Intrapleural Streptokinase for Tuberculosis Loculated Pleural Effusion

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Summary: *Intrapleural streptokinase was performed to a 25-year-old-male with loculated pleural effusion due to tuberculosis infection. The effusion was improved significantly after fibrinolytic and antituberculosis therapy. Before insertion of intrapleural streptokinase, the pleural volume drained twice with in total volume was 1700 ml, but no significant changes were seen on the chest X-ray. After streptokinase use, the volume drained was almost 1800 ml and the chest X-ray showed significant improvement, as well as the patient condition. Intrapleural streptokinase is an effective procedure in improving drainage of loculated pleural effusion due tuberculosis.*

Key words: *Pleural effusion,Streptokinase, fibrinolytic*

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INTRODUCTION

Loculated pleural effusions are most commonly caused by complicated parapneumonic effusions and empyema followed by tubercular pleural effusions, empyema, hemothorax and malignant effusions. Loculations develop due to delayed initiation and inappropriate use of antibiotics, and delayed initiation of pleural drainage. The presence of loculations and thick viscous fluid leads to failed pleural drainage in spite of tube being patent and correctly positioned.[1] In Spain, up to 23% of all patients with tuberculosis present tuberculous pleural effusion, and tuberculosis is the most frequent cause of Pleural Effusion (PE) in patients under age of 35.[2]

The management options in such cases consist of either use of minimally invasive Video Assisted Thoracic Surgery (VATS) or more invasive conventional thoracotomy. In spite of being effective, VATS is not easily accessible and affordable in developing countries, including Indonesia. The use of intrapleural fibrinolytics is a safer, easier and cost effective option and various uncontrolled and small randomized studies have shown it to be a useful alternative.[1] Streptokinase, for its part, has been successfully used since the 1960sto treat purulent pleurisy and complicated pleural effusions. Intrapleural fibrinolytic agents provide a safe and effective treatment for loculated pleural effusion, reducing morbidity and the need for surgery.There are in fact several studies that assess the use of intrapleural streptokinase to treat encapsulated PE.[2]

Recent studies showed that fibrinolytics intervention due to complicated parapneumonic effusions and empyema followed by tubercular pleural effusions significantly improved clinical symptoms such as dyspnea, reduced pleural thickening on chest X-ray, and also decreased inhospitality time. Most of the benefits may be related to the total amounts of fluid drained with the fibrinolytics intervention. In this paper, we present a streptokinase intervention case on loculated pleural effusion due to tuberculosis.[2]

CASE PRESENTATION

A-25-year-old male complained dyspnea, intermittent mid to high grade fever and pain in the right chest upon deep breathing since one week

prior to admission. Fever was present since one week before admission, continuously, improved only with antipyretics. He also lost his body weight, 5 kg in the past few months. Physical examination revealed pleural effusion in the right lung. The laboratory examination showed anemia (Hb: 11,3 gr/dL), thrombocytosis (thrombocyte 463.000 cells/mm), elevated ESR 55 mm/hr, elevated liver enzyme (ALT 34 U/L and AST 67 U/L), and hypoxia (PO2 77.1 mmHg, Oxygen saturation 94,5%). The chest X ray showed right pleural effusion at level IV intercostalis space [Figure 1]. Thoracosentesis and pleural catheter insertion was performed, resulting in 900 ml of serous fluid, that later known to be transudate and the cytology showed none of malignant cells. However, there was no significant difference in clinical conditions and chest X-ray after the first thoracocentesis. Thoracosentesis was performed for the second time, resulting in 20 ml of pleural fluid, before then chest ultrasonography was decided to be performed showing loculated effusion with fibrins. The third thoracosentesis resulted in 800 ml of serous fluid, but there was no significant improvement afterward. The patient still complained dyspnea. At day five of treatment, the Adenosine Deaminase (ADA) test from the pleural drainage showed positive result (106,6 U/L). The patient was diagnosed with tuberculosis with loculated right pleural effusion, treated with anti tuberculosis and fibrinolytic intrapleural streptokinase (300.000 IU in 100 ml saline). A total of 1712 ml was successfully evacuated after the streptokinase interventions (900 ml at day 6, 500 ml at day 7, 300 ml at day 8, and 12 ml at day 9). The period time of dyspnea was decreasing, the fever was gone, and the oxygen saturation was improved (98.6%, with PO2 132 mmHg with nasal canule 3 lpm). Afterwards, the follow up chest X-ray showed improvement in effusion. At day 12, the dyspnea and fever were gone. His condition improved significantly, the patient was then sent home, and continue to follow up at the outpatient clinic.

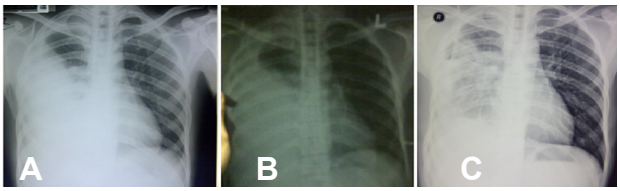

Figure 1A-C. The chest X-ray before thoracosentesis (A), after the 1st thoracosentesis, 900 ml volume pleural drainage (B), and after 2nd thoracosentesis, 800 ml pleural drainage (C) .

DISCUSSION

Pleural effusion is a common complication of bacterial pneumonia occurring in 20-60% of patients with bacterial pneumonia.[3] Mortality is higher in patients with pleural effusion than without pleural effusion.[4] The majority of patients with pleural effusions (PE) resolve with effective antibiotic treatment. However, morbidity and mortality is higher in patients with pneumonia and parapneumonic effusions (PPE) compared to patients with pneumonia alone, which may partly reflect inadequate management of the pleural effusion.[5]

In many areas of the world, tuberculosis continues to be the most common cause of pleural effusions in the absence of demonstrable pulmonary disease. According to WHO in 2011, the prevalence of tuberculosis is 680.000 and the incidence is 450.000 of 242.326.000 population in Indonesia. Moreover, there was 14.054 incidence of extrapulmonary tuberculosis notified including pleural effusion in 2011.[7] Rupture of a subpleural caseous foci into the pleural area can cause tuberculous protein enters the pleural space and generates a hypersensitivity reaction that is responsible for most of the clinical manifestations.[5] A loculated PPE develops from the intrapleural fibrinous and fibrous adhesion, which can be unilocular or multilocular.[6]

It is considerably difficult to diagnose a tuberculosis effusion or infection, even in high prevalence country such as Indonesia. Pleural effusion in tuberculous pleuritis manifests as an acute illness that mimic acute bacterial pneumonia, as found in this patient. The diagnosis of tuberculosis in the patient was confirmed with increased pleural ADA test result (106.6 U/L). Adenosine deaminase levels above 40 U/L distinguishes tuberculous effusions from other lymphocytic pleural effusions (ie, malignancies, lymphoma, collagen vascular diseases),as do interferon-gamma levels above 140 pg/mL.[6,9] The patient's chest X-ray did not differentiate tuberculosis with other bacterial infection. Coexistence of parenchymal disease is visible on standard radiographs in 19% of patients.[6] Tuberculosis effusion is usually an exudate with more than 50% lymphocytes in the white cell differential count.[5] However transudate effusion does not exclude tuberculosis infection, as showed in this case report. Smears for acid fast bacilli are only positive in 10–20% of tuberculous effusions and are only 25–50% positive on pleural fluid culture.[8] Although our case report does not show any of this

result, ADA test alone may provide high sensitivity and specificity to 89% and 92.7%, respectively.[10]

There are three phases in development of pleural effusion[11]: the exudative phase, in which pleural fluid culture is negative for bacteria, fluid pH is >7.20, normal glucose range and lactate dehydrogenase remains <3 times the upper limit of normal.[4] The second phase called fibrinopurulent phase, is characterized by positive microbial cultures and the effusion which now is referred to as "complicated". Pleural infection during this stage may respond to antibiotics and chest tube drainage but often requires invasive intervention. The third is the organizing phase, in which the thick pleural peel restricts chest mechanics and often requires surgical decortications to address restrictive impairment.

In our patient, the thoracosentesis at the first time was not able to evacuate all the pleural efussion because of the loculated effusion that was formed by fibrins in pleural space. This condition could be confirmed by ultrasonography of pleural effusion that was performed later in this patient, showed that there was amounts of fibrins layed in right pleural space resulting loculated pleural effusion. The condition suggested that the patient fell into the second stage of the development of pleural effusion.

If the pleural fluid is loculated due to a parapneumonic effusion, draining the fluid is important. The pleural infection cannot be treated unless the fibrin membrane encasing the lung is eradicated[3], in which why streptokinase were chosen. Failure of draining the effusion was associated with the presence of pleural thickening (2mm) that can be seen with CT-scan imaging (p=0.0031, OR 3, 95% CI 1.46 to 6.57), and bleeding which later not to be found associated with any factors.[12]

There are many articles reporting the efficacy of fibrinolytics in the treatment of loculated parapneumonic effusions.[3] The theory behind their use is that the loculations are produced by fibrin membranes and the fibrinolytics could destroy these membranes and facilitate drainage of the pleural fluid.[13]

Although streptokinase has existed for so long, its indication criteria are still a matter of debate between experts.[3] Whether this procedure with streptokinase may improve the total amounts of fluid to the drainage is still unclear. Chung *et al* conclude that intrapleural streptokinase is effective in resulting more total drainage fluids from tuberculosis pleural effusion.[14] While Diacon *et al* did not show any significant results.[15] This may related to variety of underlying diseases and comorbidities, such as advanced emphyema that might delay interaction of fibrinolitic.

CONCLUSION

Here we present another successful case of intrapleural streptokinase to improve loculated pleural effusion due to tuberculosis infection. Intrapleural streptokinase may be an effective procedure in improving the total amounts of fluids drained from loculated pleural effusion.

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