**Pneumomediastinum and Spontaneous Subcutaneous Emphysema in COVID-19 Patients Using High Flow Nasal Cannula (HFNC)**

***Rizki Suhadayanti1, Arie Zainul Fatoni2, Wiwi Jaya2, Aswoco Andyk Asmoro2***

*1Resident of the Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Brawijaya, RSUD Dr. Saiful Anwar, Malang*

*2Anesthesia Specialist & Intensive Care Consultant, Faculty of Medicine, Universitas Brawijaya, RSUD Dr. Saiful Anwar, Malang*

*Malang, East Java*

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| **Abstract**  **Background:** Spontaneous pneumothorax, pneumomediastinum, and subcutaneous emphysema are rare complications without mechanical ventilation, with 0.81% of all COVID-19 patients. During the COVID-19 pandemic, a High Flow Nasal Cannula (HFNC) was used to support respiratory failure in critically ill patients. However, there are no clinical trials to explain its safety and effectiveness. Hypoxaemic normocapnic respiratory failure is an indicator of the use of HFNC. This study reports a case of associated spontaneous subcutaneous pneumomediastinum and emphysema in a COVID-19 patient using HFNC.  **Case Report:** A male patient aged 30 years came to the hospital with the main complaint of shortness of breath that was getting worse and confirmed COVID-19. Physical examination found a good airway, spontaneous breathing with a frequency of 28 times/minute, SpO2 97% with HFNC Flow 60 FR 60%, SpO2 97%, blood pressure 102/69mmHg, pulse 65 times per minute. On the second day of treatment in the ICU, the patient did not have any disturbances in desaturation and hypotension. Patent airway, Spontaneous Breathing, and oxygenation were started using NRBM 10lpm with a target SpO of 97%, RR 30-32x/minute. On the fifth day, disturbances in desaturation and hypotension were no longer found.  **Conclusion:** Clinical improvement was found in COVID-19 patients with Pneumomediastinum and Spontaneous Subcutaneous Emphysema using High Flow Nasal Cannula (HFNC).  **Keywords:** Pneumomediastinum, Spontaneous Subcutaneous Emphysema, High Flow Nasal Cannula | **Correspondence email:** |

**INTRODUCTION**

COVID-19 is an emerging infectious disease caused by a new coronavirus called SARS-CoV2.1 Acute respiratory distress syndrome (ARDS) is a major and fatal complication with an incidence of 41% of hospitalized patients with COVID-19.2 Based on data from Johns Hopkins Hospital, on 14th April 2022, 501,512,915 cases of COVID-19 were found worldwide and caused 6,188,577 deaths.3 Based on Distribution Data from the Ministry of Health in Indonesia as of 13th April 2022, we found 6,036,909 positive cases of COVID -19 in Indonesia with 155,746 recorded deaths.4

Spontaneous pneumothorax, pneumomediastinum, and subcutaneous emphysema are rare complications without mechanical ventilation in 0.81% of all COVID-19 patients.5 Pulmonary interstitium causing pneumomediastinum. Pulmonary barotrauma from mechanical ventilation, especially with high positive end-expiratory pressure (PEEP), is a risk factor for pneumomediastinum and pneumopericardium. High intra-alveolar pressure makes the alveolus prone to rupture, allowing air to be dissected along the bronchovascular sheath toward the mediastinum.2

The incidence of subcutaneous emphysema and spontaneous pneumomediastinum is extremely rare in the general population (1.2 and 3.0 per 100,000, respectively).6 Pneumomediastinum can be divided into spontaneous pneumomediastinum, mainly caused by tobacco and recreational drug use, and secondary pneumomediastinum. Common symptoms of pneumomediastinum are tightness, retrosternal chest pain and cough. The diagnosis is confirmed by chest X-ray, showing signs of radiolucent lines and bubbles in and around the mediastinum. In addition, a CT scan of the thorax to evaluate the severity of the pneumomediastinum.7

*A high-flow nasal cannula* (HFNC) is a ventilation support capable of providing a high flow of optimally heated and humidified air. This method can distribute oxygen effectively and allows an increase in the fraction of inhaled oxygen (FiO2), from 21% to almost 100%, to prevent oxygen dilution with room air.1 HFNC can produce oxygen (FiO2) fractions up to 100%. The use of HFNC in patients with acute respiratory failure (ARDS) results in lower positive pressure in the upper airway and an increased positive end-expiratory pressure (PEEP) effect. Another physiological effect of HFNC is to reduce respiratory rate and improve diffusion. The use of HFNC has been shown to reduce the need for mechanical ventilation and reduce mortality in ARDS patients in the ICU.8

During the COVID-19 pandemic, a High Flow Nasal Cannula (HFNC) was used to support respiratory failure in critically ill patients. However, there are no clinical trials to explain its safety and effectiveness. Hypoxaemic normocapnic respiratory failure is an indicator of the use of HFNC. Pneumomediastinum and pneumothorax are not currently indicators of the use of HFNC. Baudin et al. described 177 episodes of HFNC involving 145 subjects. Among this population, six with a history of pneumothorax (3%) were identified before HFNC initiation, and no worsening occurred after HFNC insertion. However, we found two episodes (1%) of new pneumothorax.1 HFNC results in increased positive pressure within the airways, potentially causing air leakage. We found radiological evidence of spontaneous air leak in six patients with an onset of 10.33 ± 1,86. Two of the six patients required intubation, but all pneumomediastinum/pneumothorax events occurred before intubation.9

**CASE REPORT**

A male patient aged 30 years came to the hospital with the main complaint of shortness of breath that was getting worse. Cough since six days before admission to the hospital, where phlegm is found, phlegm is difficult to come out. The cough was severe one day before admission to the hospital; the complaint was accompanied by fever and shortness of breath. On physical examination, found a good airway, spontaneous breathing with a frequency of 28 times/minute, SpO2 97% with HFNC Flow 60 FR 60%, SpO2 97%, blood pressure 102/69mmHg, pulse 65 times per minute, GCS 456, defecate small using a dower catheter, urine output of 0 ccs per 4 hours, fluid balance 280cc / hour. Distention, residue, oedema and cyanosis were not found.

On assessment, the patient was suspected with a diagnosis of severe COVID-19 pneumonia in the critically ill confirmed cases and Severe Acute Respiratory Distress Syndrome. In the treatment plan, the patient was given oxygen ventilation with HFNC while being evaluated and treated in the HCU room. After the second day nurse in the HCU, the patient felt the condition was getting tighter, and Spo2 decreased to 94% then added with complaints of headaches and neck pain; we assessed the clinical evaluation and ROX Index and checked CXR. Then we consulted the patient for ICU care. The patient was then transferred to the ICU with worsening shortness of breath, chest pain and neck pain. Physical examination found a good airway, spontaneous breathing with a frequency of 30 breaths/minute, 97% SpO2 with HFNC Flow 40 FiO2 60%, blood pressure 100/59mmHg, the pulse of 67 beats per minute, with the additional diagnosis of subcutaneous emphysema. A chest CT scan revealed pneumomediastinum. The treatment plan carried out in the ICU was for weaning Flow 40 of 60% fraction, then changed to NRBM. The swab examination was positive. Laboratory tests are found in Table 1 below.

Table 1. Patient Laboratory Examination

|  |  |  |
| --- | --- | --- |
| **Inspection** | **17/06/2021** | **20/06/2021** |
| White Blood Cells | **7,540\*** | **12,530** |
| Hb | 13.2 | 13.2 |
| Hematocrit | 39% | 39.3% |
| PLT | 335,000 | 397,000 |
| MCV | 77.8 | 78.8 |
| MCH | 26.6 | 26.5 |
| MCHC | 34.2 | 33.6 |
| Eosinophil | 0.00% | 1% |
| Basophil | 0.00% | 0.1% |
| Neutrophil | 79.20% | 83% |
| Neutrophil Absolute | **5970\*** | 10,460 |
| Lymphocytes | 11.90% | 9.9% |
| absolute lymphocytes | **900\*** | 1240 |
| monocytes | 8.9 | 690 |
| NLR | 6.63 | 8.44 |
| Fibrinogen | **514.4\*** | 361.9 |
| D dimer | 0.39 | 1.73 |
| LDH | 461 | 1.1 |
| Quantitative  C-Reactive Protein | 5.9 | 6.1 |
| Ferritin | **983.7\*** | 0.06 |
| Calcium | 8.5 |  |
| ELISA | Reactive (COI 9.45) |  |
| Antigen swabs | **POSITIVE\*** |  |
| BGA Artery/Vena | 17/06/21 | 20/06/21 |
| Arteries | Arteries |
| pH | 7.35 | 7.43 |
| pCO2 | 31.2 | 29.2 |
| pO2 | 120.8 | 64.5 |
| HCO3 | 17.3 | 19.4 |
| BE | -8.6 | -5.1 |
| O2 saturation | 98.20% | 92.70% |
| Hb | 12.9 | 12.7 |
| Lactate | 2.4 |  |

Table 2. Examination of Clinical Presentation Parameters

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameters of clinical percentage | Enter the Hospital | Enter the ICU | First Treatment Day | Third Treatment Day | Fifth Day of Care (transfer from ICU) |
| Clinical | Cough +, fever +, shortness of breath + | The tightness is getting worse +, headache +, Neck pain + | Shortness of breath + reduced, neck pain + reduced, | Shortness of breath -, neck pain - | No complaints |
| Blood pressure | 102/69mmHg | 100/59mmHg | 118/78mmHg | 119/73 mmHg | 120/70 mmHg |
| Pulse | 65x/minute | 67x/minute | 92x/minute | 60 x/minute | 68x/minute |
| F. Breath | 28x/min | 30x/minute | 26x/minute | 24x/minute | 22x/minute |
| HFNC Flow | 60 | 60 | 40 |  |  |
| Fi02 | 60% | 60% | 60% |  |  |
| SpO2 | 97% | 94% | 97% | 98% | 98% |
| Rox Index | 6.2 |  |  | 7.0 |  |

Where oxygenation is given by HFNC and administration of drugs, examination of the chest x-ray shows the results shown in Figure 1.

A picture containing x-ray film, looking, blurry, close

Description automatically generated

Figure 1. Thorax Photos of Staircase Patients 17-June-2021 and 18-June-2021

X-ray of a person's chest

Description automatically generated with low confidence

Figure 2. Thorax Photos of Staircase Patients 28-June-2021 and 30-June-2021

On the second day of treatment in the ICU, the patient did not have any disturbances in desaturation and hypotension. Patent airway, Spontaneous Breathing, and oxygenation were started using NRBM 10lpm with a target SpO of 97%, RR 30-32x/minute. A blood pressure examination showed a 118/78 mmHg value and a pulse of 92x/minute. On the fifth day, disturbances in desaturation and hypotension were no longer found. Patent airway, Spontaneous Breathing, NRBM 10lpm with a target SpO of 98%, RR 30-32x/minute. A blood pressure examination showed a value of 110/67 mmHg and a pulse of 95x/minute. On the fifth day, urinate on the Dower Catheter with a urine production of 1000 cc/14 hours with a fluid balance of about 365 cc/14 hours. The situation was getting better and clinical evaluation and ROX Index were carried out with a plan to change oxygenation from NRBM to Simple Mask and move to a regular room. Subcutaneous emphysema disappeared on the 4th day, so the patient moved room. The patient received therapy with Ramdesivir, Dexamethasone, and enoxaparin during treatment.

**DISCUSSION**

The incidence of subcutaneous emphysema and spontaneous pneumomediastinum is extremely rare in the general population (1.2 and 3.0 per 100,000, respectively). Spontaneous pneumothorax, pneumomediastinum, and subcutaneous emphysema are rare complications without mechanical ventilation, with a prevalence of 0.81% of all COVID-19 patients.10 In this case, a 30-year-old male patient complained of worsening shortness of breath. On assessment, the patient was suspected with a diagnosis of severe COVID-19 pneumonia in the critically ill confirmed case and Severe Acute Respiratory Distress Syndrome. Then after the history and physical examination, we established an additional diagnosis of subcutaneous emphysema. A chest CT scan revealed pneumomediastinum.

One of the main methods for detecting the SARS-CoV-2 virus in upper and lower respiratory tract specimens is the Real-Time Reverse Transcriptase (RT)–PCR Diagnostic Panel. Take swabs on days 1 and 2 for diagnosis. If the examination on the first day is positive, there is no need for another examination on the second day. If the examination on the first day is negative, then an examination is required on the next day (second day). Chest CT scans in patients with COVID-19 most frequently showed ground-glass opacification (56.4%), consistent with viral pneumonia, with or without consolidation abnormalities.11

Subcutaneous emphysema (SE) and pneumomediastinum are conditions with air in the subcutaneous and mediastinal tissues, respectively. Most patients have mild hypoxia, but initial vital signs are stable. Symptoms are non-specific and are predominantly respiratory, with the main symptom being dyspnea.12 Clinical manifestations of MSS include retrosternal chest pain exacerbated by deep breathing and coughing, progressive dyspnea, dysphagia, or neck pain, but some patients may be asymptomatic. Physical examination reveals crepitus in the cervical region on auscultation (Hamman's sign) and palpation, especially with concomitant subcutaneous emphysema. Vital signs may indicate tachycardia, tachypnea, or hypotension. The SPM can be visualized on chest computed tomography (CT) imaging.13

Patients with the main complaint of shortness of breath that is getting worse. When the patient entered the ICU, the patient complained of worsening shortness of breath, headache, and neck pain. Cough since six days before admission to the hospital, where phlegm is found, phlegm is difficult to come out. The cough was severe one day before admission to the hospital; the complaint was accompanied by fever and shortness of breath. Physical examination found a good airway, spontaneous breathing with a frequency of 28 times/minute, SpO2 97% with HFNC Flow 60 FR 60%, SpO2 97%, blood pressure 102/69mmHg, pulse 65 times per minute, GCS 456. A swab examination was found positive. On assessment, the patient was suspected with a diagnosis of severe COVID-19 pneumonia in the critically ill confirmed case and Severe Acute Respiratory Distress Syndrome. In the treatment plan, The patient was given oxygen ventilation with HFNC while evaluated and being treated in the ICU. On physical examination, we found the airway to be good, spontaneous breathing with a frequency of 30 breaths/minute, SpO2 97% with HFNC Flow 40 FiO2 60%, blood pressure 100/59mmHg, pulse 67 beats per minute, with the additional diagnosis of subcutaneous emphysema. A chest CT scan revealed pneumomediastinum.

Treatment protocol for patients with severe COVID-19 is the administration of vitamin C 200-400 mg/8 hours in 100 cc of 0.9% NaCl discharged in 1 hour given intravenously (IV) during treatment, vitamin B1 1 ampoule/24 hours Intravenous and vitamin D in supplement form: 400 IU-1000 IU/day (available as tablets, capsules, effervescent tablets, chewable tablets, lozenges, soft capsules, powder, syrup) or 1000-5000 IU/day drugs ( available as 1000 IU tablets and 5000 IU chewable tablets). Suppose there is a sepsis condition that is strongly suspected to be due to bacterial co-infection. In that case, the selection of antibiotics is adjusted to the clinical condition, the focus of infection and risk factors present in the patient. Blood cultures should be performed, and sputum cultures (with special care) should be considered.14

Antivirals that can be given are favipiravir (200 mg dosage) loading dose 1600 mg/12 hours/oral on the 1st day and then 2 x 600 mg (days 2-5), OR Molnupiravir (200 mg dosage, orally), 400 mg 12 hours, for five days, OR Nirmatrevir/Ritonavir (Paxlovid) (150 mg/100 mg in combo), Nirmatrevir 2 tablets every 12 hours, Ritonavir 1 tablet every 12 hours, given for five days, OR Remdesivir 200 mg IV drip (day 1) followed by 1x100 mg IV drip (day 2-5 or day 2-10) according to the availability of drugs in each health facility. Dexamethasone at a dose of 6 mg/24 hours for ten days or other equivalent corticosteroids such as methylprednisolone 32 mg, or hydrocortisone 160 mg in severe cases receiving oxygen therapy or severe cases on a ventilator. Hospitalized patients with moderate or severe COVID-19 are considered for standard dose LMWH 1x0.4 cc subcutaneously or UFH 5,000 units 2x daily. Enoxaparin can be given by injection of 2000 anti-Xa IU/0.2 mL (20 mg), 4000 anti-Xa IU/0.4 mL (40 mg), 6000 anti-Xa IU/0.6 mL (60 mg) ( subcutaneously).

Oxygen therapy is the mainstay of treatment and can be administered through an oxygen mask, non-invasive ventilation, including high flow nasal cannula (HFNC), bilevel positive airway pressure (BIPAP), and in severe cases through invasive ventilation. Severe COVID-19 often progresses to acute hypoxemic respiratory failure requiring high concentrations of inspired oxygen fraction (FiO2). A high-flow nasal cannula (HFNC) is a strategy to improve oxygenation and carbon dioxide clearance. HFNC is currently the first choice in Critical COVID-19 patients. The use of HFNC can reduce the need for mechanical ventilation. Pneumomediastinum and subcutaneous emphysema are generally benign and self-limited conditions. Management of pneumomediastinum is non-specific and generally involves symptomatic treatment. Oxygen therapy is given to increase the resorption of free air in the secondary mediastinum with higher nitrogen concentrations. Follow-up treatment for COVID-19 is also important because the virus can continue to destroy type II pneumocytes in the lungs, damaging the alveolar membranes.14,15

Patients were planned to be treated in the ICU to weaning Flow 40 60% fraction, then changed to NRBM. Oxygenation is given by HFNC and administration of drugs. On the fifth day, the situation was getting better. Clinical evaluation and ROX Index were carried out to change oxygenation from NRBM to Simple Mask and move to a regular room. Subcutaneous emphysema disappeared on the 4th day, so the patient moved room. The patient received therapy with Ramdesivir, Dexamethasone, and enoxaparin during treatment.

**CONCLUSION**

COVID-19 is an emerging infectious disease caused by the SARS-CoV2 coronavirus. Spontaneous pneumothorax, pneumomediastinum, and subcutaneous emphysema are rare complications without mechanical ventilation, with a prevalence of 0.81% of all COVID-19 patients. Subcutaneous emphysema (SE) and pneumomediastinum are conditions with air in the subcutaneous and mediastinal tissues, respectively. Increased alveolar pressure and diffuse alveolar injury are pathognomonic of COVID-19 pneumonia. This makes the alveoli more susceptible to rupture, especially in patients with a severe cough. The alveolar rupture causes pneumomediastinum via the Macklin phenomenon.

This patient was diagnosed with severe COVID 19 in a critically ill confirmed case and Severe Acute Respiratory Distress Syndrome. The patient received oxygen ventilation with HFNC with ICU care. Later, the patient was diagnosed with additional subcutaneous emphysema during the treatment, and a chest CT scan revealed pneumomediastinum.

*A high-flow nasal cannula* (HFNC) is a ventilation support capable of providing a high flow of optimally heated and humidified air. However, HFNC has the potential to generate an increase in positive pressure within the airways, which could potentially lead to air leakage. Pneumomediastinum or subcutaneous emphysema may be associated as a sequela of COVID-19 with prolonged non-invasive ventilation. However, pneumomediastinum and subcutaneous emphysema are generally benign and self-limited conditions. Management of pneumomediastinum is non-specific and generally involves symptomatic treatment.

**BIBLIOGRAPHY**

1. Simioli, F.; Annunziata, A.; Polistina, GE; Coppola, A.; Di Spirito, V.; Fiorentino, G. The Role of High Flow Nasal Cannula in COVID-19 Associated Pneumomediastinum and Pneumothorax. Healthcare 2021, 9, 620.https://doi.org/10.3390/healthcare9060620
2. Hazariwala V; Hadid H; Kirsch D; Big C. Spontaneous pneumomediastinum, pneumopericardium, pneumothorax and subcutaneous emphysema in patients with COVID-19 pneumonia, a case report. Journal of Cardiothoracic Surgery (2020) 15:301
3. Johns Hopkins University & Medicine. COVID-19 Dashboard. JHU. 2021. Available from:<https://coronavirus.jhu.edu/map.html>[Accessed on 14th March 2022]
4. Covid-19 task force. Data on the Distribution of COVID-19 in Indonesia. Indonesian Ministry of Health. 2021. Available from:<https://covid19.go.id/>[Accessed on 14th March 2022]
5. Hamouri S; Alqudah M; Albawaih O; Al-zoubi N; Syaj S. Spontaneous pneumothorax, pneumomediastinum and subcutaneous emphysema in non-ventilated COVID-19 patients. Future Science. OA (2021) FSO771
6. Manna S; Maron SZ; Cedillo MA; Voutinas N; Toussie D; Finkelstein M; et al. Spontaneous subcutaneous emphysema and pneumomediastinum in non intubated patients with COVID-19. Clinical Imaging. 2020; 67:207–213
7. Heijboer F, Oswald L, Cretier S, et al. pneumomediastinum in a patient with COVID-19 due to diffuse alveolar damage. BMJ Case Rep 2021;14:e242527. doi:10.1136/bcr-2021-242527
8. Irianto B; Khairsyaf O; Russilawati. Pneumothorax and Subcutaneous Emphysema Related to Use of HFNC in Critically Ill COVID-19 Patient. Journal of Human Care. 2021; 6(2): 484-490.
9. Wadhawa R, Thakkar A, Chhanwal HS, Bhalotra A, Rana Y, Wadhawa V. Spontaneous pneumomediastinum and subcutaneous emphysema in patients with COVID❤19. Saudi J Anaesth 2021;15:93-6.
10. Nishiga M; Wang DW; Han Y; Lewis DB; Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nature Reviews. 2020. 17:543-558.
11. Cascella M; Rajnik M; Aleem A; Dutebohn SC; Naples RD. Features, Evaluation, and Treatment of Coronavirus (COVID-19). StatPearls. 2022. Available from:<https://www.ncbi.nlm.nih.gov/books/NBK554776/>[Accessed on 3rd April 2022]
12. Gennaro FD; Pizzol D; Marotta C; Antunes M; Racalbuto V; Veronese N; et al. Coronavirus Disease (COVID-19) Current Status and Future Perspectives: A Narrative Review. int. J. Environ. res. Public Health 2020, 17, 2690; doi:10.3390/ijerph17082690
13. Susilo A; Rumende M; Pitoyo CW; Santoso WD; Yulianti ; Herikurniawan; et al. Coronavirus Disease 2019: Review of Current Literatures. Indonesian Journal of Internal Medicine. 2020; Vol. 7, No. 1: 1-23.
14. PAPDI. Revision of the COVID-19 Treatment Protocol. PAPDI. 2021
15. Yuki K; Fujiogi M; Koutsogiannaki. COVID-19 pathophysiology: A review. Clinical Immunology. 2020; 215:108427.