Pneumothorax and pneumomediastinum in COVID-19 acute respiratory distress syndrome

Amos Lal¹, Ajay Kumar Mishra², Jamal Akhtar³, Christoph Nabzdyk⁴

¹Department of Medicine, Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN; ²Department of Medicine, Saint Vincent Hospital, Worcester, MA; ³Department of Sleep Medicine, Montefiore Medical Center, Bronx, New York, NY; ⁴Department of Anesthesiology and Perioperative Medicine, Division of Critical Care, Mayo Clinic, Rochester, MN, USA

Abstract

COVID-19 has involved numerous countries across the globe and the disease burden, susceptible age group; mortality rate has been variable depending on the demographical profile, economic status, and health care infrastructure. In the current clinical environment, COVID-19 is one of the most important clinical differential diagnoses in patients presenting with respiratory symptoms. The optimal mechanical ventilation strategy for these patients has been a constant topic of discussion and very importantly so, since a great majority of these patients require invasive mechanical ventilation and often for an extended period of time. In this report we highlight our experience with a COVID-19 patient who most likely suffered barotrauma either as a result of traumatic endotracheal intubation or primarily due to COVID-19 itself. We also aim to highlight the current literature available to suggest the management strategy for these patients for a favorable outcome. The cases described are diverse in terms of age variance and other comorbidities. According to the literature, certain patients, with COVID-19 disease and spontaneous pneumothorax were noted to be managed conservatively and oxygen supplementation with nasal cannula sufficed. Decision regarding need and escalation to invasive mechanical ventilation should be taken early in the disease to avoid complications such as patient self-inlicted lung injury (P-SILI) and barotrauma sequelae such as pneumothorax and pneumomediastinum. Recent systematic review further supports the fact that the use of non-invasive ventilation (NIV) in certain patients with COVID-19 pneumonia may give a false sense of security and clinical stabilization but has no overall benefit to avoid intubation. While invasive mechanical ventilation may be associated with higher rates of barotrauma, this should not mean that intubation and invasive mechanical ventilation should be delayed. This becomes an important consideration when non-intensivists or personnel with less experience provide care for this vulnerable patient population who may rely too heavily on NIV to avoid intubation and mechanical ventilation.

Introduction

COVID-19 affects the entire globe and the disease burden, susceptible age group; mortality rate varies depending on the demographical profile, economic status, and health care infrastructure [1-3]. Many studies have shown that factors like advanced age, diabetes, pregnancy, cancer, individuals with HIV/AIDS are specifically at higher risk of severe disease and poor outcomes [4]. Clinically, the respiratory system appears to be predominantly affected initially, though COVID-19 may progress to a multi dysfunction syndrome with cytokine storm, systemic vasculitis and associated thromboembolic events. These appear to be related to the viral load and associated immune response [5]. In the current clinical environment, COVID-19 is one of the most important clinical differential diagnoses in patients presenting with respiratory symptoms. Serological studies, and computed tomography are two major diagnostic tools, but results should be analyzed depending upon the test sensitivity and specificity, and clinical probability of having the disease [6]. Laboratory parameters like elevated d-dimers, thrombocytopenia, lymphopenia, high ferritin levels are prognostic factors associated with worse clinical
outcome. The optimal mechanical ventilation strategy for these patients has been a constant topic of discussion and very importantly so, since a great majority of these patients require invasive mechanical ventilation and often for an extended period of time. In this report we highlight our experience with a COVID-19 patient who most likely suffered barotrauma either as a result of traumatic endotracheal intubation or primarily due to COVID-19 itself. We also aim to highlight the current literature available to suggest the management strategy for these patients for a favorable outcome.

Case Report

A 65-year-old healthcare worker who tested positive for SARS-CoV-2 was admitted with hypoxemic respiratory failure to an ICU at an outside facility. Pertinent laboratory data on admission is summarized in Table 1. Chest X-ray done at the time of admission showed bilateral patchy airspace disease suggestive of multifocal pneumonia or ARDS (Figure 1A). The patient was a lifelong nonsmoker, though without a diagnosis of cardiopulmonary comorbidities. Upon admission the patient was noted to be hypoxicemic with a P/F ratio less than 100, qualifying as severe ARDS. The patient was non-invasively ventilated (NIV) for more than 48 hours prior to intubation and mechanical ventilation. The intubation was technically challenging and required 3 attempts. However, no obvious mechanical trauma to the oropharynx or the upper airway was noted by the proceduralist.

A few hours after intubation, the patient was noted to be developing swelling in the right side of the neck with elevated peak (40 cm H2O) and driving pressures (20 cm H2O) while she was mechanically ventilated with a tidal volume of 6 ml/kg (300 ml) of ideal body weight and a positive end expiratory pressure (PEEP) of 14 cm H2O. An emergently obtained chest x-ray demonstrated large amount of subcutaneous air, a possible right-sided pneumothorax and pneumomediastinum (Figure 1B). Concordant computed tomography of chest obtained shortly thereafter confirmed the findings, prompting the placement of a right-sided chest tube with a vacuum dressing, due to persistent pneumothorax and elevated peak pressure noted on the mechanical ventilator. This eventually led to the resolution of pneumothorax, pneumomediastinum and complete re-absorption of the subcutaneous emphysema of the chest and neck (Figure 1D). While in the ICU, the patient underwent 3 bronchoscopies to evaluate for a possible tracheobronchial injury or upper airway trauma secondary to traumatic intubation, but no site of injury was noted. However, due to persistent hypoxemia the patient was initiated on VV-ECMO, and though the patient had a protracted clinical course thereafter in the ICU for the next 4 weeks, she eventually made a full recovery.

Table 1. Laboratory data upon admission.

| Variable                | Reference value or range | Value  |
|-------------------------|--------------------------|--------|
| Serum ferritin          | 11-307 mcg/L             | 691 mg/L|
| C-reactive protein      | <=8.0 mg/L               | 109.1 mg/L|
| Interleukin 6           | <=1.8 pg/L               | 50.5 pg/L|
| D-Dimer                 | <=500 ng/mL              | 1584 pg/L|
| Procalcitonin           | <=0.08 ng/mL             | 0.69 ng/mL|
| Serum creatinine        | 0.59-1.04 mg/dL          | 0.48 mg/dL|
| 5th generation troponin | <=10 ng/L                | 13 ng/L|
| White cell count        | 3.4-9.6x10^9/L           | 25.6x10^9/L|
| Arterial blood gas      |                          |        |
| pH                      | 7.35-7.45                | 7.36   |
| pCO2                    |                         | 50     |
| pO2                     |                         | 48     |
| FiO2                    |                         | 1.0    |
| HCO3                    |                         | 27     |
| Base excess             |                         | 2      |

Discussion

Various hypothesized mechanisms that could explain this phenomenon of spontaneous pneumothorax and pneumomediastinum in COVID-19 patients come from the currently available literature. Some of the COVID-19 patients developed cavitation and pulmonary infarction [6-9]. These pathological changes in the lung parenchyma are not limited to patients receiving positive pressure ventilation which may also suggest that barotrauma might not be the only cause of pneumothorax and pneumomediastinum in these patients [10]. In later stages of ARDS these patients frequently develop small (less than 1 cm) sized subpleural cysts [11,12]. Some literature suggests that ARDS independently can result in cyst formation [13]. Negative outcomes in such patients appear to be associated with gender; men being more commonly affected as compared to women, age between 60-80 years, history of having pre-existing pulmonary diseases, and a significant smoking history [7,14].

Larger studies revealed a pneumothorax prevalence ranging between 1-2% in adult COVID-19 patients [14-17]. ARDS associated with COVID-19 vary from usual ARDS demonstrating fairly preserved lung mechanics with profound hypoxemia [18]. Some of these patients are known to have profound hypoxemia despite the preserved lung compliance; this has been attributed to a loss of lung perfusion regulation and pulmonary vasoconstriction secondary to hypoxia [18,19]. Optimal ventilation strategy in COVID-19 ARDS depends on the underlying phenotype (type L or type H) and can vary significantly [19]. Due to the initially reported high mortality rates of mechanically ventilated COVID-19 patients and the effects of self-proning on oxygenation, there has been reluctance by some clinicians to intubate patients and rather prolong NIV therapy [20-22]. This is a major departure from traditional ARDS management and may be highly relevant given that delayed intubation in non-COVID-19 ARDS patient has been associated with increased mortality [23]. One has to remember that much of the early data was obtained under extreme circumstances where normal critical care service lines had been overwhelmed to a degree that even commercial ventilator alternatives have been considered [24]. An excess in mortality during such times could at least partly be attributed to strained resources.

Despite multiple attempts to evaluate the potential airway injury from a difficult intubation, no evidence was found that the patient had a trachea-bronchial injury. Although, larger tidal vol-
umes delivered through NIV can increase the risk for patient self-inflicted lung injury (P-SILI), translating to worsening gas exchange and increase risk of barotrauma we cannot be fully certain that there is a cause-effect relation in our patient’s case [25]. More recent literature has shed light on more of such similar cases where patients have developed spontaneous pneumothorax in COVID-19 pneumonia and ARDS (Table 2). Optimal ventilation strategy in COVID-19 ARDS depends on the underlying phenotype (type L or type H) and can vary significantly [20]. Thus, the appropriate levels of PEEP and driving pressures can be quite variable and dynamic in the individual patient. Decision regarding need and escalation to invasive mechanical ventilation should be taken early in the disease to avoid complications such as P-SILI and barotrauma. A recent systematic review further supports the fact that the use of NIV in certain patients with COVID-19 pneumonia may give a false sense of security and clinical stabilization but has no overall benefit to avoid intubation [20]. In clinically difficult cases ROX index and HACOR score can be helpful in predicting NIV failure [26,27]. In addition, extended NIV use may increase the risk of transmission of COVID-19 to healthcare workers. Progression of respiratory failure, lack of improvement in oxygenation after brief trial (closely monitored) of noninvasive ventilation and supportive medical care, evolving hypercapnia, increasing work of breathing and change in mental status should trigger early intubation and mechanical ventilation. Hemodynamic instability and multiorgan failure in the presence of encephalopathy by itself should preclude trial of noninvasive ventilation in these clinically tenuous patients. Our current literature search as highlighted in Table 2 provides current knowledge on similar case.

In comparison to the cases described in the Table 2, our patient...
did not have any underlying lung disease, she was given a trial of non-invasive ventilation prior to making the decision of invasive mechanical ventilation. The duration of symptoms was relatively shorter, but it appeared that the disease progressed with a faster pace and severity requiring invasive strategies such as ECMO, need for bilateral tube thoracostomies etc. Despite the turbulent course of disease, our patient made a complete recovery. The cases described are spread apart in terms of age variance and other comorbidities. Certain patients in the review of literature, with COVID-19 disease and spontaneous pneumothorax were noted to be managed conservatively and oxygen supplementation with nasal cannula sufficed. But in more severe cases that required escalation of respiratory support such as NIV, the patients had poor outcomes [28]. The literature on COVID-19 related ARDS is evolving and thus there is limited data on risk factors for the propensity of suffering barotrauma. Data on barotrauma in COVID-19 patients is conflicting at best. Barotrauma in patients with COVID-19 infection and requiring invasive mechanical ventilation occurred at higher than expected rates and was associated with longer hospital stay and death. Among the group of patients requiring invasive

Table 2. Review of literature, highlighting similar cases in the recently published English literature.

| Study                      | Age/gender | Pulmonary risk factors in addition to COVID-19 infection | Duration of symptoms | Previous history of pneumothorax | Mechanical ventilation characteristics | Management strategy | Outcome |
|----------------------------|------------|----------------------------------------------------------|----------------------|----------------------------------|----------------------------------------|---------------------|---------|
| Aydin et al. [44]          | 24/M       | Healthy                                                  | None                 | Managed without mechanical ventilation | Tube thoracostomy, Tube details not available | Full recovery       |
| Flower et al. [45]         | 36/M       | Childhood asthma, smoking                                | 3 weeks              | Managed without mechanical ventilation | Emergency needle decompression 12-French chest drain | Full recovery       |
| Hollingshead et al. [46]   | 50/M       | Not available                                            | Approx. 4 weeks      | Managed without mechanical ventilation | Tube Thoracostomy, (details not available) | Full recovery       |
| López Vega et al. [28]     | 84/F*      | None                                                     | 5 days               | Unknown                          | Managed without mechanical ventilation | Full recovery       |
| López Vega et al. [28]     | 67/M       | None                                                     | 5 days               | Unknown                          | Managed without mechanical ventilation | Full recovery       |
| López Vega et al. [28]     | 73/M**     | Obstructive sleep apnea, obesity concurrent pulmonary embolism | 5 days               | Non-invasive positive pressure ventilation | Conservative management | Died     |
| Spiro et al. [47]          | 47/F       | History of HIV                                           | Approx. 4 weeks      | Managed without mechanical ventilation | 12-French chest drain | Full recovery       |
| Romano et al. [48]         | 30/M*      | None                                                     | Unclear              | Details not available             | Details not available               | Full recovery       |
| Romano et al. [48]         | 65/M*      | None                                                     | Unclear              | Details not available             | Details not available               | Full recovery       |
| Alhakeem et al. [49]       | 49/M       | None                                                     | Approx. 3 weeks      | Managed without mechanical ventilation | Tube thoracostomy, (details not available) | Full recovery       |
| Mallick et al. [50]        | 40/M       | Smoker                                                   | 1 week               | Managed without mechanical ventilation | Tube thoracostomy, (details not available) | Died     |
| Mallick et al. [50]        | 68/M       | None                                                     | 4 weeks              | Managed without mechanical ventilation | Bilateral tube thoracostomy, (details not available) | Full recovery       |
| Mallick et al. [50]        | 58/F**     | None                                                     | Details not available | Managed without mechanical ventilation | Conservative management            | Full recovery       |
| Rachidi et al. [51]        | 34/F       | None                                                     | 1 week               | Managed without mechanical ventilation | Conservative management | Recovery in process |
| Sun et al. [15]            | 38/M*      | None                                                     | Approx. 2 months     | Managed without mechanical ventilation | Non-invasive positive pressure ventilation followed by high flow nasal cannula (HFNC) | Conservative management | Recovery in process |
| Ucpinar et al. [52]        | 82/F*      | None                                                     | Details not available | Managed without mechanical ventilation | Tube thoracostomy, (details not available) | Full recovery       |
| Our patient                | 65/F       | Obstructive sleep apnea                                  | 1 week               | Managed without mechanical ventilation | Non-invasive positive pressure ventilation followed by Mechanical ventilation and ECMO | Multiple tube thoracostomies, 20-French | Full recovery |

*Patient with pneumomediastinum with pneumothorax; †patient with pulmonary embolism.
mechanical ventilation (IMV) patients at NYU Langone Health in New York City during the pandemic surge from March 1 to April 6, barotrauma occurred in 15% of those with COVID-19 and 0.5% of those without it (p<0.001) [29]. However some earlier papers have described a lower incidence of barotrauma in COVID-19 (approximately 2%) as compared to conventional ARDS, where it can occur in up to 10% of patients [30,31].

In our case, the clinical team did forgo proning the patient due to concerns of tracheobronchial injury though arguably, a CT chest and repeated bronchoscopies could not delineate a definitive tracheal injury. Bedside bronchoscopy and CT chest with 3D reconstruction remain the gold standard for diagnosing airway trauma [32-37]. Needless to say, a high index of clinical suspicion is of paramount importance to avoid any delay in diagnosis. Smaller injuries (less than 2 cm) can be managed conservatively in cases where adequate ventilation has been achieved in the presence of a secured and patent airway and no concern for mediastinitis exists [32].

ECMO can be lifesaving for patients with profound and refractory hypoxemia in COVID-19 ARDS. Due to extensive hospital resource utilization, availability of equipment and invasive nature of ECMO; it remains to be used as a salvage therapy for patients in which despite optimal mechanical ventilation strategies, adequate oxygenation or ventilation cannot be achieved [38-40]. As per the recent ELSO (extracorporeal life-support organization) guidance paper; PaO2:FIO2 less than 80 mm Hg for more than 6 hours or PaO2:FIO2 less than 50 mm Hg for less than 3 hours should prompt an early ECMO consult [41]. The decision of offering ECMO as a lifesaving modality needs to be considered after taking in accounts multiple patient and hospital related factors. If other modalities of improving oxygenation and ventilation such as prone positioning, pharmacological paralysis to improve ventilator synchrony and reduced work of breathing should be tried first [9,33,39,42,43]. Fortunately, early ECMO initiation was lifesaving in our patient.

COVID-19 has taught us once again that clinical research is messy and humbling as patients with COVID-19 may have dynamic clinical courses with unfortunately very different outcomes. Despite millions of cases worldwide and thousands of related research articles, it remains difficult to predict the individual patient’s outcome. Vigilance, ARDS net guidelines, and attention to detail in the clinical care remain the best recipe for a good outcome until we identify metrics that allow for reliable statistical inferences. We understand that no concrete hypothesis can be drawn from a single patient experience; therefore, well designed studies exploring this issue become even more important. The evolving literature is bringing forth new information with more cases having spontaneous pneumothorax and pneumomediastinum in COVID-19 patients. To determine a better sense of managing these complications we need to collate more data of similar presentations in the COVID-19 disease. This case highlights a spectrum of problems that can occur in patients suffering from severe COVID-19 pneumonia and ARDS. Our intent is to alert the treating physicians with regards to the appropriate monitoring of these patients if the trial of NIV is given, it may provide a false sense of security in progressively worsening disease. Prolonged periods of NIV, especially in the absence of clinical improvement should trigger consideration for repeat cross-sectional imaging to illustrate the evolution of the injury to the lung parenchyma. Persistent or worsened lung injury may warrant intubation and/or early ECMO consultation to provide optimal lung rest even in the absence of extreme hypoxemia. Current literature provides ambiguous information about its utility in severe cases of COVID-19 pneumonia and early intubation should be considered to avoid complications of p-SILI and barotrauma. While invasive mechanical ventilation may be associated with higher rates of barotrauma, this should not mean that intubation and invasive mechanical ventilation should be delayed. This becomes an important consideration where non-intensivists or personnel with less experience and familiarity taking care of this vulnerable patient population have to rely on NIV to avert or delay the need for intubation and mechanical ventilation.

Conclusions

Despite the risk of developing pneumothorax and pneumomediastinum, a closely monitored trial of NIV or high flow nasal cannula is not unreasonable and should be attempted in a subset of these patients. Based on current literature and, the cause of pneumothorax and pneumomediastinum in these patients may not only be barotrauma from mechanical ventilation; other contributing factors such as severity of the disease, underlying preexisting lung diseases and smoking may also be responsible for increasing the risk of negative events. NIV therapy in COVID-19 ARDS is not a benign intervention in patients with worsening parenchymal injury. Lack of clinical progress may warrant re-imaging and possibly consideration of elective intubation or VV-ECMO cannulation to maximize lung protection in these high risk patients.

References

1. Sahu KK, Mishra AK, Lal A. Comprehensive update on current outbreak of novel coronavirus infection (2019-nCoV). Ann Transl Med 2020;8:393.
2. Sahu KK, Mishra AK, Lal A. COVID-2019: update on epidemiology, disease spread and management. Monaldi Arch Chest Dis 2020;90:1292.
3. Sahu KK, Mishra AK, Lal A. Novel coronavirus (2019-nCoV): Update on 3rd coronavirus outbreak of 21st century. QJM 2020;113:384-6.
4. Wu Z, McGoogan JM. Characteristics of and Important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323:1239-42.
5. Soy M, Keser G, Atagündüz P, et al. Cytokine storm in COVID-19: pathogenesis and overview of anti-inflammatory agents used in treatment. Clin Rheumatol 2020;39:2085-94.
6. Lal A, Mishra AK, Sahu KK. CT chest findings in coronavirus disease-19 (COVID-19). J Formos Med Assoc 2020;119:100-1.
7. Martinelli AW, Ingle T, Newman J, et al. COVID-19 and pneumomediastinum: A multicentre retrospective case series. Eur Respir J 2020;56:2002697.
8. Lal A, Mishra AK, John K, et al. Corticosteroids and rehabilitation in COVID-19 survivors. J Formos Med Assoc Online ahead of print 2020;S0929-6646(20)30605-7.
9. Lal A, Mishra AK, Sahu KK. Prevention of early ventilator-associated pneumonia. N Engl J Med 2020;382:1671-2.
10. Liu K, Zeng Y, Xie P, et al. COVID-19 with cystic features on computed tomography: a case report. Medicine (Baltimore) 2020;99:e20175.
11. Bor C, Demirag K, Uyar M, et al. Recurrent spontaneous pneumothorax during the recovery phase of ARDS due to H1N1 infection. Balkan Med J 2013;30:123-5.
12. Gattinoni L, Caironi P, Pelosi P, et al. What has computed tomography taught us about the acute respiratory distress syndrome? Am J Respir Crit Care Med 2001;164:1701-11.

13. Joynt GM, Antonio GE, Lam P, et al. Late-stage adult respiratory distress syndrome caused by severe acute respiratory syndrome: abnormal findings at thin-section CT. Radiology 2004;230:339-46.

14. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.

15. Sun R, Liu H, Wang X. Mediastinal emphysema, giant bulla, and pneumothorax developed during the course of COVID-19 pneumonia. Korean J Radiol 2020:21:541-4.

16. Cheng ZJ, Shan J. 2019 Novel coronavirus: where we are and what we know. Infection 2020;48:155-63.

17. Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus Disease 2019 (COVID-19): A systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020;215:87-93.

18. Gattinoni L, Coppola S, Cressoni M, et al. COVID-19 does not lead to a “typical” acute respiratory distress syndrome. Am J Respir Crit Care Med 2020;201:1299-300.

19. Gattinoni L, Chiurillo D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med 2020;46:1099-102.

20. Schünemann HJ, Khabisa J, Solo K, et al. Ventilation techniques and risk for transmission of coronavirus disease, including COVID-19: A living systematic review of multiple streams of evidence. Ann Intern Med 2020;173:204-16.

21. Arulkumaran N, Brealey D, Howell D, et al. Use of non-invasive ventilation for patients with COVID-19: a cause for concern? Lancet Respir Med 2020;8:e45.

22. Patel BK, Kress JP, Hall JB. Alternatives to Invasive ventilation in the COVID-19 pandemic. JAMA 2020;324:43-4.

23. Kangelaris KN, Ware LB, Wang CY, et al. Timing of intubation and clinical outcomes in adults with acute respiratory distress syndrome. Critical Care Med 2016;44:120-9.

24. Kwon AH, Slocum AH Jr., Vareldmann D, et al. Rapidly scalable mechanical ventilator for the COVID-19 pandemic. Intensive Care Med 2020;46:1642-4.

25. Brochard L, Slutsky A, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J RespirCrit Care Med 2016;195:438-42.

26. Duan J, Han X, Bai L, et al. Assessment of heart rate, acidosis, consciousness, oxygenation, and respiratory rate to predict non-invasive ventilation failure in hypoxic patients. Intensive Care Med 2017;43:192-9.

27. Roca O, Messika J, Caralt B, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxic respiratory failure: The utility of the ROX index. J Crit Care 2016;35:200-5.

28. López Vega JM, Parra Gordo ML, Diez Tascón A, et al. Pneumome diastinum and spontaneous pneumothorax as an extrapulmonary complication of COVID-19 disease. Emerg Radiol 2020;27:727-30.

29. McGuinness G, Zhan C, Rosenberg N, et al. High incidence of barotrauma in patients with COVID-19 Infection on invasive mechanical ventilation. Radiology 2020;297:e252-62.

30. de Durante G, del Turco M, Rustichini L, et al. ARDSNet lower tidal volume ventilatory strategy may generate intrinsic positive end-expiratory pressure in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2002;165:1271-4.

31. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475-81.

32. Prokakis C, Koletsis EN, Dedelias P, et al. Airway trauma: a review on epidemiology, mechanisms of injury, diagnosis and treatment. J Cardiothorac Surg 2014;9:117.

33. Lal A, Akhtar J, Jindal V, et al. Rare cause of respiratory failure: A twist in the tale. Am Am Thorac Soc 2018;15:880-3.

34. Lal A, Akhtar J, Khan MS, et al. Primary endobronchial amyloidosis: A rare case of endobronchial tumor. Respir Med Case Rep 2018;23:163-6.

35. Lal A, Akhtar J, Pinto S, et al. Recurrent pulmonary embolism and hypersensitivity pneumonitis secondary to aspergillus, in a compost plant worker: Case report and review of literature. Lung 2018;196:553-60.

36. Lal A, Davis MJ, Akhtar J, et al. Serious cover-up: Hodgkin's lymphoma masked by organizing pneumonia. Am J Med 2018;131:1174-7.

37. Lal A, Mishra AK, Sahu KK, et al. The return of Koch's: Ineffective treatment or re-infection. Enferm Infecc Microbiol Clin 2020;38:144-5.

38. Lal A, Nabzdyk C, Ramakrishna H, et al. Consider heightened awareness of propofol infusion syndrome after extracorporeal membrane oxygenation (ECMO) decannulation. J Cardiothorac Vasc Anesth 2020;34:2174-7.

39. Lal A, Mishra AK, Sahu KK, et al. Spontaneous pneumomediastinum: Rare complication of tracheomalacia. Arch Bronconeumol 2020;56:185-6.

40. Seelhammer TG, Plack D, Lal A, Nabzdyk CGS. COVID-19 and ECMO: An unhappy marriage of endothelial dysfunction and hemostatic derangements. J Cardiothorac Vasc Anesth 2020;34:3193-6.

41. Bartletth RH, Ogino MT, Brodie D, et al. Initial ELSO guidance document: ECMO for COVID-19 patients with severe cardiopulmonary failure. ASAIO J 2020;66:472-4.

42. Lal A, Pena ED, Sarcilla DJ, et al. Ideal length of oral endotracheal tube for critically ill intubated patients in an Asian population: Comparison to current western standards. Cureus 2018;10:e3590.

43. Lal A, Mishra AK, Sahu KK. Vitamin E acetate and e-cigarette or vaping product-associated lung injury (EVALI): An update. In J Infect Public Health 2020;13:e235861.

44. Spairo JE, Siscovic S, Ockert B, et al. Secondary tension pneumothorax following COVID-19 pneumonia. IDCases 2020;21:e00868.

45. Aydin S, Oz G, Dumanli A, et al. A case of spontaneous pneumothorax in Covid-19 pneumonia. J Surg Res 2020;3:096-101.

46. Flower L, Carter J-PL, Rosales Lopez J, et al. Tension pneumothorax in a patient with COVID-19. BMJ Case Rep 2020;13:e235861.

47. Hollingshead C, Hanrahan J. Spontaneous pneumothorax following COVID-19 pneumonia. IDCases 2020;21:e00868.

48. Spiro JE, Siscovic S, Ockert B, et al. Secondary tension pneumothorax in a patient with COVID-19 pneumonia: a case report. Infection 2020;48:941-4.

49. Romano N, Fischetti A, Melani EF. Pneumome diastinum related to Covid-19 pneumonia. Am J Med Sci 2020;360:e19-e20.

50. Alhakeem A, Khan MM, Al Soub H, et al. Case Report: COVID-19–associated bilateral spontaneous pneumothorax - A literature review. Am J Trop Med Hyg 2020;103:1162-5.

51. Mallick T, Dinesh A, Engdahl R, Sabado M. COVID-19 complicated by spontaneous pneumothorax. Cureus 2020;12:e9104.

52. Rachidi SA, Motiaa Y. Spontaneous pneumothorax associated by Covid-19 pneumonia. Cureus 2020;12:e9104.

53. Ucpinar BA, Sahin C, Yane U. Spontaneous pneumothorax and subcutaneous emphysema in COVID-19 patient: Case report. J Infect Public Health 2020;13:887-9.