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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

COVID-19 pneumonia complicated by late presentation of bilateral spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema

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SUMMARY

Introduction Over the last few months the coronavirus disease 2019 (COVID-19) pandemic has created overwhelming challenges for physicians around the world. While much has been described in the literature about lung infiltrates and respiratory failure associated with infection of coronavirus 2 (SARS-CoV-2), pneumothorax is reported as a rare (a rate of 1%) but a life-threatening complication of COVID-19 pneumonia. Late bilateral spontaneous pneumothorax has been described in few cases. The aim of the report is to consider pneumothorax as a possible complication of COVID-19 pneumonia, which is also one of the causes of respiratory deterioration and potentially fatal outcome in these patients.

Case outline This article describes the clinical course of the patient who tested positive for SARS-CoV-2 on reverse-transcriptase polymerase chain reaction (RT-PCR) testing of nasopharyngeal and oropharyngeal swab specimens and who presented with COVID-19 pneumonia complicated by bilateral, spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema. He had no underlying lung disease nor risk factors for pneumothorax, except administered non-invasive ventilation/continuous positive airway pressure during first hospitalization. The patient was successfully treated with surgical (chest drainage, thoracoscopy and pleural abrasion) and non-surgical methods (by application of drugs and other supportive therapies).

Conclusion This review demonstrates that the possibility of a late pneumothorax should be kept in mind in patients with, or recovering from, COVID-19 disease with progressive dyspnea. The timely diagnosis and management of pneumothorax will reduce COVID-19 associated mortality.

Keywords: COVID-19; complications; management

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been recognized as a worldwide pandemic [1]. COVID-19 is a systemic infectious disease. This infection has a broad spectrum of presentations that can range from asymptomatic disease to fatal acute respiratory distress syndrome (ARDS) with death due to multi-organ failure [2].

Initial chest X-ray (CRX) may be normal but patients may later develop radiological signs of COVID-19 pneumonia. In critically ill patients with marked respiratory symptoms, CRX can be diagnostic for COVID-19 pneumonia. Some patients with PCR confirmed COVID-19 infection had changes on initial computed tomography (CT) and radiographs were false negative. Therefore, these imaging methods can help both in diagnosis and in the management of COVID-19 patients [3, 4].

The important causes of sudden respiratory deterioration associated with COVID-19 pneumonia are ARDS, pulmonary embolism and pneumothorax. They need a prompt diagnosis and intervention in order to reduce COVID-19 associated mortality [5, 6]. The aim of the report is to consider pneumothorax as a possible complication of COVID-19 pneumonia, which is also one of the causes of respiratory deterioration and potentially fatal outcome in these patients.

CASE REPORT

We report a case of a 47-year-old white male with no history of pulmonary disease, nonsmoker, weightlifter (BMI 30.7), who presented with symptoms of muscle and joint pain, malaise, and hemoptysis five days prior to hospitalization. On admission day, he developed a fever up to 38°C (100.4°F) and dyspnea. CRX revealed signs of bilateral pneumonia, O2 saturation 94%, heart rate 80/minute, leucopenia 3.06 × 109 and C-reactive protein 65.7 mg/L. Nasopharyngeal and oropharyngeal swab for COVID-19 PCR testing were positive. On the second day of hospitalization, he was transferred to Intensive care unit (ICU) due to respiratory failure, where non-invasive ventilation/continuous positive airway pressure was administered. After detection of high levels of

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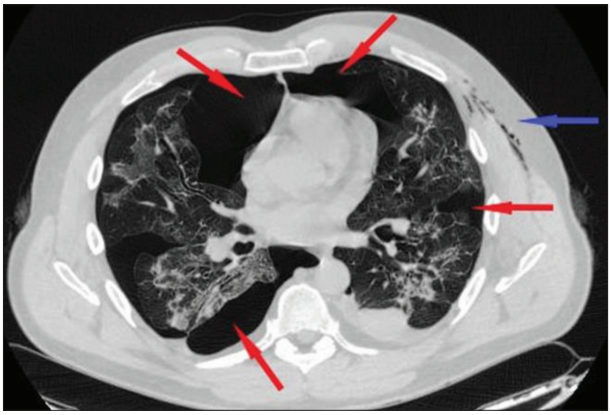

Figure 1. Chest computed tomography scan on admission; red arrows show bilateral pneumothorax; blue arrow shows subcutaneous emphysema

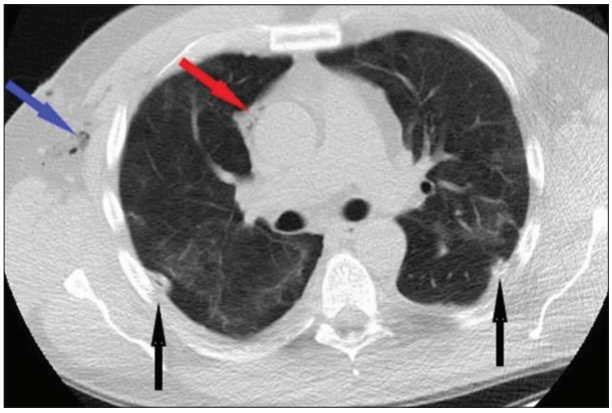

Figure 2. Chest computed tomography scan after bilateral chest tube placement; black arrows show chest tubes; the blue arrow shows subcutaneous emphysema; the red arrow demonstrates the Macklin effect

IL-6, tocilizumab was administered during the second and third day of ICU treatment in doses of 8 mg/kg. Total length of ICU treatment was 10 days. After stabilization of respiratory function (arterial SO_2 98% on 4/L min of O_2) COVID-19 PCR testing was repeated negative in two samples. During the hospitalization he was treated with dexamethasone 6 mg/24h for 10 days. Piperacillin/tazobactam was discontinued on the 14th day. On the 20th day of hospitalization, severe dyspnea was reported with CRX showing signs of complete left sided pneumothorax. Chest tube No. 22F was inserted and connected to water seal and active suction of -20 cm H_2O. After placement of chest tube there were no signs of air leak, so the drain was removed on the fifth day after placement, with fully expanded lungs on CRX. He was discharged after 25 days of hospitalization.

The day after he was discharged, the patient developed signs of severe dyspnea. Chest CT showed complete bilateral pneumothorax (Figure 1).

After admission to the thoracic surgery clinic, bilateral chest drainage was performed with 22F chest tubes. The chest tubes were connected to water seal and active suction -20 cm H_2O with severe bilateral air leakage and hemorrhagic secretion up to 200 ml/24h in combination with necrotic detritus. Initial CRX after drainage showed complete lung expansion. Due to the prolonged air leak on the right chest drain, control chest CT was performed on day 11 of admission (Figure 2).

CT described a full expansion of the left lung, partial right sided pneumothorax, subcutaneous emphysema, mediastinal Maclin effect and signs of bilateral ground glass opacity in regression. The left chest tube was clamped for 24 hours on day 12 after no signs of air leak was present for three days. Left sided chest tube was removed on day 13. Right sided chest tube was connected to Medela Thopaz pump -2kPa (Medela HQ., Baar, Switzerland) with air loss measuring in range from 10–80 ml/min. On day 15, the air leak stopped, but CRX showed signs of complete right sided pneumothorax. Inactive right sided chest tube, blocked with necrotic detritus, was removed and drainage was performed with chest tube No. 24F. Due to the prolonged and severe air leak after the drainage, accompanied

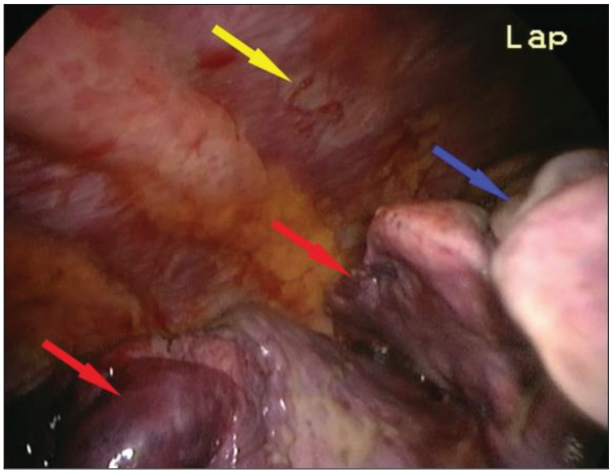

Figure 3. Video-assisted thoracoscopic surgery procedure; red arrows show necrotic posteriors segments with bullae; the blue arrow shows fibrin deposits on visceral pleura; the yellow arrow shows inflamed parietal pleura

with the complete lung collapse on CRX, the patient was operated in general anesthesia on day 15 of hospitalization. Uniportal right sided video-assisted thoracoscopic surgery was performed. During the operation signs of partial necrosis of S2, S6, and S8–10 lung segments were detected, with fibrin deposits on visceral pleura (Figure 3).

No obvious spots of air leak were detected. Complete abrasion of parietal pleura was performed with placement of two chest tubes No. 28F. Samples of parietal pleura were sent to pathophysiology: acute purulent inflammation of the pleura. On the first postoperative day there were no signs of air leak. CRX showed fully expended lungs. On the seventh postoperative day one chest tube was removed. The following day the second chest tube was clumped for 24 hours. CRX showed signs of full lung re-expansion, so the following day the last chest tube was removed. He was discharged after 25 days of rehospitalization.

Three months after discharge control chest CT was performed (Figure 4): No signs of pneumothorax and pneumomediastinum. Complete regression of ground-glass opacification with few reticular intestinal lesions in regression. SARS-CoV-2 IgM and IgG antibodies were present.

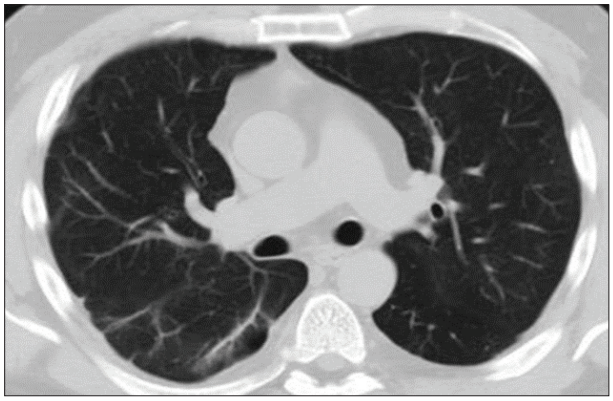

Figure 4. Control chest computed tomography scan three months after discharge

Written consent to publish all shown material was obtained from the patient.

DISCUSSION

Radiology frequently shows typical changes of COVID-19 pneumonia [4]. Chen et al. [7] first reported pneumothorax as a rare radiologic feature in 1% of patients with COVID-19. Late bilateral spontaneous pneumothorax has not yet been widely reported in the literature [6, 8]. Patients can develop pneumothorax at different stages of the COVID-19 disease course [9]. It is important to consider the diagnosis of pneumothorax in COVID-19 patients, if there is a sudden increase in work of breathing, decreased oxygen saturation, or the patient complains of chest tightness. In case of sudden deterioration, urgent CRX, ultrasound or computed topography scan should be done, and expert help sought [6, 7, 8].

Like many other authors, we believe that the combination of severe inflammation and prolonged duration of illness in COVID-19 patients contributed to the pulmonary parenchymal injury (degenerative changes in the lung parenchyma) in patients with the development of air leaks leading to pneumothorax, and/or pneumomediastinum, and subcutaneous emphysema [10, 11, 12]. The lungs of patients with COVID-19 who have significant interstitial involvement appear physiologically small, with low compliance and reduced elasticity. This thickened, stiff tissue makes it difficult for the lungs to work properly, and sustained-pressure ventilation may be necessary to obtain acceptable gas exchanges. In this setting, parenchyma is prone to rupture, with consequent risk of pneumothorax [10]. In some cases, progression to ARDS causes diffuse alveolar damage and a pro-inflammatory cytokine storm, which can induce alveolar rupture and the development a new lesion - pneumatoceles and pneumothorax [13, 14]. Likewise, severe airway inflammatory damage from the release of cytokines in COVID-19 can lead to weakening of the bronchial walls [15].

The most common causes of pneumothorax in respiratory infection have been associated with barotraumas in mechanically ventilated patients or increased airway pressure due to ARDS. Pneumothoraxes that developed in patients with COVID-19 and ARDS have been attributed to the same etiologies [5, 16]. Endotracheal intubation and mechanical ventilation are known to cause iatrogenic pneumomediastinum, subcutaneous emphysema, and pneumothorax [5, 16]. Our patient did not have ARDS based on criteria and was not intubated. He developed both a severe pneumonia and unilateral pneumothorax, and later in the course of the disease bilateral pneumothorax, which may be a consequence not only of COVID-19 pneumonia, but also as a consequence of non-invasive ventilation/continuous positive airway pressure application. Although pneumothorax can be a complication of positive airway pressure in patients with ARDS receiving mechanical ventilation, most of the COVID-19 patients, did not receive any form of ventilation pneumothorax [5]. The diffuse alveolar damage seen in both ventilated and unventilated COVID-19 patients may cause development of bullae and create predisposition for pneumothorax in different stages of disease [5, 9, 17].

The pathogenesis of pneumomediastinum follows the so-called "Macklin effect". The Macklin effect seen on thoracic CT suggests that air leakage is caused by rupture of the alveoli and rupture of the mediastinal pleural traces along the broncho-vascular sheath to the mediastinum, and then to the subcutaneous tissue and in the pleural space. This is likely to happen in patients with COVID-19 due to cough, which is known to increase intra-alveolar pressure [18].

The appearance of pneumothorax in patients with COVID-19 pneumonia might be caused by underlying pulmonary diseases. Patients with chronic obstructive pulmonary disease and pulmonary emphysema are at higher risk of pneumothorax when infected with SARS-CoV-2 [19]. Signs suggestive of potential comorbidities on CRX might be obscured by signs of COVID-19 pneumonia [20]. However, in some cases, COVID-19 pneumonia changes might be so widespread that features suggestive of comorbidities are obscured.

It was found that pneumothorax can occur in patients with COVID-19 pneumonia without preexisting lung disease [12]. Our patient did not have a history of pneumothorax, underlying pulmonary disease and had no history of smoking. Therefore, it is our opinion that the development of these pneumothoraxes are results of advanced alveolar damage, bronchiolar distortion leading to pulmonary bullae formation and tissue necrosis, predominantly of posterior lung segments. Moreover, the severe cough associated with viral infections increases the intrapulmonary pressure. This may precipitate bullae rupture and pneumothorax formation [18].

When pneumothorax occurs in COVID-19 patients, chest drainage represents first-line of treatment [21]. Managing pneumothorax in these patients is crucial to prevent the development of life-threatening tension pneumothoraxes. We note that the initial treatment of unilateral pneumothorax with a tube thoracostomy provided a satisfactory but temporary outcome, most likely due to massive pulmonary changes in our patient. It is our belief

that the final outcome of pneumothorax in patients with COVID-19 pneumonia depends on the severity (and progression) of lung disease, and therefore prompt surgical treatment of pneumothorax in these patients provides appropriate outcomes. The patient was treated with steroid therapy based on institutional policy for severe disease. Therefore, we believe that the use of drugs and other supportive therapies has also contributed to a favorable treatment outcome. After chest tube placement, a wait-and-see strategy was preferred over the aggressive pleurectomy or pleural abrasion because of doubts about the effectiveness of the procedure. However, in case of persistent or repeating pneumothorax, thoracoscopy and pleurectomy/pleural abrasion or even apical blebs resection (when present) can be feasible options to reduce air leakage and improve ventilation [21, 22]. The ideal timing of minimally invasive treatment (video-assisted thoracoscopic surgery) is unclear. Even in cases of repeated and persistent pneumothorax in patient with COVID-19 pneumonia, we recommend delaying thoracoscopic operative management in the light of uncertain course of the disease and potential progression of lung tissue damage. While operative management in this patient had a good outcome, it seems that prolonged management with chest tubes is needed for resolution of air leaks from injured and fibrotic pulmonary parenchyma.

The worsening status of patients infected with SARS-CoV-2 should not always be attributed to disease progression, but also pneumothorax. Early diagnosis and timely treatment of this complication can improve the therapeutic effect and reduce mortality [23].

Conflict of interest: None declared.

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Упала плућа изазвана болешћу *COVID-19* која је компликована касном појавом обостраног спонтаног пнеумоторакса, пнеумомедиастинума и поткожног емфизема

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САЖЕТАК

Увод Током последњих неколико месеци пандемија болести изазване вирусом корона 2019 (*COVID*-19) створила је велике изазове за лекаре широм света. Иако је у литератури много писано о плућним инфилтратима и респираторној инсуфицијенцији који су у вези са инфекцијом вирусом корона 2 (*SARS-CoV*-2), пнеумоторакс је пријављен као ретка (стопа од једног процента) али по живот опасна компликација болести *COVID*-19. Касна појава обостраног пнеумоторакса описана је у само неколико случајева.

Циљ приказа је да се размотри пнеумоторакс као могућа компликација упале плућа изазване болешћу *COVID*-19, који је и један од узрока респираторног погоршања и могућег смртног исхода код ових болесника.

Приказ болесника Чланак описује клинички ток болесника чији је брис назофаринкса и орофаринкса испитиван методом *RT-PCR* био позитиван на *SARS-CoV*-2. Он је развио упалу плућа изазвану болешћу *COVID*-19 која је компликована обостраним, спонтаним пнеумотораксом, пнеумомедиастинумом и поткожним емфиземом. Болесник није имао ранију болест плућа нити факторе ризика за пнеумоторакс, осим примене неинвазивне вентилације/континуираног позитивног притиска у дисајним путевима током прве хоспитализације. Успешно је излечен хируршким (дренажом грудног коша и торакоскопском абразијом плућне марамице) и нехируршким методама (применом лекова и других супортивних мера).

Закључак Овај случај показује да треба имати на уму могућност пнеумоторакса код болесника са болешћу *COVID*-19 и оних у фази опоравка од болести а који имају прогресивну диспнеју. Правовремена дијагностика и лечење пнеумоторакса може да допринесе смањењу морталитета који је у вези са болешћу *COVID*-19.

Кључне речи: *COVID*-19; компликације; лечење