Pneumothorax and pneumomediastinum in COVID-19 acute respiratory distress syndrome

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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-inflicted 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.

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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 appears 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 hypoxemic 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 develop swelling in the right side of the neck with elevated peak (40 cm H_2O) and driving pressures (20 cm H_2O) 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 H_2O. 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 (Figure 1C) (Supplement video 1). The patient was subsequently transferred to our center for higher acuity care and consideration for extracorporeal membrane oxygenation (ECMO). Upon arrival to our ICU, the patient was overtly hypoxemic with SpO_2 in low 80s with a FiO_2 of 1.0. Prone positioning was not attempted due to concerns for trachea-bronchial injury from traumatic intubation. Rapid beside bronchoscopy did not reveal any obvious tracheobronchial tear. Ultimately, the patient required a second right-sided chest tube insertion 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 mcg/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
Procalcitonin	<=0.08 ng/mL	0.69 ng/mL
Serum creatinine	0.59-1.04 mg/dL	0.48 mg/dL
5^{th} generation troponin	<=10 ng/L	13 ng/L
White cell count	3.4-9.6x10(9)/L	25.0x10(9)/L
Arterial blood gas		
pH	7.35-7.45	7.36
pCO_2		50
pO_2		48
FiO_2		1.0
HCO_3		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 volumes 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

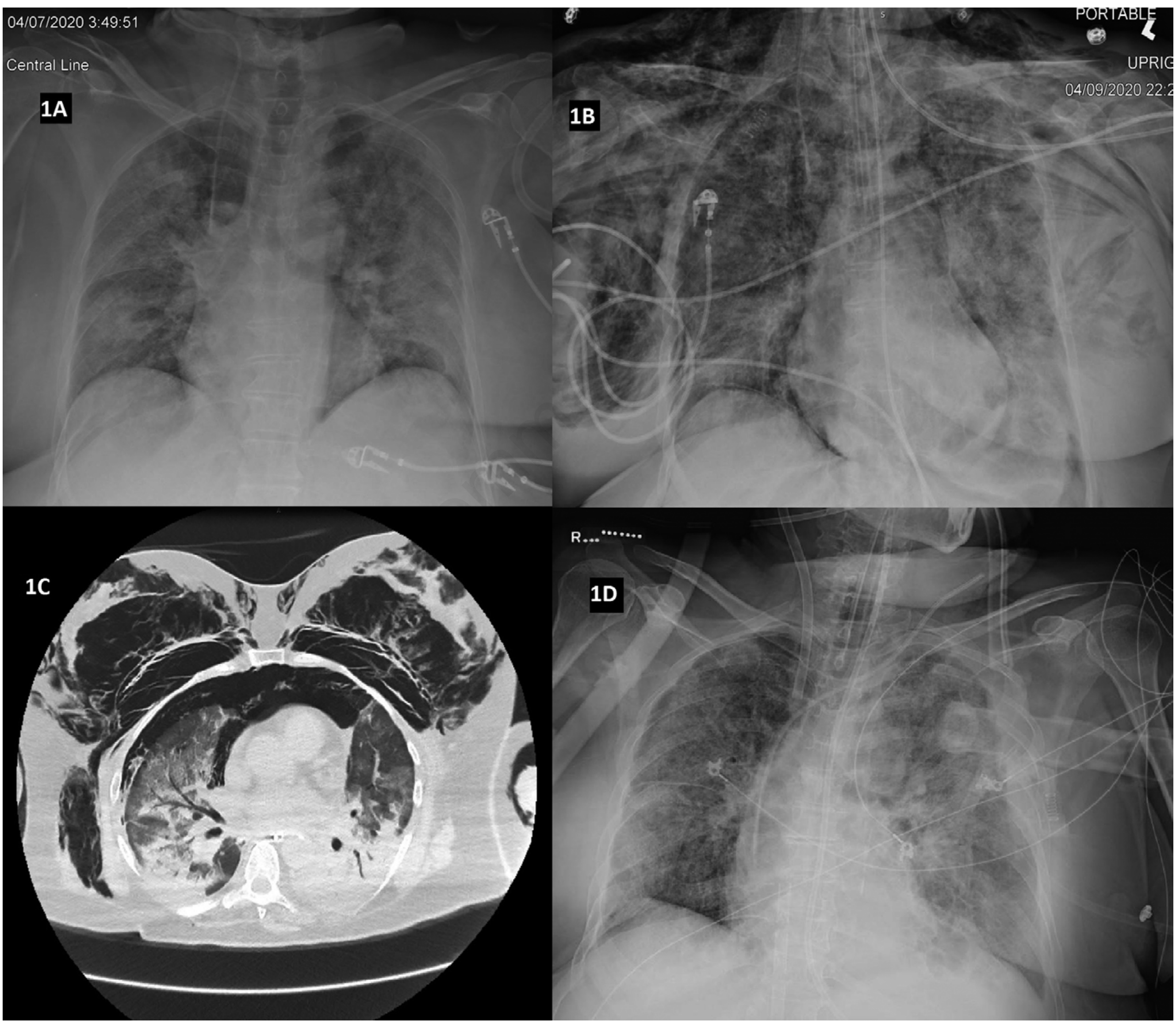

Figure 1. A) Chest x-ray showing bilateral patchy airspace disease. B) Chest x-ray showing severe subcutaneous emphysema in the neck and chest wall bilaterally, questionable right-sided pneumothorax and pneumomediastinum. C) Axial section of CT chest showing bilateral chest wall subcutaneous emphysema, right-sided pneumothorax, pneumomediastinum and bilateral dense consolidations in the lungs consistent with ARDS. D) Chest x-ray showing resolution of previously noted bilateral chest wall and neck subcutaneous emphysema, pneumothorax and pneumomediastinum. Right internal jugular and right femoral ECMO catheters are noted to be in appropriate position.

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	None	Managed without mechanical ventilation	Emergency needle decompression 12-French chest drain	Full recovery
Hollingshead *et al.* [46]	50/M	Not available	Approx. 4 weeks	None	Managed without mechanical ventilation	Tube Thoracostomy (details not available)	Full recovery
López Vega *et al.* [28]	84/F	None	5 days	Unknown	Details not available	Details not available	Died
López Vega *et al.* [28]	67/M	None	5 days	Unknown	Details not available	Details not available	Died
López Vega *et al.* [28]	73/M*#	Obstructive sleep apnea, obesity concurrent pulmonary embolism	5 days	Unknown	Non-invasive positive pressure ventilation	Conservative management	Died
Spiro *et al.* [47]	47/F	History of HIV	Approx. 4 weeks	None	Managed without mechanical ventilation	12-French chest drain	Full recovery
Romano *et al.* [48]	30/M*	None	Unclear	Unknown	Details not available	Details not available	Full recovery
Romano *et al.* [48]	65/M*	None	Unclear	Unknown	Details not available	Details not available	Full recovery
Alhakeem *et al.* [49]	49/M	None	Approx. 3 weeks	None	Managed without mechanical ventilation	Tube thoracostomy (details not available)	Full recovery
Mallick *et al.* [50]	40/M	Smoker	1 week	None	Managed without mechanical ventilation	Tube thoracostomy (details not available)	Died
Mallick *et al.* [50]	68/M	None	4 weeks	None	Details not available	Bilateral tube thoracostomy (details not available)	Full recovery
Mallick *et al.* [50]	58/F*#	None Concurrent pulmonary embolism	Details not available	None	Managed without mechanical ventilation	Conservative management	Full recovery
Rachidi *et al.* [51]	34/F	None	1 week	None	Managed without mechanical ventilation	Conservative management	Recovery in process
Sun *et al.* [15]	38/M*	None	Approx. 2 months	None	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	None	Managed without mechanical ventilation	Tube thoracostomy (details not available)	Full recovery
Our patient	65/F	Obstructive sleep apnea	1 week	None	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; PaO_2:FiO_2 less than 80 mm Hg for more than 6 hours or PaO_2:FiO_2 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 canula 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.

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