect along the bronchovascular sheaths causing SPM towards the mediastinum and may further progress to pneumothoraces and SCE. So, the patients are more likely to develop SPM, as the severity of alveolar damage increases. In most cases, the pressure in the mediastinum is relieved by decompressing into the subcutaneous spaces, causing air to enter the face and up to the thighs in several instances.[8] But in some, the diffuse alveolar damage causes dilatation of cystic air spaces, which in turn may rupture to produce pneumothorax.

Table 1: Clinical course and outcome of the patients

Parameter	Case 1	Case 2	Case 3	Case 4
Age/Sex	45 years/Male	38 years/Male	75 years/Male	43 years/Male
Symptoms at presentation	Fever ×10 days Breathlessness ×2 days	Fever ×2 days Breathlessness ×2 days Altered sensorium ×2 days	Fever ×2 days Breathlessness ×2 days	Fever ×5 days Breathlessness ×5 days Loss of taste sensation ×5 days
Room air SpO_2 at presentation	86%	94%	90%	89%
Comorbidities	Systemic hypertension, Chronic kidney disease	Post renal transplant Chronic kidney disease on maintenance hemodialysis	Diabetes mellitus, Systemic hypertension	Systemic hypertension, Coronary artery disease
COVID-19 confirmed by	RT PCR	RT PCR	RT PCR	RT PCR
abnormal routine blood investigations	Blood urea 87 mg/dl, Creatinine 1.4 mg/dl, WBC 15350 cells/ml^3	Blood urea 161 mg/dl, Creatinine 5.8 mg/dl	WBC 26500 cells/ml^3 (Neutrophils 95.3%)	Nil
Elevated inflammatory markers of COVID-19	Ferritin 579.2 ng/ml, CRP 2.4 mg/dl D dimer 1.12 µg/ml	Ferritin 322.6 ng/ml, CRP 2.4 mg/dl D dimer 5.4 µg/ml LDH 1156 U/L	Ferritin 1983 ng/ml, D dimer 805 µg/ml LDH 520 U/L	Ferritin 555.2 ng/ml CRP 8 mg/dl
Oxygen support received in hospital before development of complications	Initially NRBM 15 L of O_2, Later HFNC-50 L of 100% O_2	NRBM 10 L of O_2	HFNC-50 L of 100% O_2, NIV with PEEP 8 cm H_2O (airway pressures never increased above 15 cm H_2O)	NIV with PEEP 5 cm H_2O (airway pressures never increased above 15 cm H_2O)
COVID-19 medications (Institute protocol- Remdesivir, Dexamethasone, Azithromycin and Heparin)	Received	Received	Received	Received
Complications	SCE, SPM (on day 2 of admission)	SPM (on day 3 of admission)	SCE (on day 5 of admission)	SCE, SPM (on day 4 of admission)
Final outcome	Required intubation with endotracheal tube on day 9, expired on day 21	Required intubation with endotracheal tube on day 11, expired on day 14	Required intubation with endotracheal tube on day 12, expired on day 14	Improved and discharged home in stable condition on day 12

SpO_2 - Peripheral oxygen saturation; COVID-19 - Corona virus disease of 2019; RT PCR- reverse transcriptase polymerase chain reaction; WBC- White blood cells; CRP- C-reactive protein; LDH- lactate dehydrogenase NRBM- non rebreather mask; HFNC- high flow nasal cannula; NIV- non-invasive ventilation; PEEP- positive end expiratory pressure; SCE- subcutaneous emphysema; SPM- spontaneous pneumomediastinum.)

In the past SARS epidemic, steroid therapy was also implicated in the pathogenesis of spontaneous pneumothorax as it could delay wound healing and perpetuate air leakage.[9] All our patients had been treated with dexamethasone as a part of COVID-19 treatment and it would have partly predisposed our patients to air leaks. Valsalva manoeuvre, tobacco or marijuana smoking, illicit drug use, interstitial lung disease and lung infections are other risk factors for SPM. Our third patient was also a moderate tobacco smoker. There have been reports describing the role of large size endotracheal tubes and high PEEP values in the development of pneumomediastinum.[10] The former may cause tracheobronchial injury and the latter may result in barotrauma leading to pneumomediastinum. However, our patients were neither intubated, nor received high PEEP values (maximum of 8 cmH_2O in case 3 during NIV support) before the onset of SPM and/or SCE. We also observed elevated levels of inflammatory markers in all patients, most probably substantiating the occurrence of the cytokine storm. Studies to explore the role of immunosuppressive agents in decreasing the destruction of alveoli and the risks of developing pneumomediastinum are needed to address this issue.

Development of SPM and SCE are considered a possible indicator of worsening disease in COVID-19 patients.[11] Even in our case report, three out of four COVID-19 patients had poor hospital course and died eventually. In a pooled analysis on COVID-19 patients, the authors concluded that elevated LDH values were associated with increased severity of disease and mortality.[12] Two of our patients (case 3 and 4) also had increased levels of LDH and we lost both of them.

SPM is a rare, benign self-limiting condition that usually requires conservative treatment with rest,

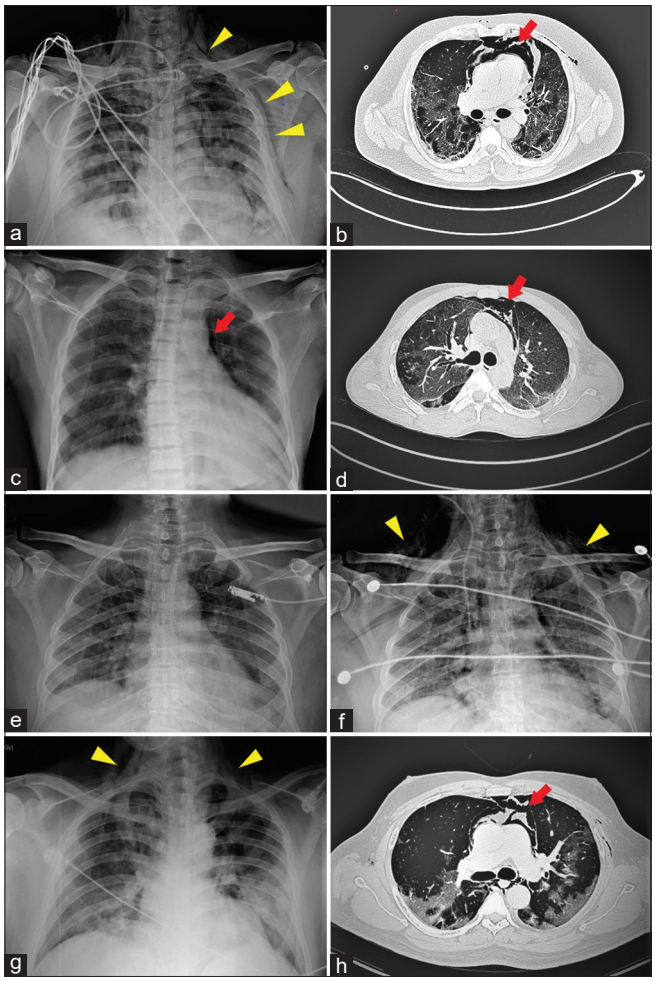

Figure 1: Radiological images. (a) Diffuse b/l infiltrates with SCE on CXR; (b) Diffuse GGO with mosaic attenuation and SPM on chest CT; (c) Air density along medial aspect of left lung on CXR; (d) Diffuse patchy GGO with mosaic attenuation, thickened vessels in right hilar region along with SPM on chest CT; (e) Patchy b/l infiltrates on CXR; (f) Diffuse b/l infiltrates with SCE on CXR; (g) B/l hilar and lower zone infiltrates with SCE on CXR; H. B/l dependent distribution of GGO and SPM on chest CT (a, b-case 1; c and d-case 2; e and f-case 3; g and h-case 4; Yellow arrow heads-SCE; Red arrows- SPM)

oxygen therapy and analgesia. However, the presence of pneumomediastinum in COVID-19 patients warrants close monitoring as it can lead to severe circulatory and respiratory pathology and also because the association is suggested as a potential indicator of worsening disease. As there were no major risk factors, we presume that acute lung injury due to COVID-19 pneumonia would have predisposed our patients to SPM and SCE.

CONCLUSIONS

Spontaneous pneumomediastinum and subcutaneous emphysema are rare complications of COVID-19 pneumonia and warrant close monitoring as they portend poor prognosis. Their oxygenation status can rapidly deteriorate. Hence, further research is justified to delineate the exact pathophysiology and to explore treatment modalities to reduce these complications in COVID-19 patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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