Chirurgia (2022) 117: 317-327
No. 3, May - June

http://dx.doi.org/10.21614/chirurgia.2719

Cervico-Thoracic Air Collections in COVID-19 Pneumonia Patients - Our Experience and Brief Review

Claudiu Eduard Nistor[1], Camelia Stanciu Gavan[1], Daniel Pantile[1], Narcis Valentin Tănase[2], Adrian Ciuche[1]

[1]Department of Thoracic Surgery, Central Military Emergency University Hospital ”Dr. Carol Davila”
”Carol Davila” University of Medicine and Pharmacy Bucharest, Romania
[2]Department of Intensive Care, Central Military Emergency University Hospital ”Dr. Carol Davila”
”Carol Davila” University of Medicine and Pharmacy Bucharest, Romania

*Corresponding author:
Claudiu-Eduard Nistor, MD
Department of Thoracic Surgery
Central Military Emergency
University Hospital ”Dr. Carol Davila”
Calea Plevnei 134, 010825
Bucharest Romania
E-mail: ncd58@yahoo.com

Received: 26.03.2022
Accepted: 28.05.2022

Rezumat

Revărsate aeriene cervico-toracice la pacienții cu pneumonie COVID-19: experiența noastră și scurt review al literaturii

Introducere: COVID-19 (boala Coronavirus 19), o nouă entitate clinică secundară infecției cu SARS-CoV-2, ar putea explica apariția revărsatelor aeriene cervico-toracice (pneumotorax, pneumomediastin şi emfizem subcutanat).
Material și metodă: A fost analizat un studiu retrospectiv pe o perioadă de 8 luni a cazurilor dintr-un sigur centru care prezentau concomitent infecție SARS-CoV-2 şi pneumotorax, pneumodiastin, emfizem subcutanat, singure sau asociate.
Rezultate: Toți pacienții neintubați care au prezentat complicațiile amintite mai sus au avut o evoluție favorabilă după drenajul pleural, drenajul percutan şi/sau tratament conservator. Drenajul pleural s-a practicat la pacienții cu pneumotorax; în cazurile cu pneumomediastin şi emfizem subcutanat asociat a fost necesară utilizarea de ace sau angiocatetere inserate subcutanat împreună cu masaj decompresiv manual. Tratamentul conservator a fost rezervat pacienților care aveau pneumomediastin şi disfuncție respiratorie moderat-severă.
Concluzii: Infecția SARS-CoV-2 ar trebui inclusă în clasificarea etiopatogenica a pneumotoraxului, ca o posibilă cauză de pneumotorax secundar spontan pneumoniei COVID-19. Rata de supraviețuire a fost mică (18,75%), 4 pacienți au fost vindecați, 2 au avut o evoluție favorabilă iar 26 au decedat. Drenajul pleural, obligatoriu la pacienții cu pneumonie COVID-19 complicată cu

pneumotorax, nu modifică prognosticul pacienților cu afectare pulmonară severă, la care, în majoritatea cazurilor decesul a survenit secundar ventilației prelungite şi tarelor asociate.

Cuvinte cheie: COVID-19, pneumotorax, pneumomediastin, emfizem subcutanat

Abstract
Introduction: COVID-19 (Coronavirus-19 disease), a new clinical entity caused by SARS-COV-2 infection, could explain the physiopathology of cervicothoracic air collections (pneumothorax, pneumomediastinum, and subcutaneous emphysema).
Material and Methods: We conducted an 8-months retrospective analysis of a single-center SARS-CoV-2 cases associating pneumothorax, pneumomediastinum, and subcutaneous emphysema, either alone or combined.
Results: All non-intubated patients with the complications cited above had a favorable outcome after pleural drainage, percutaneous drainage, and/or conservative treatment, while the intubated patients, with multiple comorbidities, have had an unfavorable outcome, regardless the chosen treatment. Pleural drainage was used for pneumothorax cases; pneumomediastinum with subcutaneous emphysema required insertion of subcutaneous needles or angio-catheters with manual decompressive massage. Conservative methods of treatment were used for patients with pneumomediastinum and medium or severe respiratory disfunction.
Conclusions: Etiopathogenic classification of pneumothorax should include SARS-CoV-2 infection as a possible cause of secondary spontaneous pneumothorax due to COVID-19 pneumonia. Survival rate after the occurrence of these complications was small (18,75%), 4 of the patients were cured, 2 had a favorable outcome and 26 have died. Pleural drainage which is mandatory to do for patients with pneumothorax complication in COVID -19 pneumonia, doesn't change the prognosis for those with severe affecting lungs, because the prolonged ventilation and the other comorbidities have led to death in most of these cases.

Key words: COIVD-19, pneumothorax, pneumomediastinum, subcutaneous emphysema

Introduction

Several pneumonia cases of unknown etiology were reported in Wuhan, Hubei province, China in December 2019. The etiopathogenic agent for this type of pneumonia was found to be a novel coronavirus SARS-CoV-2, leading to COVID-19 disease (1).

COVID-19 disease was declared a public health emergency by World Health Organization (WHO) on January, 30th, 2020, and pandemic on March, 12th, 2020 (2).

SARS-CoV-2 belongs to betacoronavirus family, along with the viruses responsible for severe acute respiratory syndrome (SARS) and for Middle East respiratory syndrome (MERS) (SARS-CoV-1, respectively MERS-CoV). SARS-CoV-2 is the SARS-CoV virus with receptor for human cells (3).

Spontaneous pneumothorax can be found in 1-2% of the COVID-19 pneumonia patients who need hospitalization (4), while 15% of the cases are represented by pneumothorax associated with pneumomediastinum, subcutaneous emphysema, pleural effusions in ventilated patients, secondary to barotrauma (5). Current literature reports are based on a small number of patients, 1,7% of these hospitalized patients associating only spontaneous pneumothorax, as a complication of SARS-CoV-2 associated severe acute respiratory syndrome (6).

This article reports the experience of a single Romanian center on SARS-CoV-2 patients with associated pneumothorax, pneumomediastinum and subcutaneous emphysema who required thoracic surgery management. Thirty patients with SARS-CoV-2 infection who were admitted to the intensive care unit (ICU) and two patients with pneumothorax and positive testing for SARS-CoV-2 were included.

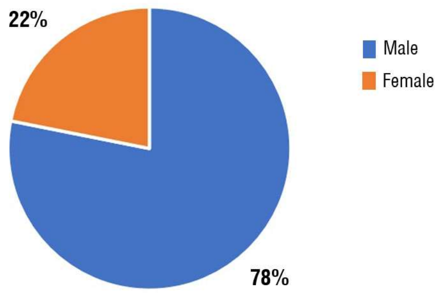

Figure 1. Patients' distribution according to sex

Material and Methods

An anonymized and retrospective targeted chart and imaging review was performed using the hospital's database. The study was approved by the research ethics commission no. 441 / 3.03.2021.

Patients and Clinical Information

Inclusion criteria were limited to COVID-19 patients associating either pneumothorax, pneumomediastinum, with or without subcutaneous emphysema, who were admitted in our hospital between July 2020 and February 2021.

Patients with cervicothoracic air collections (pneumothorax, pneumomediastinum, subcutaneous emphysema) without COVID-19 disease were not included in this study.

A total of 32 patients were selected according to the agreed inclusion and exclusion criteria.

Most of the patients were males n=25, (78%) and women n= 7 (22%), aged between 30-84 years old, with a median of 61.5 years (*Figs. 1, 2*).

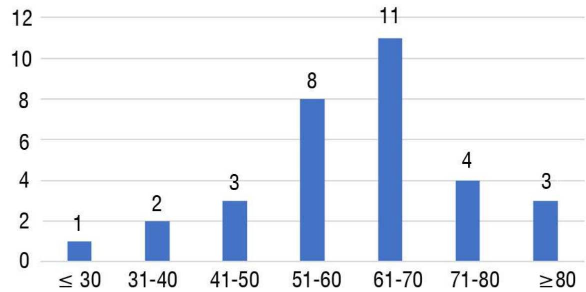

Figure 2. Patients' distribution according to their age group

Patients' history revealed 5 patients were never smokers, 15 are currently smokers, 10 formerly smokers, and for 2 patients we have no available data due to critical state at admission (*Fig. 3*).

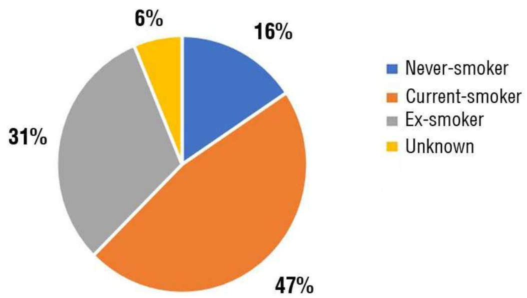

Figure 3. Patients' distribution based on their somking status

Two patients were admitted to the ER with spontaneous pneumothorax. For the remaining 30 patients, the air leaks were diagnosed as COVID-19 complications occurring days 1 – 10 after admission: pneumothorax, pneumomediastinum and subcutaneous emphysema, either alone or associated. Invasive ventilation through an endotracheal tube was used in 21 patients, while 9 patients required non-invasive ventilation.

Complications described during the evolution of COVID-19 include severe pneumonia, pulmonary edema (7), pneumothorax, pneumomediastinum, subcutaneous emphysema (8), pneumopericardium (9), hemopneumothorax (10), severe acute respiratory syndrome, and multiple organ failure with subsequent death (7). Several unfavorable risk factors for

COVID-19 infection were identified: obesity (7), smoking (11), diabetes mellitus (7), chronic obstructive pulmonary disease (12,13), and barotrauma in intubated patients (14).

The rupture of the alveolar wall or of the subpleural structures represents the background for pneumothorax in most of the cases (12). The Macklin effect is involved in the physiopathology of the pneumomediastinum. This mechanism describes a significant pressure gradient between the alveoli and the interstitium, resulting in air leaks movement to the surrounding bronchovascular sheath (15). Specific interactions between the surfactant system and glycocalyx at the level of the alveolar epithelium might contribute to the maintenance of alveolar homeostasis, especially to the alveolar micromechanics and to the functional integrity of the blood-air barrier, to the regulation of the thickness and viscosity of the alveolar protective layer and to defense against inhaled pathogens (16). COVID-19 diagnosis is based on viral detection by using a real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay (17).

Computed tomography (CT) is of paramount importance in the early diagnosis of COVID-19 pneumonia and is recommended for the evaluation of the diseases's evolution and of the diffuse interstitial pulmonary lesions (18,19).

Procedure

COVID-19 patients who required thoracic surgery evaluation and management were selected. All imaging studies (CT scans) before and after drainage for pneumothorax were analyzed (cutaneous punctions with manual decompressive cervico-thoracic massage for subcutaneous emphysema were also included), and the post therapeutic evolution of all the selected patients was evaluated. Seriated thoracic CT scans were performed and compared for the pneumomediastinum cases, assessing the evolution of these patients.

Laboratory evaluation in all patients consisted of complete blood count, D-dimer, ferritin, C reactive protein, lactate dehydrogenase.

Statistical Analysis

Statistical analysis of the patients' data was performed and is presented in tables and figures; we established correlations between the different variables. A p value $<.05$ was considered statistically significant.

Results

Two patients without previously known pulmonary pathology, presented to the emergency room with moderate dyspnea, and the thoracic computed imaging detected pneumothorax. Both patients had a positive COVID-19 rapid antigen test. The other 30 patients (23 men and 7 women) were initially diagnosed with COVID-19 and developed complications during the admission, such as pneumothorax, pneumomediastinum, and/or subcutaneous emphysema, requiring thoracic surgery evaluation and treatment.

Associated pulmonary conditions included chronic obstructive pulmonary disease (8 patients), bronchial asthma (5 patients), bronchiectasis (4 patients) or no available data (2 patients) – *Fig. 4*. Relevant comorbidities other than pulmonary conditions were: essential hypertension (19 cases), cardiac disease (13 cases), diabetes mellitus (12 cases), chronic kidney disease (8 cases), atrial fibrillation (3 cases), tachycardia (3 cases), obesity (18 cases) – *Fig. 5*.

Among all COVID-19 positive patients, 3 patients associated pneumothorax, pneumomediastinum and subcutaneous emphysema, 5 patients associated pneumothorax and pneumomediastinum, 14 patients associated pneumomediastinum and subcutaneous emphysema, 4 patients associated hydropneumothorax and pneumomediastinum, 4 patients had only pneumomediastinum and 2 patients had only pneumothorax features (*Fig. 6*).

When comparing the mean age for patients with pneumothorax to patients with other air collections secondary to COVID-19, we

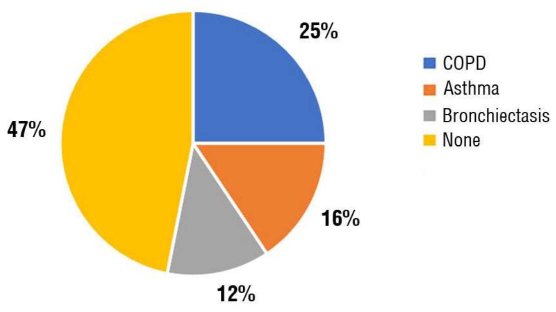

Figure 4. Patients' distribution based on their respiratory comorbidities

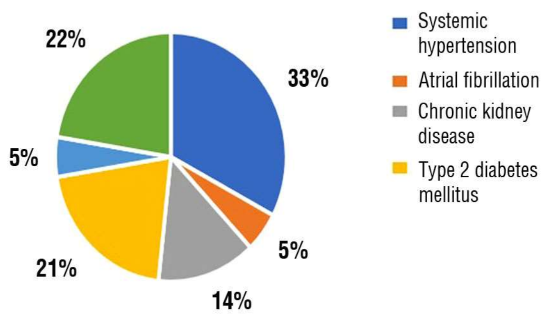

Figure 5. Patients' distribution based on their non-respiratory comorbidities

observed no statistical differences (*Tables 1, 2*). As a result, age should not be considered when asserting the risk for patients developing a certain air collection.

For patients (n=2) only with pneumothorax and a favorable outcome after chest drain insertion, it was established that the respiratory failure was secondary to air accumulation in the pleural cavity and not secondary to COVID-19 disease.

Aggravation of dyspnea was recorded in all 30 RT-PCR SARS-COV-2 positive patients admitted in the dedicated COVID-19 unit, with altered or severe general status. Repeated CT scans confirmed the presence of

Table 1. Comparison of mean age for patients with pneumothorax and patients with pneumomediastinum

	Total cases	Pneumothorax	Pneumomediastinum
N	32	14	30
male	25	11	26
women	7	3	4
%		43.75%	93.75%
Mean age	30-84 age	61.36	62.26
Standard Deviation		15.73	13.28
Standard error		4.559	
95% confidence interval		-8.29 to 10.11	
t test		.20	
p value		.84	

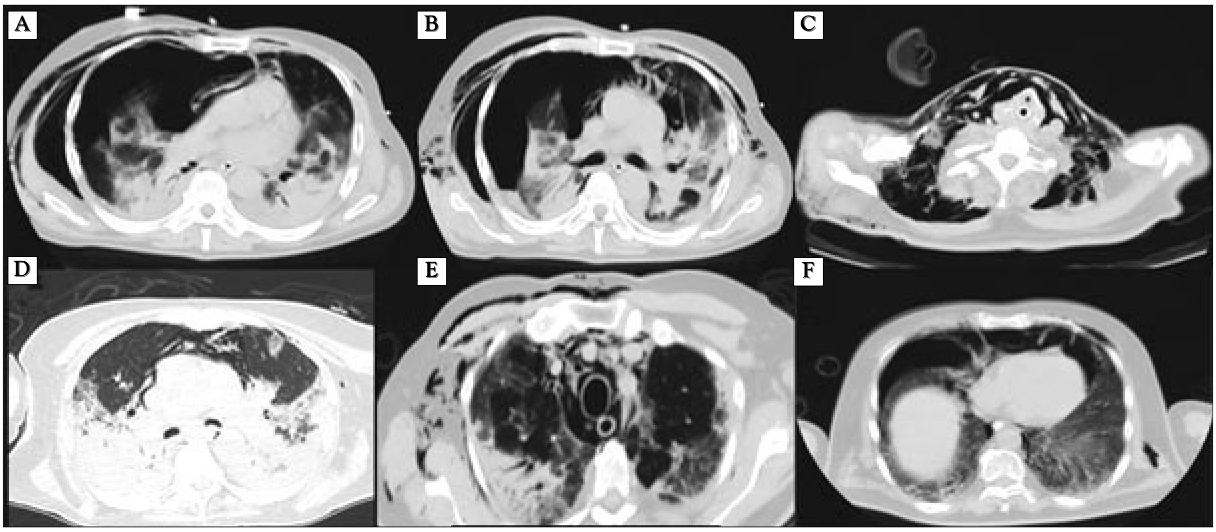

Figure 7. CT imaging. **(A, B)** – right thoracic subcutaneous emphysema with right pneumothorax, ground-glass opacities in the left lung parenchyma; **(C)** – massive cervical subcutaneous emphysema; **(D)** – ground-glass opacities in both lungs; **(E)** – thoracic subcutaneous emphysema and pneumomediastinum; **(F)** – right pneumothorax and ground-glass opacities

Table 2. Comparison of mean age for patients with pneumothorax and patients with subcutaneous emphysema

	Total cases	Pneumothorax	Subcutaneous emphysema
N	32	14	17
male	25	11	13
women	7	3	4
%	100%	43.75%	53.13%
Average age	30-84 age	61.36	62.94
Standard Deviation		15.73	12.06
Standard error		4.999	
95% confidence interval		-8.62 to 11.78	
t test		.317	
p value		.75	

pneumothorax, pneumomediastinum, and/or subcutaneous emphysema.

Imaging aspects suggestive for SARS-COV-2 infection, such as ground-glass opacities covering 40-80% of the lung parenchyma, subsegmental atelectasis, and diffuse fibrosis were identified in all admitted patients. For patients with negative initial RT-PCR tests, but highly suspicious imaging aspects for COVID-19, bronchoalveolar lavage was performed and all patients were identified to be COVID-19 positive.

Standard tube thoracostomy was performed in all patients diagnosed with pneumothorax (19,20). Patients associating pneumomediastinum and pneumothorax were treated conservatively and carefully monitored by repeated CT scans.

In *Table 3*, some of the characteristics of the patients with COVID-19 and pneumothorax requiring a surgical procedure are analyzed. We did find a significant statistical correlation between the need for a surgical procedure and the presence of CPAP ventilation. All other analyzed parameters regarding the sex, smoking status, the presence of pulmonary or cardiac disease were not influenced by the need of a surgical procedure.

Also, the statistical analysis didn't find any correlation between the patients; death and the need for a surgical procedure.

In *Table 4* we analyze the characteristics of the patients with COVID-19 and subcutaneous emphysema requiring a surgical procedure. We did not find any significant statistical correlation between the need for a surgical procedure and the analyzed parameters regarding the sex, smoking status, or the presence of pulmonary or cardiac disease.

Also, we did not find any significant statistical correlation between the need for a surgical procedure and the analyzed para-

Table 3. Chi squared correlations between patients' characteristics and the presence of pneumothorax for patients with Covid-19 needing a surgical procedure

	Total cases	Chi squared	p value
Sex	32	.65	.42
male	25		
women	7		
Smoker	15	1.05	.30
Pulmonary disease			
COPD	8	.17	.68
Asthma	5	1.36	.24
Bronchiectasis	4	.07	.79
Cardiac disease			
Systemic hypertension	19	.25	.62
Atrial fibrillation	3	.71	.4
Tachycardia	3	.71	.4
Heart Disease	13	.91	.34
Type of breathing			
Spontaneous breathing	2	0.29	.1
Intubated and ventilated	21	0.18	.3
CPAP	9	0.41	.01
Deceased	26	0.16	.37

Table 4. Correlations between patients' characteristics and the presence of subcutaneous emphysema for patients with Covid-19 needing a surgical procedure

	Total cases	Chi squared	p value
Sex	32	.38	.54
Male	25		
Women	7		
Smoker	15	1.95	.16
Pulmonary disease			
COPD	8	.38	.54
Asthma	5	.11	.74
Bronchiectasis	4	.88	.35
Systemic hypertension	19	.43	.51
Atrial fibrillation	3	.52	.47
Tachycardia	3	.52	.47
Heart Disease	13	1.89	.17
Type 2 diabetes mellitus	12	.21	.65
Type of breathing			
Spontaneous breathing	2	N/A	N/A
Intubated and ventilated	21	.06	.81
CPAP	9	.3	.86
Deceased	26	.06	.81

meters regarding the sex, smoking status, or the presence of pulmonary or cardiac disease in patients with COVID-19 and pneumomediastinum requiring a surgical procedure.

Conservative treatment was applied to 4 patients with pneumomediastinum, tube thoracostomy was performed in 14 patients with pneumothorax and for the cases associating subcutaneous emphysema we inserted multiple percutaneous angiocathethers and performed cutaneous pressure massage, allowing air elimination from the cervical soft tissues.

Regarding the laboratory findings, elevated levels of plasma lactate dehydrogenase, which are correlated to cell death secondary to plasmatic membrane disruption and lung parenchyma injury (12), were found in all patients, regardless of the treatment approach.

Discussions

The first SARS-CoV-2 infection was recorded in Romania on February 26th, 2020. According to WHO guidance, the Health Ministry of Romania has elaborated on August 7th, 2020, a protocol for the treatment of the infection with the SARS-Cov-2 virus, effective August 10th, 2020, which was published in The Official Gazette of Romania (Monitorul Oficial) part I, No 719 of August 10th, 2020.

Pneumothorax can occur in COVID-19 ICU patients for various reasons: either spontaneously in patients without previously known SARS-CoV-2 infection, or in patients already diagnosed with COVID-19 who are under invasive/non-invasive ventilation. The latest can develop pneumothorax due to pulmonary barotrauma secondary to mechanical ventilation (22).

In 9 patients who were admitted with general altered status but spontaneously breathing, the evolution was unfavorable, necessitating non-invasive ventilation. In 2 of these, pneumothorax was associated with severe COVID-19 pneumonia and 1 was critical. Not all severe COVID-19 pneumonia cases associating pneumothorax necessitated high flow nasal oxygen therapy (HFNC), invasive mechanical ventilation, or non-invasive ventilation (Helmet continuous positive airway pressure – CPAP).

Invasive mechanical ventilation was used from the beginning in 21 patients with severe illness. Critical COVID-19 pneumonia associated pneumothorax was found in 9 of these patients.

Pneumothorax incidence is increased (14-87%) in patients presenting severe respiratory distress syndrome, despite protective mechanical strategies, low tidal volume, and reduced driving pressure (23,24,25).

Our findings suggest that isolated pneumomediastinum can occur in 3,7% of the patients requiring invasive ventilation. In such cases, the clinical evolution of the patients was aggravated by the occurrence of pneumothorax, but the quo ad vitam prognosis was not influenced. Vital prognosis in these patients depends entirely on the severity of multiple organ dysfunction and on the response to personalized therapy (corticosteroids, anticoagulants, immunomodulatory therapy – tocilizumab, anakinra).

Our results are similar to those reported by Martinelli who performed retrospective multicenter retrospective case series on pneumothorax in COVID-19 patients (4).

Laboratory evaluation in all patients consisted of complete blood count, D-dimer, ferritin, C reactive protein, lactate dehydrogenase. Elevated levels of plasma lactate dehydrogenase are correlated to cell death secondary to plasmatic membrane disruption and lung parenchyma injury (12).

Pathology aspects in COVID-19 pneumonia are represented by diffuse alveolar modifications with evident desquamation of pneumocytes, cellular fibromyxoid exudates, and hyaline membrane formation (8,26). In the cases studied by us, we observed the modification of the laboratory analyzes, respectively the decrease of the albumin values, the increase of the values for the C-reactive protein, high lactate dehydrogenase, lymphopenia, high rate for erythrocyte sedimentation rate.

Patient evaluation every 4-5 days by both clinical monitoring of ventilation parameters and repeated portable chest radiography/CT scan, even in the absence of modifications of the general status or ventilation parameters, is extremely useful. The purpose of such investigations is early diagnosis of pneumothorax, allowing immediate management (25). According to this monitoring protocol, we found the appearance of cervicomediastinal air effusions. in our patients, a few days after hospitalization.

Inflammatory alveolar diffuse lesions are believed to represent the underlying pathogenesis for COVID-19 associated pneumothorax, leading to alveolar rupture with consequent air loss (27, 28). Several theories have described the mechanism of these complications: Macklin effect (29), Hamman effect (30, 31), barotrauma (14), and coughing (7,8). Alveolar rupture can occur secondary to an infection, as well. Knowing these mechanisms, we found that in 9 patients who were on CPAP and in 21 patients with orotracheal intubation in our group, these cervicomediastinal effusions appeared.

Hamman effect leads to spontaneous subcutaneous emphysema, due to trauma, infection, or iatrogenic (postprocedural barotrauma). One of the iatrogenic causes leading to subcutaneous emphysema in mechanically ventilated patients is barotrauma caused by elevated plateau pressure over 35 cm H2O. Subcutaneous emphysema and pneumomediastinum are less frequent in COVID-19 patients and are believed to be sequelae of alveolar membrane rupture, secondary to type I and II pneumocyte infection (30,31,32).

Macklin effect is represented by an acute intra-alveolar pressure rise (i.e., respiratory airways inflammation, Valsalva maneuver, coughing, vomiting, and barotrauma) leading to alveolar rupture and consecutive dissociation along the bronchovascular sheath in the mediastinum under the effect of the intrathoracic air leak (29).

Severe cough in COVID-19 infection leads to alveolar rupture by increased transpulmonary pressure. Cough effort increases thoracic pressure, especially in smokers, leading to rapidly progressive pneumothorax, interstitial emphysema and pneumomediastinum (8). In our group of patients 15 were smokers, 10 former smokers 5 non-smokers and 2 patients did not state if they smoked.

Usually, subcutaneous emphysema has scarce symptoms and spontaneous resolution, but massive extension (cervical, thoracic or abdominal), and can become life-threatening by alteration of the general status, severe respiratory acidosis and death secondary to severe progression of its underlying cause (33). We found the presence of subcutaneous emphysema in 17 patients.

Post intubation barotrauma. SARS-CoV-2 patients with acute respiratory distress syndrome (ARDS) were ventilated with higher positive expiratory pressure and lower tidal volumes per kilogram of predicted body weight compared to patients without ARDS (26). The occurrence of complications (pneumothorax, pneumomediastinum, subcutaneous emphysema) in ARDS patients was associated with high positive end-expiratory pressure associated with assisted ventilation (14). We also found the presence of these cervicomediastinal airflows in 21 patients who were intubated.

Obesity and COVID-19. Obesity represents a strong independent risk factor for increased morbidity and mortality in SARS-CoV-2 infected patients. Visceral obesity and hyperglycemia in non-diabetic patients are significant independent risk factors for severe COVID-19 (32). We had 18 obese patients in the study group.

Disease evolution in smokers. Several meta-analyses have studied the effect of smoking on COVID-19 prevalence and severity (34,35). Multiple studies were included, with large differences regarding the number of patients included, demonstrating that severity and mortality rate is higher in COVID-19 active smokers compared to COVID-19 non-smokers (36). We found that all smokers died, survived, improved a former smoker and a non-smoker and cured 3 non-smokers and a former smoker.

Septic shock in COVID-19. Clinical signs of septic shock must be observed in due time (altered mental status, bradycardia, tachycardia, increased capillary filling, tachypnea, cold skin, petechia, purpura, elevated lactate dehydrogenase, oliguria, hyperthermia, or hypothermia), thus allowing for early management, as recommended by WHO (27). These clinical and paraclinical signs were found in all patients who died in the study group.

Personalized treatment. COVID 19 heterogeneity requires personalized clinical reasoning and management. Clinicians need to carefully evaluate and monitor each patient, keeping in mind the potential benefits as well as the adverse effects of the treatment in use. According to laboratory test results, three clinical COVID-19 hospitalization patterns were identified: inflammatory, co-infection and thrombotic (37). The patients we studied benefited from a personalized therapeutic scheme.

Antibiotherapy ± antiviral therapy. Current data doesn't recommend specific anti-COVID-19 treatment. Several ongoing clinical studies advise for the use of various antiviral therapeutic agents (27). Our personalized approach in such patients included surgery, medication (antivirals, antibiotics, anti-inflammatory drugs, anticoagulants) and oxygen therapy. Pleural drainage tubes for pneumothorax simple or associated with pneumomediastinum or subcutaneous emphysema have been fitted, percutaneous angiocatheter in patients with subcutaneous emphysema or associated with pneumomediastinum. In pneumothorax, chemical pleurodesis is performed with betadine (38). We did not perform any type of chemical pleurodesis in these patients.

This paper describes a single center COVID-19 associated pneumothorax, pneumomediastinum and subcutaneous emphysema cases, including non-ventilated and invasive and non-invasive ventilated patients. Although heterogeneous, these cases offer important data on the associations between pneumothorax, pneumomediastinum, emphysema and COVID-19.

Management was oriented towards management of acute respiratory failure and acute respiratory distress. Emergency drainage of the pleural space was the optimal therapeutic option. Several methods have been described in literature for subcutaneous emphysema decompression, irrespective of its mechanism. Early subcutaneous decompression by subcutaneous trocar-type chest tube (39), percutaneous angiocatheter (40, 41, 42) or by bilateral 3-cm infraclavicular incisions down to the pectoralis fascia (43), are good therapeutic options in such patients.

In most of the subcutaneous emphysema cases needle decompression for subcutaneous emphysema associated with cutaneous cervico-thoracic pressure massage were used, as applied by Brenton Robinson (41).

We encountered several pneumomediastinum cases, with or without subcutaneous emphysema, who did not require surgery. Interdisciplinary assessment in COVID-19 unit established the necessity of thoracic surgery evaluation and treatment.

Conclusions

Our findings suggest that the mechanism underlying the occurrence of pneumothorax and pneumomediastinum can be the SARS-CoV-2 infection.

Since COVID-19 is a recent clinical entity, we consider it should be included in the etiopathogenic classification of both secondary pneumothorax and pneumonia.

Early imaging examination is essential, and it allows optimal timing of the management and diagnosis. COVID-19 complication rate can be thus reduced, and treatment can reduce mortality. Although the pleural drainage did not influence the evolution of the disease in severe COVID-19 patients, it allowed a better ventilation of the patients. We thus recommend pleural drainage as soon as possible for these patients.

Pneumomediastinum is a severe complication of COVID-19 disease with unpredictable evolution in most non-intubated patients.

In COVID-19 pneumonia suspected or confirmed cases, aggravation of dyspnea and rapid alteration of general status is very suggestive for pneumomediastinum and/or pneumothorax

In most cases, pneumomediastinum is spontaneous and requires conservative management only, consisting of continuous monitoring, bed rest, analgesia, and oxygen therapy. At the same time, any aggravating factor must be identified.

Author's Contributions

Conceptualization CEN; resources CSG and AC; data Curation DP, CSG writing-original draft preparation. All authors have written, reviewed, edited, read and agreed to the published version of the manuscript.

Funding

This research received no external funding

Conflicts of Interest

The authors have no conflict of interest to disclose and received no funding for this study.

Institutional Review Board Statement

The study protocol was approved by the coordinator ethics committee (n. 441, date of approval 3rd of March 2021).

Informed Consent Statement

Patient consent was waived due to the retrospective nature of this study and the problems related to the pandemic.

Data Availability Statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy policy of the centers involved in the study.

References

1. Brogna B, Bignardi E, Salvatore P, Alberigo M, Brogna C, Megliola A, et al. Unusual presentations of COVID-19 pneumonia on CT scans with spontaneous pneumomediastinum and loculated pneumothorax: A report of two cases and a review of the literature. Heart Lung. 2020;49(6):864-868.
2. WHO: Coronavirus disease 2019 (COVID 19) Situation Report. https://www.who.int/emergencies/diseases/novel coronavirus 2019/situation reports/. Updated September 28, 2020.
3. Petrosillo N, Viceconte G, Ergonul O, Ippolito G, Petersen E. COVID-19, SARS and MERS: are they closely related?. Clin Microbiol Infect. 2020; 26(6):729-734.
4. Martinelli AW, Ingle T, Newman J, Nadeem I, Jackson K, Lane ND, et al. COVID-19 and pneumothorax: a multicentre retrospective case series. Eur Respir J. 2020;56(5):2002697.
5. McGuinness G, Zhan C, Rosenberg N, Azour L, Wickstrom M, Mason DM, et all. Increased incidence of barotrauma in patients with COVID-19 on invasive mechanical ventilation. Radiology. 2020;297(2):E252-E262.
6. Centers for Disease Control and Prevention Announcement New ICD 10 Code for Coronavirus 2 20 2020; 2020 [Accessed 8 JUN 2020].
7. 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.
8. Shan S, Guangming L, Wei L, Xuedong Y. Spontaneous pneumomediastinum, pneumothorax and subcutaneous emphysema in COVID-19: case report and literature review. Rev Inst Med Trop Sao Paulo. 2020; 62:e76. doi: 10.1590/S1678-9946202062076. eCollection 2020.
9. Hazariwala V, Hadid H, Kirsch D and Big C. Spontaneous pneumomediastinum, pneumopericardium, pneumothorax and subcutaneous emphysema in patients with COVID-19 pneumonia, a case report. J Cardiothorac Surg. 2020;15(1):301.
10. Long A, Grimaldo F. Spontaneous hemopneumothorax in a patient with COVID-19. Am J Emerg Med. 2021;40:228.e1-228.e2.
11. Wenzl T. Smoking and COVID-19- A review of studies suggesting a protective effect of smoking against COVID-19; JRC TECHNICAL RAPORT. European Commission. Luxembourg: Publications Office of the European Union, 2020. EU Science Hub https://ec.europa.eu/jr
12. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. Travel Med Infect Dis. 2020;34:101623.
13. Higham A, Mathioudakis A, Vestbo J, Singh D. COVID-19 and COPD: a narrative review of the basic science and clinical outcomes. Eur Respir Rev. 2020;29(158):200199.
14. Kargirwar KV, Rathod D, Kumar V, Patel M, Shah M, Choudhury H, et al. Clinical profile of patients with severe acute respiratory syndrome coronavirus 2 infection developing pulmonary barotrauma on mechanical ventilation. Indian J Crit Care Med. 2022;26(5):613-618.
15. Nistor CE, Ciuche A, Stanciu-Gavan C. Spontaneous Pneumothorax - Therapeutic Attitude – Brief Review. International J Cardiov and Thor Surg. 2020;6(4):49-53.
16. Elhakim TS, Abdul HS, Romero CP, Rodriguez-Fuentes Y. Spontaneous pneumomediastinum, pneumothorax and subcutaneous emphysema in COVID-19 pneumonia: a rare case and literature review. BMJ Case Rep. 2020;13(12):e239489.
17. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn. 2020;20(5):453-454.
18. Dong J, Peng H, Zhang D. Early clinical and CT manifestations of coronavirus disease 2019 (COVID-19) pneumonia. AJR. 2020:1–6.
19. Pan F, Ye T, Sun P, et all. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology. 2020. https://doi.org/10.1148/radiol.2020200370
20. Nistor C, Ciuche A, Horvat T. Pneumotoraxul spontan. In: Popescu I , Horvat T, Tratat de Chirurgie, Vol IV Chirurgie Toracica. Bucuresti: Editura Academiei Romane; 2008. p. 261-269.
21. Ciuche A, Nistor C, Pantile D, Marin D, Tudose A. Spontaneous pneumothorax in a case of pulmonary langerhans cell histiocytosis. Maedica (Bucur). 2011;6(3):204-9.
22. Wang W, Gao R, Zheng Y, Jiang L. COVID-19 with spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema. J Travel Med. 2020;27(5):taaa062.
23. Wang XH, Duan J, Han X, Liu X, Zhou J, Wang X, et al. High incidence and

mortality of pneumothorax in critically Ill patients with COVID-19. Heart Lung. 2021;50(1):37-43.
24. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes?. Intensive Care Med. 2020;46(6):1099-1102.
25. Martinelli AW, Ingle T, Newman J, Nadeem I, Jackson K, Lane ND, et al. COVID-19 and pneumothorax: a multicentre retrospective case series. Eur Respir J. 2020;56(5):2002697.
26. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-422.
27. WORLD HEALTH ORGANIZATION- Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance 13 March 2020 https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf
28. Lemmers DHL, Hilal MA, Bnà C, Prezioso C, Cavallo E, Nencini N, et al. Pneumomediastinum and subcutaneous emphysema in COVID-19: barotrauma or lung frailty? ERJ Open Res. 2020;6(4):00385-2020.
29. Manna S, Maron SZ, Cedillo MA, Voutsinas N, Toussie D, Finkelstein M, et al. Spontaneous subcutaneous emphysema and pneumomediastinum in non intubated patients with COVID-19. Clin Imaging. 2020;67:207-213.
30. Oshovskyya V, Poliakova Y. A rare case of spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema in the II stage of labour. Int J Surg Case Rep. 2020;70:130-132.
31. Hazariwala V, Hadid H, Kirsch D and Big C. Spontaneous pneumomediastinum, pneumopericardium, pneumothorax and subcutaneous emphysema in patients with COVID-19 pneumonia, a case report. J Cardiothorac Surg. 2020;15(1):301.
32. Stefan N, Birkenfeld AL, Schulze MB. Global pandemics interconnected - obesity, impaired metabolic health and COVID-19. Nat Rev Endocrinol. 2021;17(3):135-149.
33. Al-Azzawi M, Douedi S, Alshami A, Al-Saoudi G, Mikhail J. Spontaneous Subcutaneous Emphysema and Pneumomediastinum in COVID-19 Patients: An Indicator of Poor Prognosis? Am J Case Rep. 2020; 21:e925557.
34. Zhang R, Ouyang H, Fu L, Wang S, Han J, Huang K, et al. CT features of SARS-CoV-2 pneumonia according to clinical presentation: a retrospective analysis of 120 consecutive patients from Wuhan city. Eur Radiol. 2020; 30(8):4417-4426.
35. Vardavas CI, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. Tob Induc Dis. 2020;18:20.
36. Eakin MN and Neptune E. Smoking and COVID-19: The Real Deal. Ann Am Thorac Soc. 2021;18(10):1610-1613.
37. Garcia-Vidal C, Moreno-García E, Hernández-Meneses M, Puerta-Alcalde P, Chumbita M, Garcia-Pouton N, et al. Personalized therapy approach for hospitalized patients with COVID-19. Clinical Infectious Diseases. Oxford Academic 2020. https://doi.org/10.1093/cid/ciaa964
38. Nistor C, Ranetti AE, Ciuche A, Pantil D, Constantin LM, Brincoveanu R. Betadine (R) in chemical pleurodesis. Farmacia. 2014;62(5):897-806.
39. Terada Y, Matsunobe S, Nemoto T, Tsuda T, Shimizu Y. Palliation of severe subcutaneous emphysema with use of a trocar-type chest tube as a subcutaneous drain. Chest. 1993;103(1):323.
40. Mustafa A, Heleno C, Summerfield DT. Rapid resolution of severe subcutaneous emphysema causing respiratory failure with subcutaneous drain. SAGE Open Med Case Rep. 2021;9:2050313X21997196.
41. Robinson B. Rapid resolution of severe subcutaneous emphysema with simple percutaneous angiocatheter decompression. J Surg Case Rep. 2018; 2018(7):rjy173.
42. O'Reilly P, Chen HK, Wiseman R. Management of extensive subcutaneous emphysema with a subcutaneous drain. Respirol Case Rep. 2013;1(2): 28-30.
43. Herlan DB, Landreneau RJ, Ferson PF. Massive spontaneous subcutaneous emphysema. Acute management with infra-clavicular "blow holes". Chest. 1992;102(2):503-5.