OLGU SUNUMU CASE REPORT

Non-Invasive Mechanical Ventilation Related Pneumothorax and Subcutaneous Emphysema in COVID-19 Pneumonia

COVID-19 Pnömonisinde Noninvaziv Mekanik Ventilasyon İlişkili Pnömotoraks ve Subkütan Amfizem

Melis SUMAK HAZIR^a, ¹⁰ Dilek YAZICIOĞLU ÜNAL^a

^aDepartment of Anesthesiology and Reanimation, University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Türkiye

This case report was presented as an oral presentation at 23rd International Intensive Care E-Symposium, 19-22 May 2021, Online.

ABSTRACT One of the most serious complications of coronavirus disease-2019 (COVID-19) is atypical pneumonia with diffuse bilateral lung involvement. Severe cases present with acute respiratory failure and lung injury and may require ventilatory support. In COVID-19 patients, ventilatory support is provided with oxygen via nasal-cannula or face-mask, high frequency nasal oxygenation (HFNO), non-invasive mechanical ventilation (NIMV) or invasive mechanical ventilation depending on the severity of lung injury. Each ventilation support modality has advantages and disadvantages, and should be tailored according to patient's oxygen demand. This article aims to present NIMV and HFNO related pneumothorax and subcutaneous emphysema developing due to barotrauma in a patient with COVID-19 pneumonia and highlight the issues of lung protective mechanical ventilation with these modalities.

Keywords: COVID-19; pneumothorax; subcutaneous emphysema

Pneumothorax (PTX) and subcutaneous emphysema (SE) is the presence of air in the pleural space and subcutaneous area, most common causes are trauma, surgery, infection and iatrogenic causes.¹ A complication of invasive mechanical ventilation (IMV), barotrauma and associated PTX and SE may also occur during non-invasive mechanical ventilation (NIMV) or even with high flow nasal oxygenation (HFNO).² ÖZET Koronavirüs hastalığı-2019'un [coronavirus disease-2019 (COVID-19)] en ciddi komplikasyonlarından biri bilateral akciğer tutulumu ile seyreden atipik pnömonidir. Akut solunum yetersizliği ve akciğer hasarı ile seyreden hastalarda mekanik ventilasyon ihtiyacı gelişebilir. COVID-19 hastalarında, nazal kanül, oksimask, yüksek akımlı nazal kanül oksijenasyon [high frequency nasal oxygenation (HFNO)], noninvaziv mekanik ventilasyon (NIMV) ve invaziv mekanik ventilasyon uygulamaları ile oksijenasyon sağlanabilir. Her ventilasyon desteği hastanın oksijen ihtiyacına göre ayarlanmalıdır. Bu olguda, COVID-19 pnömonisi nedeniyle NIMV ve HFNO ile takip edilen bir hastada barotravma nedeniyle gelişen pnömotoraks ve subkütan amfizem ile akciğer koruyucu mekanik ventilasyon stratejileri ele alınmıştır.

Anahtar Kelimeler: COVID-19; pnömotoraks; subkütanöz amfizem

Lung protective ventilation (LPV) strategies are well established for IMV; however there is lack of evidence for NIV and HFNO practice.³

This case report describes NIV-HFNO related PTX and SE in a patient with coronavirus disease-2019 (COVID-19) pneumonia and issues of LPV during these modalities are addressed.



CASE REPORT

A 89-year-old female presented with a three-day cough, fever, weakness, new onset shortness of breath. Her history revealed Alzheimer's disease. She was respiratory distressed, respiratory rate (RR): 25 breath.min⁻¹; heart rate: 115 beats.min⁻¹; blood pressure: 124/52 mmHg. Lung auscultation revealed bilateral rhonchus in the lower lung areas. Peripheral oxygen saturation (SpO₂) was 85%, and increased to 94% after nasal oxygen 8L.min⁻¹. Laboratory findings were significant for leukocytosis, lymphopenia and elevated lactate dehydrogenase, C-reactive protein, ferritin and fibrinogen. Arterial blood gas (ABG) analysis revealed hypoxemia. Chest X-ray and computerized tomography showed bilateral peripheral ground-glass opacities with consolidation, suggestive of viral pneumonia (Figure 1). The reverse transcriptase chain reaction was positive for COVID-19.

The patient was admitted to the intensive care unit (ICU). HFNO [AIRVO2[™] device, Optiflow[™] nasal interface (Fisher&Paykel, New Zealand)] with 80% inspired oxygen fraction (FiO₂) and 60 L/min flow in the prone position for 12 hours, and in order to prevent the loss of the advantage of prone positioning, NIV with continuous positive airway pressure (CPAP, Biosis, Biovent, Turkey) via facemask with 80% FiO₂, 8 mmHg positive end expiratory pressure (PEEP) and 10 mmHg pressure support in the supine position was initiated, ventilatory support was titrated to maintain $SpO_2 \ge 90\%$ and according to ABG analysis results. Medical treatment consisted of antiviral, antibacterial, antithrombotic and steroid medications.

At 7th day of her ICU admission, patient's respiratory distress worsened, she deteriorated, and widespread SE was detected. Lung ultrasound (US) (Esaote, MyLab SixtyTM, Italy) revealed PTX. The patient was intubated and IMV was commenced. Chest X-ray revealed PTX in the right lung; a chest tube was placed; the PTX and SE resolved after 14 hours; chest tube was removed after 3 days without further complications. However the patients' respiratory status continued to worsen and by the 11th day of ICU admission the patient died from respiratory failure (Table 1). Written informed consent was obtained. Approval from the Ministry of Health was obtained for this study.



FIGURE 1: Chest computerized tomograpy on admission (1-2-3-4): Bilateral peripheral ground-galss opacities with consolidation, consistent with COVID-19 pneumonia. Chest X-ray evaluation of the patient (5-6-7): 1st radiograph: Bilateral pneumonic involvement on the 2nd day of hospilalization; 2nd radiograpy: Pneumothorax and subcutaneous diffuse emphysema in the right lung; 3rd graph: Radiography at 24th hour after chest tube completely subcutaneous and pneumothorax resolved, from left to right respectively.

					TABLE 1:	Clinical cour	se of the pa	tient.						
Day of illness	-	2	e	4	5	9	7	8	6	10	11	12	13	14
		Home							ICU					
Cough, fever, myalgi										PTX-SE				Exitus
Respiratory failure														
Lung injury														
										Chest tube				
Ventilatory support						HFNO/(CROP					SIMV		
			FiO ₂	0.8	0.8	0.8	0.8	0.8	0.7	1.0	1.0	1.0	1.0	1.0
			Fllow	60	60	60	60	60	60					
			PEEP	8	ø	8	80	80	8	10	10	10	10	10
			Pasb	10	10	10	10	10	10	12	12	12	12	12
			RR	25	22	23	24	23	20	14	14	14	14	14
			Τv							470	470	470	470	470
			PO ₂	61.9	42.3	58	59.2	60	34.9	60	49.1	60	57	55
			PCO ₂	32.9	36	53	37	43	53	47	43.6	35.4	47	49
			SpO ₂	89	73.8	83	89.7	85.5	61.8	88.9	75.4	89.6	77.6	75.2
			Ph	7.40	7.38	7.25	7.47	7.38	7.34	7.38	7.33	7.32	7.25	7.24
			ROX	4.4	4.1	4.5	4.6	4.6	4.2					
Medical treatment				Favipiravir: 1	,600mg twice	daily loading:	600 mg twice	daily mainten	ance					
				Levofloxacin	:750 mg daily t	or 14 days								
				Methylpredn	isolone: 1 g da	ily for 5 days f	followed by do	ose reduction i	n 10 days					
				Enoxaparin :	sodium: 40 mg	twice daily su	Ibcutaneous							
										Neropinephi	rine 0.1-1µg k	kg ⁻¹ min ⁻¹		
Laboratory evaluations										Propofol 2-6	3 mg kg ⁻¹ h ⁻¹			
Hemoglobin			12.2	11.8	11.4	10.5	10.8	12.1	11.5	11	10.4	10.3	10.4	9.9
White blood cells (x10 ⁹ /L)			15.45	9.21	15.46	12.77	12.96	24.7	20.95	20.7	16.34	19	25.6	24
Absolute lymphocyte count (x	(10 ³ /mcL)		0.51	0.43	0.37	0.26	0.19	0.51	0.39	0.31	0.3	0.37	0.47	0.52
Platelets (x10 ⁹ /L)			190	241	283	253	226	307	156	197	170	149	199	183
Ferritin (ng/mL)			723					-7.38				,		
D-dimer (ng/mL)			0.73	0.92				2.2		0.86	0.83	1.02	,	
Lactate dehydrogenase (U/L	(;		307		378	,		378		,		,	,	
C-reactive protein (mg/L)			248.08	152.36				41.65	36.41					
Alanine aminotransferase (U	I/I)		5	23	19	15	15	22	19	12	80	13	,	30
Aspartate aminotransferase	(n/L)		16	49	29	23	20	35	22	13	15	20	,	57
Creatinine (mg/dL)			1.36	1.16	1.09	0.83	0.67	0.71	0.73	0.68	0.64	0.89		1.18
Procalcitonin			3.2	1.91	0.85	,		0.15	0.34	0.4	0.34	0.49	0.46	
ICU: Intensive care unit; PTX: Pneum tory pressure; Pasb: Inspiratory suppc	nothorax; Se: Subc ort pressure; RR: F	utaneous emphy Respiratory rate;	/sema; HFNO: Hig TV: Tidal volume;	h flow nasal oxyge ROX: Ratio of oxy	nation; CRAP: Co gen saturation by	ontinuous positive pulse oximetry/F	e airway pressure	e; SIMV. Synchro y rate index.	nized intermitten	t mandatory ventil	ation; FiO ₂ : Insp	bired oxygen fract	ion; PEEP: Posi	tive and expira-

DISCUSSION

In COVID-19 patients, ventilatory support is provided with oxygen via nasal-cannula or facemask, HFNO, NIV or IMV depending on the severity of lung injury. The utilization of HFNO and NIV in the ICU course of COVID-19 related severe lung damage may prevent intubation and ICU length of stay can be shortened.⁴

The pathophysiology of barotrauma associated PTX is explained by the Macklin phenomenon; high pressure gradient between marginal alveoli and lung interstitium results in rupture and air leakage from the bronchovascular bed; either excessive aeration in the alveoli or narrowing of pulmonary vessel diameters may lead to this pressure gradient.⁵

NIV-associated barotrauma is more common HFNO-associated barotrauma and than the mechanism is more clearly understood. During NIV, increased pressure gradient between alveoli and PEEP, of interstitium due to formation emphysematous areas due to rapid increase in inspiratory peak pressure with coughing, and development of small airway and bronchoalveolar bed disruptions are the reasons for alveolar rupture.² In HFNO-associated barotrauma, the high flow in the inspiratory phase is suggestive of high airway pressures.⁶ Patients may also trigger lung injury; this self-inflicted injury is a result of the increased inspiratory effort of spontaneous breathing and consequent diffuse or regional transpulmonary pressure changes in the lung.⁷

LPV is a well established approach in acute lung injury, the strategies include tidal volume <8 mL.kg⁻¹, plateau pressure<30 cmH₂O, a patient-specific PEEP setting, and a low driving pressure.³

There are recommendations for low tidal volume, low driving pressure, and high PEEP for NIV, however, a protocol driven NIV management for COVID-19 pneumonia does not exist.⁸ Additionally, spontaneous breathing of the patient may also cause deviations from the ventilator settings; predetermined tidal volume may not be delivered and there may be deviations from predetermined pressures because of air leakage and

the patients' inspiratory effort and inspiratory-time variations. Moreover during HFNO, ventilation cannot be monitored at all.

Monitoring patients on NIV or HFNO is important as the detection of failure or complications require timely conversion to IMV. While the efficiency of gas exchange can be monitored by pulse oximetry and periodical ABG analyses, monitoring of ventilation parameters is more complex.⁹ This is partially due to the qualifications of the ventilator, but also due to the fact that NIV and HFNO are semi-open systems. Differences between ventilator-software reported values and real values were previously demonstrated and patient ventilator asynchrony can influence efficacy.^{10,11} Recording of the electrical activity of the diaphragm and pressure changes in the oesophagus can be used to detect asynchrony.¹²

In the present case, there was no underlying lung disease. The only intervention that the patient had undergone was ventilatory support. We suggest that the high pressure in the respiratory tract might have increased the pressure gradient between the alveoli and surrounding tissues leading to alveoli rupture. PTX and SE occurred while our patient was on NIV-CPAP, and while HFNO is used to increase FiO₂ it is the CPAP that generates pressure, thus it is more likely that the reason was NIV. However, we cannot speculate which of the ventilatory support modalities caused this result. According to the ROX index (the ratio of SpO₂ as measured by pulse oximetry/FiO₂ to RR), which is proposed for the assessment of progress and the risk of intubation in COVID-19 pneumonia, our patient was not at high risk for intubation.¹³ We could not monitor the airway pressure during HFNO and the pressure support and PEEP during CPAP ventilation was not high, however the cough attacks of the patient may have rapidly increased the peak inspiratory pressure. Also lung fraility due to COVID-19 may be a precipitating factor for this outcome. A seven-fold increase in the incidence of pneumomediastinum/SE, in patients with acute respiratory distress syndrome due to COVID-19 pneumonia, despite the use of LPV, was previously reported and it was stated that an increased lung frailty could explain this finding more than barotraumas.14

Barotrauma-related complications should be managed according to the oxygenation and hemodynamic status; oxygenation was severely impaired after the development of PTX and SE in our patient, so IMV was initiated. LPV was provided with plateau pressure of $<30 \text{ cmH}_2\text{O}$ and tidal volumes were determined to predicted body weight and PEEP was titrated according to ABG analysis.

In the present case, PTX was first diagnosed by US with the presence of lung point and absence of dynamic pleural sliding, B-lines and lung pulse and chest radiography thereafter.¹⁵

Minimal PTX and SE are benign and selflimiting. In this case, the PTX and SE completely resolved in less than 24 hours after insertion of a chest tube. One the other hand, PTX associated with severe lung injury may result in mortality.² We suggest that this was the case in our patient; although PTX and SE resolved rapidly, the patient could not recover in correlation with the severity of the lung damage.

In the course of COVID-19 pneumonia, PTX should be considered in the differential diagnosis in

case of sudden deterioration and increase in oxygen demand. PTX and SE during NIV or HFNO is highly suggestive of severe lung damage and mortality. Evidence regarding LPV strategies for HFNO and NIV is limited and there is need for protocol driven NIV and HFNO management during COVID-19.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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