CASE REPORT

Spontaneous Air-leak Syndrome and COVID-19: A Multifaceted Challenge

Pranshuta Sabharwal[1], Sangeeta Chakraborty[2], Niraj Tyagi[3], Rahul Kumar[4], Ashutosh Taneja[5]

Abstract

Spontaneous air-leak syndromes have emerged as rare but significant complication of Coronavirus disease-2019 (COVID-19) pneumonia in the last few months. This complication has been documented in both spontaneous and mechanically ventilated patients. Although few studies have used computed tomographic scans to confirm the diagnosis, this could be challenging in resource-limited setup. We present a series of 15 cases that highlight the clinical heterogeneity with respect to stage of illness, ventilatory status, and varied clinical scenarios at the time of development of these syndromes. All cases in our series were diagnosed clinically and confirmed by bedside chest X-ray and were managed promptly. Though mortality was not so infrequent in our experience, these air-leak syndromes were not directly attributed as cause of death in these patients. Therefore, high level of clinical suspicion and vigilance is necessary to identify and manage cases of air-leak syndrome.

Keywords: Air-leak syndrome, COVID-19, Pneumomediastinum, Pneumothorax, Subcutaneous emphysema.

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-23819

Introduction

Coronavirus disease-2019 (COVID-19) has emerged as a multisystemic disorder over the last few months, leading to a myriad of complications. Pneumothorax and subcutaneous emphysema with or without pneumomediastinum have been reported in small number of patients with COVID-19, although the frequency and significance of this association remain uncertain. The incidence of spontaneous pneumothorax as reported varies from 1[1] to 1.1%.[2] These pathologies were well-documented complications of severe acute respiratory syndrome coronavirus(SARS-CoV-1) and Middle East respiratory syndrome (MERS) and were indicative of severe disease with poor prognosis.[3] The current literature comprises of case reports and retrospective cohort studies, all pointing toward clinical heterogeneity and indeterminate causal association of these complications in COVID-19 pneumonia. We hereby report the largest single-center case series of spontaneous pneumothorax and/or subcutaneous emphysema with or without mediastinal emphysema in both ventilated and nonventilated patients from a tertiary care intensive care unit in India over 4 months.

Case Descriptions

Cases 1–15

Out of the 15 patients documented in our series, nine were on invasive ventilation, five were on noninvasive ventilation (NIV), and one patient (Case 11) presented with spontaneous pneumothorax from home. This patient developed it as a sequelae of COVID-19 pneumonia, 15 days after discharge. This patient came with breathlessness and was managed with intercostal drain (ICD) insertion. During his first admission in ICU, the patient was managed with high-flow nasal cannula. Patient had no apparent risk factors for spontaneous pneumothorax.

Out of the five patients on NIV, four developed subcutaneous emphysema and one developed pneumothorax requiring ICD insertion and rescue intubation with invasive mechanical ventilation (Case 2). Two of them also had evidence of pneumomediastinum in the high-resolution computed tomography (HRCT) chest. All five patients were ventilated with a target minute ventilation of 10 to 15 mL/minute and positive end-expiratory pressure (PEEP) not exceeding 10 cm of H_2O.

Out of the nine patients on invasive mechanical ventilation, four patients developed tension pneumothorax necessitating ICD insertion. Rest of the patients developed subcutaneous emphysema with evidence of mediastinal emphysema in only 3 cases in chest X-ray. HRCT thorax could not be done in these patients due to logistic reasons. All these patients were ventilated following lung-protective ventilation (LPV) strategy with the target of maintaining plateau pressure below 30 cm of H_2O and tidal volume and PEEP not exceeding 6 mL/kg of IBW and 15 of H_2O, respectively.

Most of the patients developed these complications in second week of illness and beyond but at different stages of illness, for example, one even in weaning phase (Case 10) and one patient while on extracorporeal life support (Case 13). Out of the 15 cases, only two had underlying lung condition which was chronic obstructive pulmonary disease (Case 1) and the other was interstitial lung disease (Case 6). None of the patient had any procedure (central venous cannulation/bronchoscopy/tracheostomy) done 24–48 hours prior to the development or detection of pneumothorax/subcutaneous emphysema. Eight out of nine intubated patients

[1-5]Department of Critical Care Medicine, Sir Ganga Ram Hospital, New Delhi, India

Corresponding Author: Sangeeta Chakraborty, Department of Critical Care Medicine, Sir Ganga Ram Hospital, New Delhi, India, Phone: +91 9830356827, e-mail: brightsky@rediffmail.com

How to cite this article: Sabharwal P, Chakraborty S, Tyagi N, Kumar R, Taneja A. Spontaneous Air-leak Syndrome and COVID-19: A Multifaceted Challenge. Indian J Crit Care Med 2021;25(5):584–587.

Source of support: Nil

Conflict of interest: None

Table 1: Details of all 15 cases of pneumothorax

Cases	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*
Age/sex	59/M	51/M	48/M	57/M	46/M	73/F	71/M	53/M	56/M	40/M	61/M	73/M	57/M	42/M	41/F
Ventilation status/mode	Invasive CMV	NI PSV	NI PSV	Invasive CMV	NI PSV	Invasive CMV	Invasive CMV	Invasive CMV	NI PSV	Invasive CMV	Spontaneous on room air at home	Invasive CMV	Invasive ECMO/ PCV	NI PSV	NI PSV
Day of intubation(onset of illness)	D11	D14	D16	D10		D2	D5	D8		D28		D9	D18		
Day of pneumothorax/S C emphysema	D17	D14	D19	D17	D21	D22	D10	D16	D12	D55	D47	D15	D35	D15	D10
X-ray finding	Pneumothorax (L)	Pneumothorax (L)	Pneumomediastinum and SC emphysema	Pneumothorax (R)	SC and mediastinal emphysema	SC emphysema	SC emphysema	Pneumothorax (L)/SC emphysema	SC emphysema	Prior to intercostal drain insertion X-ray not done	(R) Large pneumothorax	SC emphysema and pneumomediastinum	SC and mediastinal emphysema	SC emphysema	SC emphysema
ANC	16,553	20,640	27,081	30,827	15,842	34,560	34,032	30,559	25,906	2,755	12,617	17,466	35,514	17,242	18,050
ALC	160	731	300	280	448	85	110	152	363	440	210	480	461	36	380
NLR at admission	48:1	12:1	17:1	15:1	7:1	24:1	31:1	54:1	23:1	10.6	23:1	23:1	23:1	11:1	13:1
Ferritin	33,511	511	609	816	4,115	5,780	2,913	211	2,446	1,265	72,454	1,515	2,180	3,017	104
D-dimer	8.22	8.45	1.36	1. 1	0.96	3.45	0.59	9.48	8.0	3.69	0.89	0.62	1.16	1.12	4.94
IL-6	1,487	>1,500	224	>1,500	>1,500	68.8	466	223	1,208	343	658	91	357	124	23
Outcome	Death on D19	Death on D17	Death on D61	Death on D20	Death on D25	Death on D26	Death on D16	Death on D18	Still in ICU	Death on D65	Death on D50	Death on D28	Death on D53	Death on D31	Shifted to ward

CMV, controlled mode of ventilation; NI PSV, noninvasive pressure support ventilation; SC emphysema, subcutaneous emphysema; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; NLR, neutrophil lymphocyte ratio; IL-6, interleukin 6

highest value of ANC, ferritin, D-dimer IL6, lowest value of ALC during the illness and at admission NLR taken into consideration

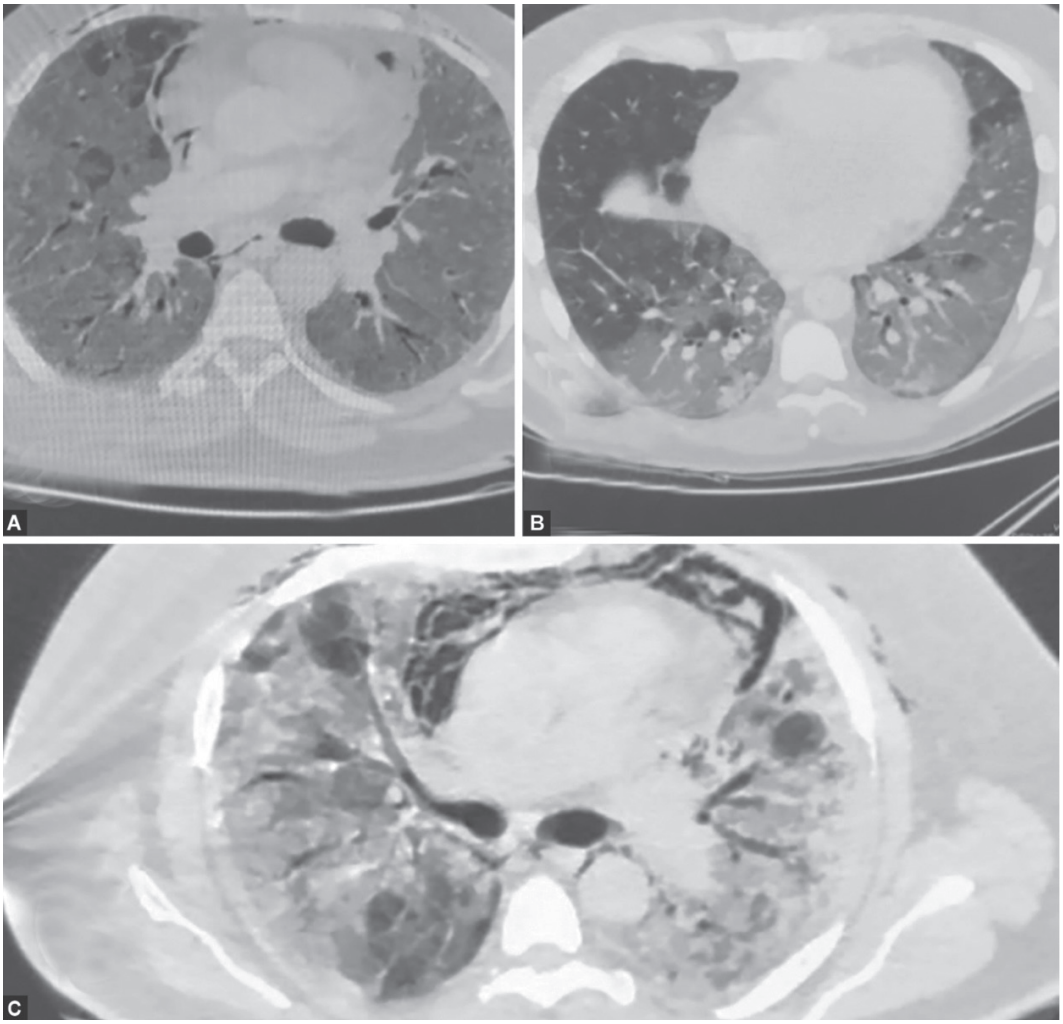
received prone ventilation. Hemodynamic instability was associated with all cases of pneumothorax along with hypoxemia and increased peak airway pressures that resolved after ICD placement. Rest of the cases were clinically identified by the presence of crepitus in neck region and later confirmed by chest radiograph and HRCT thorax whichever possible (Figs 1 and 2). Although the mortality was high in the patients in this series (13/15), the primary cause of death was not directly attributed to air-leak syndrome (Table 1).

Discussion

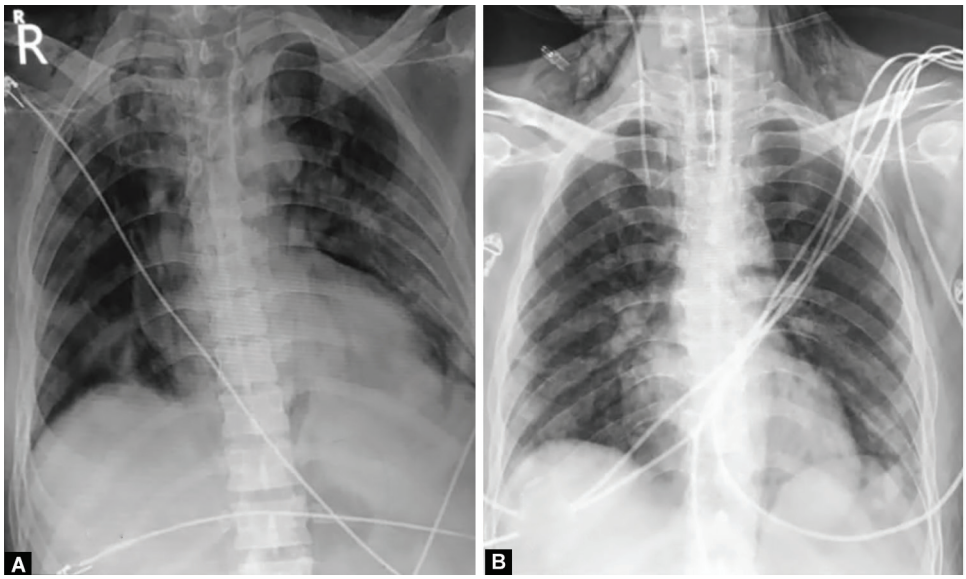
Pneumothorax, subcutaneous emphysema, and mediastinal emphysema are components of air-leak syndrome, documented to occur in acute respiratory distress syndrome (ARDS). Contribution of barotrauma, volutrauma, atelectrauma, and biotrauma has been implicated in pathological lung damages in ARDS patients on mechanical ventilation termed as ventilator-induced lung injury (VILI). Clinical and experimental data over the years have supported the use of LPV strategies to prevent VILI and therefore recommended in COVID-19-related ARDS.[4] Our case series describes 15 cases of air-leak syndrome, out of which nine patients were on invasive mechanical ventilation. Although LPV was largely achieved, it was insufficient in preventing the development of air-leak syndrome in these patients. The insufficiency of LPV in preventing air-leak syndrome has also been documented in other studies,[5] indicating that the pathological lung damages occurring in COVID-19 is much more complicated and multifactorial.

The consistent finding in most patients in this series is of laboratory parameters, suggesting a severe inflammatory state characterized by neutrophilia, lymphopenia, high neutrophil–lymphocyte ratio (NLR), and high inflammatory markers. Previous experience with SARS-CoV-1/ MERS showed that association of pneumothorax was consistent with higher neutrophil counts, more severe disease, and prolonged duration of lung inflammation.[6]

Earlier studies have attempted to explain pathological processes leading to air-leak syndromes that include consolidation, interstitial pneumonia, and *in situ* thrombosis leading to friable lung and pleura.[4] These findings were demonstrated in our patients on X-ray. However, *in situ* thrombosis could not be confirmed in all but one patient. Although indirect evidence of thrombosis was suggested by elevated D-dimer levels. A few studies demonstrated the presence of bullae,[6] subpleural blebs, ground-glass opacities (GGO),[7] crazy paving patterns,[8] and pneumatocele[6] in HRCT thorax of patients presenting with air-leak syndrome (Fig. 1). Subpleural



Figs 1A to C: (A) Subcutaneous emphysema, pneumomediastinum, subpleural blebs, ground-glass opacities; **(B)** Ground-glass opacities only; **(C)** Subcutaneous emphysema, pneumomediastinum, subpleural blebs, ground-glass opacities, crazy paving, reverse halo sign



Figs 2A and B: Subcutaneous emphysema and thin rim of mediastinal air

blebs, GGO, and crazy paving patterns could be demonstrated in HRCT thorax of our patients.

The occurrence of air-leak syndrome in spontaneously breathing patients raises further question on possible association of patient self-inflicted lung injury (P-SILI). Large swings in a minute ventilation could not be avoided, which may have put patients on NIV at risk of P-SILI. The possibility of P-SILI contributing to air-leak syndromes has also been suggested in other studies.[9,10]

Considering the possible factors putting patients at risk of air-leak syndromes, few probable preventive strategies could be to strictly maintain low driving pressure (plateau pressure—PEEP) and ultra-low tidal volume, prevent all possible patient ventilator asynchrony by maintaining appropriate sedation even in patients on NIV, and prevent cough as far as possible.

Conclusion

Our series presents a heterogeneous clinical scenario of air-leak syndrome. In a resource-limited setup where HRCT thorax is not possible in all patients, clinical diagnosis is paramount to identify air-leak syndrome. A high level of alertness, clinical suspicion, and prompt action are mandatory to prevent fatal consequences. Further randomized controlled studies are warranted for better understanding of pathogenesis of air-leak syndromes in COVID-19.

Highlights

This series highlights the heterogeneity of COVID-19-induced air-leak syndrome in terms of clinical presentation, day of illness from first symptom, mode of ventilation, and radiological features. However, the laboratory values in all our patients point toward a state of severe inflammatory response characterized by lymphopenia, high NLR, and higher value of other inflammatory markers. Further studies are required to understand the pathophysiology and predictors of air-leak syndrome associated with COVID-19 for better management of these patients.

Orcid

Pranshuta Sabharwal https://orcid.org/0000-0003-3914-5867
Sangeeta Chakraborty https://orcid.org/0000-0003-1331-1572
Niraj Tyagi https://orcid.org/0000-0001-5862-9731
Rahul Kumar https://orcid.org/0000-0001-9231-2359
Ashutosh Taneja https://orcid.org/0000-0002-5821-8868

References

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395(10223):507–513. DOI: 10.1016/S0140-6736(20)30211-7.
2. Yang F, Shi S, Zhu J, Shi J, Dai K, Chen X. Analysis of 92 deceased patients with COVID-19. J Med Virol 2020:10.1002/jmv.25891. DOI: 10.1002/jmv.25891.
3. Das KM, Lee EY, Al Jawder SE, Enani MA, Singh R, Skakni L, et al. Acute middle east respiratory syndrome coronavirus: temporal lung changes observed on the chest radiographs of 55 patients. Am J Roentgenol 2015;205(3):W267–W274. DOI: 10.2214/AJR.15.14445.
4. Berlin DA, Gulick RM, Martinez FJ. Severe covid-19. N Engl J Med 2020. DOI: 10.1056/NEJMcp2009575.
5. Jones E, Gould A, Pillay TD, Khorasanee R, Sykes R, Bazo-Alvarez JC, et al. Subcutaneous emphysema, pneumomediastinum, and pneumothorax in critically ill patients with coronavirus disease 2019: a retrospective cohort study. Crit Care Explor 2020;2(9):e0210. DOI: 10.1097/CCE.0000000000000210.
6. Mallick T, Dinesh A, Engdahl R, Sabado M. COVID-19 complicated by spontaneous pneumothorax. Cureus 2020;12(7):e9104. DOI: 10.7759/cureus.9104.
7. Do Lago VC, Cezare TJ, Fortaleza CMCB, Okoshi MP, Baldi BG, Tanni SE. Does COVID-19 increase the risk for spontaneous pneumothorax? Am J Med Sci 2020;S0002-9629(20)30320-7. DOI: 10.1016/j.amjms.2020.07.024.
8. Zantah M, Dominguez Castillo E, Townsend R, Dikengil F, Criner GJ. Pneumothorax in COVID-19 disease- incidence and clinical characteristics. Respir Res 2020;21(1):236. DOI: 10.1186/s12931-020-01504-y.
9. Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. JAMA 2020;323:2329–2330. DOI: 10.1001/jama.2020.6825.
10. Brochard L, Slutsky A, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J Respir Crit Care Med 2017;195:438–442. DOI: 10.1164/rccm.201605-1081CP.