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Air Leak in COVID-19 Patients

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Abstract

COVID-19 has been associated with multiple complications including Acute Respiratory Distress Syndrome (ARDS), thrombo-embolism, and septic shock. A rare complication is a Spontaneous pneumomediastinum (SPM), pneumothorax (PNX), and subcutaneous emphysema (SCE) unrelated to positive pressure ventilation. These complications can become life threatening if a large amount of air is present and cannot escape to the neck or retroperitoneum causing obstructive shock or tension pneumothorax. Studies suggest that the cytokine storm in COVID-19 can result in diffuse alveolar injury, which can result in the alveolar wall being vulnerable to rupture. It is also speculated that the cause of the alveolar rupture is due to the diffuse alveolar damage resulting in air leak to the mediastinum. A recent case series of COVID19 autopsies have identified the microthrombi formation and the mononuclear response that leads to diffuse alveolar damage. In addition, recent studies have shown that COVID 19 infected patients are associated with worse clinical outcomes and increase intra and postoperative pulmonary complications and mortality risk. Meaning that patients with SPM had a higher chance of intubation and a higher chance of death. For anesthesiologists, the preoperative evaluation and risk assessment have always been a crucial step in determining whether it is safe to take a patient for surgery. Studies have shown that patients who test positive for COVID 19 are associated with worse clinical outcomes and increase postoperative complications and mortality. Obtaining accurate information, using clinical judgement and having open communication with surgeons may help reduce these risks.

About COVID-19

Towards the end of 2019, health officials from Wuhan City of China identified multiple cases of pneumonia with unknown etiology complicated by Acute Respiratory Distress Syndrome(ARDS)[1]. Later on, nucleic acid sequence tests of samples from lung, posterior pharynx, and blood demonstrated a novel coronavirus, later named SARS-CoV2. It was determined that most of these patients visited an outdoor market that sells fish and wild animals[2]. It is thought that the most common route of transmission is in droplet form human to human, although aerosol transmission is possible[3]. The virus can remain viable and infectious on different surfaces for hours after being shed[4-5].

Coronavirus is a positive-stranded RNA virus with spike glycoproteins on its envelope, which gives it the appearance of a crown[6-7]. The incubation period is typically 2-14 days and it typically precedes symptoms like fever, fatigue, cough, myalgia, dyspnea, headache, dizziness, loss of taste and smell, abdominal discomfort, nausea, vomiting, and diarrhea[8]. In general, most cases present with mild symptoms while others can progress to pneumonia, sepsis, ARDS, and multi-organ failure[8].

Spike proteins on SARS-COV2 bind directly to angiotensin-converting enzyme 2 (ACE2) expressed on alveolar epithelium type 2 cells[9]. Analysis has shown that ACE2 can facilitate viral invasion and replication in the lungs. ACE2 is also seen in other organ tissues like the gut epithelium, which is implicated in fecal-oral route transmission and severe complications leading to multi-organ failure[9]. Moreover, the pro-inflammatory cytokine storms seem to be the culprit for lung and tissue inflammation which leads to fibrosis[10]. Interferon-alpha, tumor necrosis factor and interleukin 6 are among the most commonly implicated[10]. Meta-analyses have shown that high LDH levels are commonly seen in patients infected with MERS-CoV[11]. This may be due to different mechanisms like upregulation of glycolysis due to decreased oxygen supply and cell death which releases LDH[11]. Serum levels of LDH are associated with an increased risk of SPM in patients with COVID19[12]. Damage can be seen on imaging as bilateral peripheral ground glass appearance is best seen on CT scan and can be identified early in the disease process[13].

Spontaneous pneumomediastinum, Pneumothorax, and Subcutaneous emphysema in COVID-19

The presence of air within the mediastinum is known as pneumomediastinum (PM) or mediastinal emphysema. In 1819, this condition was originally described by Lannec in the setting of chest trauma[14]. It was further characterized by Hamman in 1939, who described the typical findings of crackles or rub sounds heard on auscultation with each contraction of the heart[16]. Patients usually present with chest pain, dyspnea, and subcutaneous emphysema, which is due to the continuous connection of cervical fascial planes which is seen as crepitus on physical exam. PM is typically considered benign and patients usually recover spontaneously[15]. However, there is a risk for severe complications which may occur when the mediastinal pressure increases resulting in obstructive shock[15]. There is also a risk of bilateral tension pneumothorax after air dissecting into bilateral pleural spaces. The list of possible causes of PM is extensive, but it includes barotrauma from the use of mechanical ventilation or injuries directed to the chest wall[16]. It can also arise spontaneously or as secondary causes of lung or airway disease that include but are not limited to cystic fibrosis or asthma increasing the risk of pneumothorax[17]. Other risk factors include smoking tobacco or marijuana, drug use, lung infection, and interstitial lung disease[18-19].

Air Leak and The Macklin Phenomenon

Air leak is referred to the escape of air from cavities that contain air into spaces that normally do not contain air. The pathophysiology of pneumomediastinum involves alveolar rupture leading to air leak through the broncho-vascular sheath to the mediastinum[16]. The mediastinal air can take the path of the low resistance cervical fascial planes resulting in subcutaneous emphysema which is associated with significant relief of the patient's symptoms[20]. This is usually a consequence of overinflated marginal alveoli causing an increased pressure gradient between alveoli and the surrounding connective tissue[16]. Potential causes of increased intrathoracic pressure can occur with coughing, vomiting, defecating, sneezing, or asthma exacerbations[20]. Another mechanism of air leak is caused by a reduction in the caliber of pulmonary vessels without a corresponding reduction in alveolar pressures as seen with vigorous Valsalva maneuver which can decrease blood return and increase alveolar pressure[16].

Discussion

Prior to the covid 19 pandemic lung infections caused by staphylococcal, mycoplasma, fungal, bronchiolitis obliterans organizing pneumonia, and severe pertussis had been known to cause air leaks leading to SPM and PNX[21-23]. Other causes of PNX have been seen in HIV patients infected with PCP or tuberculosis[24].

Further review of the literature identified 13 patients who developed SPM with or without PNX or SCE during a community outbreak of SARS-CoV in Hong Kong 2003[12]. All patients were treated with a standard protocol of broad spectrum antibiotics, ribavirin and corticosteroids[12]. In every patient SPM occurred before assisted ventilation being non related to invasive or noninvasive positive pressure ventilation[12]. Patients had a mean of 19.6 +/- 4.6 days from onset of symptoms for the development of SPM, and those who survived took an average of 28 days to completely resolve. Most patients were managed in a conservative manner, but bilateral tube thoracostomies were needed in five patients complicated by bilateral pneumothoraces[12]. There was a total of 4 deaths. Two of the five total patients intubated died and two additional patients without intubation on surrogates' requests. Meaning that patients with SPM had a higher chance of intubation and a higher chance of death[12]. It was speculated by the authors that the cause of the alveolar rupture is due to the diffuse alveolar damage resulting in air leak to the mediastinum[17].

There are many complications reported with COVID-19 positive patients that demonstrate the potential and severity posed by this deadly virus. We have identified 16 cases of SPM occurring in patients confirmed as COVID19 positive[25-35]. Of the 15 patients, 6 patients developed associated PNX and SCE and one case of pneumopericardium was reported[25-35]. Some patients presented with these complications initially while others developed them during the hospital stay. A common factor shared among these patients is that none of them required the use of an invasive or noninvasive positive pressure ventilation before the development of these complications[25-35]. All patients were nonsmokers and had no significant comorbidities that would place them at a high risk. This may suggest that the disease process of COVID19 can directly result in air leaks. Prior studies have shown that the exaggerated immune response to SARS-CoV could be the cause of such severe lung changes that may lead to ARDS[32]. A recent case series of COVID19 autopsies have identified the microthrombi formation and the mononuclear response that leads to diffuse alveolar damage[33]. This suggests that the exaggerated immune response is responsible for the diffuse alveolar damage which makes the alveoli prone to rupture especially with uncontrolled cough or the use of positive pressure ventilation as explained by the Macklin effect. Fortunately, 11 patients spontaneously recovered with conservative management. However, four patients did not recover and eventually expired due to respiratory failure and acute respiratory distress syndrome[21-31]. Although most of the patients with SPM tend to do well, they should be closely monitored for any sudden change in respiratory status or circulatory dysfunction. An early chest CT scan may help identify these complications in any patients whose respiratory status rapidly declines.

There are certain types of surgeries that increase the chances of subcutaneous emphysema for example during laparoscopic surgery if the trocar is misplaced and CO2 is insufflated into the peritoneal cavity[36]. This may even cause gas to take the path of least resistance and track up into the thorax and mediastinum[37]. Additional risk factors are surgeries that take more than 200 minutes, or the use of additional surgical ports[37]. Although most cases resolve after the abdomen is deflated, caution for laryngeal edema should be taken by delaying extubation[36-37]. Physical exams may show crepitus in the neck and audible crunch on auscultation. Patients typically transition to a higher level of care for closer observation and tend to recover with bed rest, analgesia and oxygen therapy including mitigation of factors that increase alveolar pressure such as cough and forced expiration.

For anesthesiologists, the preoperative evaluation and risk assessment has always been a critical step for safe surgery. New studies show that patients who test positive for COVID 19 are associated with worse clinical outcomes and increase postoperative complications and mortality[38]. Recovery from COVID 19 may be slow and there is a new syndrome known as "post-COVID" resulting in deconditioning of lung function due to inflammation that may lead to fibrosis[38-39]. Some of these patients may require surgery and are at a higher risk of intra-postoperative complications. The use of lung protective strategies and peep optimization has shown to be beneficial studies are still not conclusive to its application when it comes to patients with ARDs[40]. A recent international, multicenter cohort study identified patients who tested positive for SARS-CoV-2 within 7 days prior or 30 days after surgery found an increase rate of pulmonary complications, pulmonary embolism, intensive care unit admission, reoperation, 7-day mortality, and length of hospital stay[41].

It showed that 30-day mortality was as high as 23.8% (268 of 1128) with men having higher mortality rates than women[41]. Age was also a predictor as men and women aged 70 years or older had higher rates than those younger than 70 years[39,41]. Pulmonary complications occurred in 219 (81.7%) of 268 patients who died. Among patients who developed pulmonary complications, 30-day mortality was highest in those who developed ARDS (102 [63.0%] of 162)[39,41].

Postoperative pulmonary complications may result in reintubation and/or unplanned intensive care unit admission[39]. Based on available literature COVID-19 can also cause subcutaneous emphysema and should therefore be included in your differential diagnosis as a separate reason for air leak.

In some circumstances, delaying surgery in some patients greatly outweighs the risk associated with SARS-CoV-2 infection[39]. Certain groups of patients were highly vulnerable to adverse outcomes, such as men, people aged 70 years or older, ASA grades 3-5 or with comorbidities, cancer surgeries, emergency surgeries or major[39,41].

COVID 19 continues to affect our daily life, and it is vital to keep building our understanding of the problem and investigate methods to minimize the risk for intra or postoperative pulmonary complication in COVID 19 infected patients where the surgery cannot be delayed.

Conflict of Interest

The Authors declare no conflicts of interest.

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