ARDS following talc pleurodesis
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Abstract
Recurrent and symptomatic pleural effusion is not uncommon for patients with lung malignancy. In these cases, chemical pleurodesis is used to prevent reaccumulation of the effusion as a palliative measure. Pleurodesis can be done with talc and various other chemotherapeutic agents. Talc remained the most commonly used one as it is cheaper and easily available. Pleurodesis using mixed talc (containing small talc particles) produces more lungs and systemic inflammation and more hypoxemia than graded talc which can lead to a variety of clinical manifestation from hypoxia to adult respiratory distress syndrome. These complications can be predicted based upon the clinical predictors and can be easily prevented.

INTRODUCTION
Recurrent and symptomatic pleural effusion is not uncommon for patients with lung malignancy. In these cases, chemical pleurodesis is used to prevent reaccumulation of the effusion as a palliative measure. Pleurodesis can be done with talc (either as insufflated or as slurry), the tetracycline derivatives (tetracycline, minocycline or doxycycline), corynebacterium parvum, the chemotherapeutic agents (bleomycin, interferon b, cisplatin, cytarabine, doxorubicin, mitomycin, 5-fluorouracil and etoposide), silver nitrate and iopropidone. Cases of acute respiratory failure occurring after talc pleurodesis can be due to various reasons including ARDS. We present a case of ARDS following talc pleurodesis.

CASE PRESENTATION
A 62 years old Caucasian female was admitted to the hospital because of progressively increasing shortness of breath and easy fatigability for the past one week. Her other review of systems were negative. Her past medical history includes hypertension and gout. Her physical examination revealed a moderately built female with out any apparent distress. Her vitals are stable and she was saturating 99% at room air. Her physical examination was notable for edema in the extremities and pulmonary examination was consistent with left sided pleural effusion. Her imaging studies confirmed moderate to severe left pleural effusion and diagnostic tap of the pleural fluid was consistent with adenocarcinoma. Her computed tomogram of the chest revealed left lung mass. Due to symptomatic effusion she had undergone therapeutic thoracentesis. However, on the second day of thoracentesis, she again got her pleural fluid reaccumulated on the left side. Due to rapid reaccumulation of pleural fluid, various options including pleural catheter and talc pleurodesis are presented to the patient. The patient preferred chemical pleurodesis as she cannot take care of the pleural catheter.

Powdered talc pleurodesis with 5gms of mixed talc (10-30µm mean particle size) was performed at the bedside. 2 days later, patient developed progressively worsening hypoxia. Her physical examination revealed bibasilar crackles. Her central venous pressures are normal. Blood counts are within normal limits. Blood cultures and pleural fluid culture remained negative. Her echocardiogram revealed normal ejection fraction with normal diastolic function. On day 3 after pleurodesis, patient developed hypoxic respiratory failure. Her PaO2 / FiO2 ratio was 100 and A-a gradient was 305 mmHg. CXR showed reasonably good lung reexpansion and new onset bilateral alveolar infiltrates suggestive of ARDS. CT scan of the chest revealed ground glass opacities consistent with alveolar infiltrates. The patient was not interested in active intervention and she opted for DNR / DNI status. The patient was treated with non invasive ventilation and steroids and improved slowly over a period of 10 days.
**Figure 1**
Figure 1 New onset of bilateral alveolar infiltrates on Day 2 after pleurodesis. Note that the patient is on non invasive ventilation.

**DISCUSSION**
Although talc pleurodesis remains a widely used and highly effective mechanism for palliation of malignant pleural effusions, it is not free of complications. The most common adverse effects of talc pleurodesis agents are chest pain and fever. The reported incidence, which is mostly retrospective, of chest pain varies from 7 to 40% and fever from 10 to 59% (1). Acute hypoxemia (incidence 28.9%) / ALI (5.9%) / ARDS (0.4%) are potentially lethal complications of talc pleurodesis (2). Possible causes for acute respiratory failure following talc pleurodesis include the systemic inflammatory response syndrome (SIRS) or ARDS, reexpansion pulmonary edema, excessive premedication, severe comorbid disease, widespread malignant involvement of the lungs, terminal malignancy, sepsis from unsterile talc or poor chest tube technique, and excess talc (high dose or bilateral simultaneous pleurodesis). (3). If talc is culpable, it may be due to talc with very small particle size or there is a contaminant or endotoxin in the talc. Talc dissemination accounts for acute respiratory failure observed after talc pleurodesis is supported by the following facts (4):

1. Talc has been found in all patients with acute respiratory failure after talc pleurodesis, whether in lung or bronchoalveolar lavage samples, but not in patients without acute lung failure;
2. Acute respiratory failure has not been described after nontalc pleurodesis;
3. In animal studies, talc dissemination to the lung has been reported, especially at high doses and with smaller talc particles;
4. Most patients undergoing acute respiratory failure after talc pleurodesis received talc from the United States, where smaller talc particles are used.

Pleurodesis using mixed talc (containing small talc particles) produces more lung and systemic inflammation and more hypoxemia than graded talc (sorted during manufacture to exclude the vast majority of particles of less than 10 µm). The stomas in the parietal pleura with their associated lacunas and lymphatic vessels usually absorb the particulate material with diameter less than 15 µm. It is hypothesized that the mechanism for talc pleurodesis induced hypoxemia may be the escape of very small talc particles from the pleural space through these pores (5). Acute respiratory failure may be related to the systemic dissemination of talc, leading to the elaboration of inflammatory mediators. Also, ALI can be dose dependent with a higher incidence in patients receiving >5 grams of talc (4). Higher doses of talc were associated with greater talc migration and created local and distant inflammatory responses.

Predictors for the occurrence of ALI following pleurodesis are:

- Any oxygen requirement before pleurodesis
- Presence of peripheral edema
- Having undergone chemotherapy within 14 days before pleurodesis (2)

These predicting factors simply underline the severity and chronicity of the underlying pathology.

**KEY POINTS**

The ideal agent for pleurodesis is yet to be discovered. All the available substances have their own documented side effects.

Even though talc pleurodesis is a widely available, inexpensive and effective method of dyspnea control in patients with recurrent malignant pleural effusions, an effort should be made in identifying patients at high risk to develop complications, including acute respiratory failure, as these are potentially lethal.

Also, an attempt should be made by physicians to use greater
size of talc particles and require graded talc preparations, especially for those patients at high risk.

References
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