A Case of Acute Respiratory Distress Syndrome **Following Pleurodesis With Talc**

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ABSTRACT: Management of malignant pleural effusion is a medical challenge, and several methods have been proposed to deal with it including thoracentesis, indwelling pleural catheter placement, and chemical or mechanical pleurodesis. Each method, however, has its advantages and disadvantages. Talc pleurodesis is generally recognized as the most effective and safest method for the induction of chemical pleurodesis. However, in rare cases, it can lead to acute respiratory distress syndrome (ARDS). In this article, we report the case of a patient with metastatic adenocarcinoma to the pleura who presents with shortness of breath and malignant pleural effusion, develops ARDS after pleurodesis with talc, and expires despite the partial improvement of lung involvement. The symptoms and causes of this rare side effect as well as the methods that can be used to deal with it are reviewed in this article.

KEYWORDS: Talc, acute respiratory distress syndrome, malignant pleural effusion

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Introduction

Pleural effusion is the accumulation of excess fluid in the pleural space. Malignant pleural effusion (MPE) often occurs in patients with metastatic involvement of the pleura. It affects the patients' lung function and causes dyspnea and chest pain. The survival of patients with MPE depends on the origin of the primary tumor. The most common primary tumors causing MPE are lung, breast, ovarian, and lymphoma cancers. Lung cancer, which accounts for more than one-third (1/3) of the MPE cases, reduces the life expectancy of the affected patients to less than 4months after being afflicted.1 Management of MPE has proved to be challenging. No specific medication has been discovered to date that can be injected into the pleural space via a catheter and induce lifelong pleurodesis without any side effects and any need for hospitalization. However, there are some treatment techniques such as thoracentesis (in cases with frequent recurrence of pleural effusion), indwelling pleural catheter (IPC), and chemical or mechanical pleurodesis that can be used to control the patient's condition. Pleurodesis is a procedure through which the pleural space is obliterated and, as a result, the excess fluid or air cannot build up around the lung. Talc pleurodesis is generally recognized as the most effective and safest method for conducting chemical pleurodesis. However, Acute Respiratory Distress Syndrome (ARDS) is a rare but serious complication that can develop after talc pleurodesis.²⁻⁴ ARDS is characterized by acute lung inflammation that leads to increased vascular permeability.⁵ Its clinical symptoms are hypoxemia and changes in the mechanics of the respiratory system. ARDS has 3 determining factors, which are as follows:

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onset within 1 week of a known clinical insult or new/ 1worsening respiratory symptoms;

bilateral opacities not fully explained by effusions, 2lobar/lung collapse, or nodules on chest X-ray or computed tomography;

respiratory failure not fully explained by cardiac failure 3or fluid overload

So far, no specific medication has been introduced to treat this disease.⁶ However, there are some treatment methods such as ventilation with low tidal volume, the use of tranquilizers and painkillers, and strategies for weaning from ventilation that can control it.5

Case Presentation

The patient was a 39-year-old female who had been referred to the hospital with the chief complaint of shortness of breath. Her shortness of breath had started in the last 6 months and had exacerbated 2weeks before. As her condition worsened, she was referred to the hospital with mMRC III dyspnea. The patient did not mention having fever, coughs, or sputum production accompanied by chest pain. She had been diagnosed with metastatic gastric adenocarcinoma 8 years before and had received chemotherapy. Also, she mentioned a history of recurrent pleural effusion in her left hemithorax, which had been treated with the insertion of a chest tube and permanent pleural catheter. Her oxygen hemoglobin saturation (SpO₂) was 86%, respiratory rate was 25, pulse rate was 85, and blood

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	REFERENCE VALUE	ADMISSION	ARDS	EXPIRED
WBC (cu/mm)	4000-10000	6700	19000	18800
Hb (g/dl)	12-16	8.8	9.9	10.2
MCV (fL)	80-100	90	94	101
Platelets (10 ⁶ /ml)	150-450	386	142	445
PTT (sec)	30-35	30	40	43
INR (Index)	1-1.4	1	1.4	1
Urea (mg/dl)	15-45	37	21	21
Creatinine (mg/dl)	0.5-1.4	0.7	0.6	0.6
AST(IU/L)	5-40	17		
ALT(IU/L)	5-40	7		
ALK. P(IU/L)	64-306	312		
Sodium (mEq/L)	132-145	138	135	132
Potassium (mEq/L)	3.7-5.5	3.9	4.3	4.2
Calcium (mg/dl)	8.2-10.7	7.6		
Phosphorus (mg/dl)	2.5-5	3.1		
Albumin (g/dl)	3.5-5.5	1.9	3.2	3.1
ESR (mm/h)	<20	40		
LDH (IU/L)	0-500	251	283	
CRP	Negative	3+		
CPK-MB (U/L)	0-24	19		
PCR Covid19	Negative		Negative	

Table 1. Shows the laboratory results in different stages of the patient's hospitalization.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatinine phosphokinase; Cr, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; LDH, lactate dehydrogenase; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; PCR, polymerase-chain reaction; PTT, partial thromboplastin time; WBC, white blood cells.

pressure was 130/80 mmHg. A basal bilateral decreased breath sound and hyper resonance in the left hemithorax were auscultated during the physical examination.

Chest radiography indicated a massive hydropneumothorax in the left hemithorax and a passive collapse in a large area of the left lung. Moreover, pleural effusion was observed in the right hemithorax. After the insertion of a chest tube in her left hemithorax, the fluid from pleural effusion was examined, and the results revealed that it was exudative fluid. In addition, necro inflammatory debris with fibrin deposition along with scattered epithelial cells was reported in the cytology.

Echocardiography, on the other hand, demonstrated normal ejection fraction (55%-60%), mild mitral and tricuspid regurgitation, and pulmonary artery pressure of 30. The laboratory findings are presented in Table 1. Daily follow-up continued with chest radiography. Due to the relative improvement of her symptoms (SpO₂ increased to 92%) and Imaging findings, she was prepared for discharge (Figure 1). However, a thoracic

surgery consultation was requested due to recurrent pleural effusion and her relatives asked for pleurodesis. The thoracic surgery specialist suggested that it would be beneficial. Pleurodesis was then performed by injecting 3.5 g of sterile and non-small particle size talc (Steritalc®) suspended in 100 ml of normal saline into the pleural space via chest tube. One day after injection, the patient's SpO₂ dropped to 80% and tachypnea (RR=38 per min) with gasping respiration emerged. Hence, she was intubated, and the ventilator was set to SIMV mode with Tidal volume = 450, $FIO_2 = 100\%$, PEEP = 7, PS = 15, and RR = 30. Her blood pressure decreased to 85/60, and inotropic drugs were administered. Considering the results obtained from imaging, which showed diffuse ground glass opacity (Figure 1), and other tests on the patient as well as the nature of the patient's previous disease, her use of chemotherapy drugs, and the suppression of the immune system, the primary diagnosis was primary lung infection with viral agents, mycoplasma, or other opportunistic agents such as pneumocystis

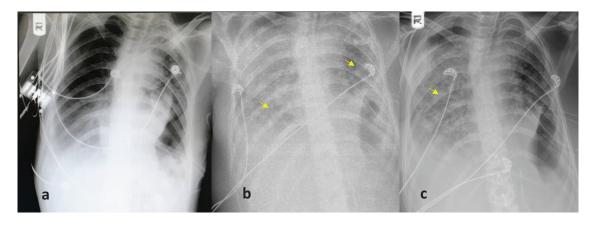


Figure 1. patient's chest radiography: (a) Pneumothorax and pleural effusion resolved after primary treatments. (b) Bilateral diffuse ground glass opacity (yellow arrow). (c) Relative improvement in lung involvement (yellow arrow).

jirovecii. Bronchoalveolar lavage was postponed as she was hemodynamically unstable. Therefore, broad-spectrum antibiotics were administered to fight against the possible infectious source of her condition. On the next day, as her condition did not improve and her moderate severity of Horowitz index ($PaO_2/FiO_2=156$), as well as imaging findings, suggested ARDS as a differential diagnosis, she was started on a high corticosteroid regimen (Methylprednisolone amp 250 mg daily) which was continued for 3 days. After 7 days, despite improvements in imaging, she did not respond to the support-ive treatment and inotropic drugs and expired following a car-diorespiratory arrest.

Discussion

In this article, we presented a case of MEF who developed symptoms of severe dyspnea after talc injection and progressed toward respiratory failure, need for mechanical ventilation, and death. Considering the findings obtained from imaging and the patient's resistance to medical treatments, and after ruling out other causes, ARDS seemed to be the most probable diagnosis. The common risk factors for ARDS are pneumonia, sepsis, aspiration of gastric contents, trauma, pancreatitis, burns, non-cardiogenic shock, the overdose of medications, transfusion-related acute lung injury (TRALI), and drowning.⁶ In addition, fungi and parasites like pneumocystis jirovecii, toxoplasma gondii, and aspergillus fumigatus might be responsible for ARDS in patients with immunodeficiency.⁷

Pain and fever are the most common side effects of talc injection; ARDS is rare in this setting but is associated with a high mortality rate.^{8,9} Evidence suggests a direct relationship exists between the particles' mean size and the complications' characteristics. It has also been demonstrated that significant hypoxemic events after the injection of graded talc products are quite rare. The concept of "graded" or "calibrated" talc products is used for the products whose powder has been processed in a way that the volume of the particles varies between 10 and $25 \,\mu$ m. Graded talc with medium or large particle volumes is less likely to cause systemic side effects.⁹ Various studies have revealed that higher doses of talc are associated with more adverse effects. However, dose-related side effects have not been studied systematically in human beings.¹⁰ Our patient received non-small particle size talc with an efficient dose, expecting that it would cause minor side effects.

Conclusion

Even though talc is a safe substance for pleurodesis, it might present inevitable side effects such as ARDS, in which the chance of survival is quite low.

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Not applicable.

Author Contributions

EI visited the patient in the hospital daily, checking and revising the manuscript. SM and MN drafted the manuscript.

Consent to Participate

Written informed consent was obtained from the patient for his participation in this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for Publication

Written informed consent was obtained from the patient to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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