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Utility of chest ultrasound and intrapleural fibrinolytics with gentamicin following failed pleurodesis

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Abstract

This is a case of a 65-year-old male patient who presented to our institution due to worsening dyspnea and respiratory failure development. The patient was admitted due to dyspnea at rest and chest pain. He had a recent medical history of lung cancer with malignant pleural effusion. The patient had already undergone pleural talc poudrage by thoracoscopy, which had not been effective. Indeed, the patient was found to have residual septate pleural effusion on ultrasound examination. A placement of transthoracic pleural drainage followed by intrapleural instillation of urokinase (100,000 units) and gentamicin (80 mg) was performed within 30 days of chemical pleurodesis, achieving re-expansion of the lung by preventing recurrence of the effusion and leading to rapid clinical improvement. The novelty of the present case concerns the effectiveness of a combined treatment of fibrinolytic and intrapleural antibiotic through a pleural drainage after failure of chemical pleurodesis.

Key words: septate pleural effusion, chemical pleurodesis, intrapleural fibrinolysis, pleural drainage, chest ultrasonography.

Introduction

Lung cancer is the leading cause of death among all cancer types and it is the second highest incidence for both males and females [1]. Malignant pleural effusion (MPE) is the most frequent complication and can be associated with many types of cancer. Pleural effusion from neoplasia is characterized by the presence of malignant cells in the pleural fluid. It is present in 8 to 15 percent of lung cancer cases. For many individuals with MPE, the main symptoms are dyspnea, cough and chest pain. The consequence is worsening respiratory function, sometimes leading to respiratory failure. When the effusion is recurrent, it requires specific treatment and management [2]. The presence of pleural effusion is often indicative of an advanced disease stage, when tumor cells have spread by blood or lymphatics or by contiguity [2].

The technique of talc pleurodesis through thoracoscopy or pleural drain insertion is indicated in recurrent effusions especially if it is malignant. It is not always effective and the use of a fibrinolytic agent is controversial [3]. The novelty of this case lies in the effective use of intrapleural fibrinolytics and antibiotics during the window period following talc pleurodesis failure.

Case Report

This is a case of a 65-year-old male who was suffering from lung cancer, specifically a non-small cell lung cancer (NSCLC) that was diagnosed in April 2023. Stage at diagnosis was already a stage 4 given the presence of nodule contralateral to the main lesion and pleural effusion later identified as malignant. The histotype was an adenocarcinoma. Molecular analyses performed on pleural biopsy showed no genetic mutations of molecules such as EGFR. The patient had a positive history of hypertension and active and passive exposure to tobacco smoke. He has been treated with immunotherapy along with chemotherapy. The combination therapy schedule included treatment with cisplatin 80 mg /mq +pemetrexed 500 mg/mq+ pembrolizumab 200 mg q 21 days. The treatment continued with pembrolizumab maintenance therapy. Subsequently, a pleurodesis with talc was performed by thoracoscopy due to a recurrent malignant pleural effusion.

Fifteen days after pleurodesis, a radiographic investigation showed the persistence of pleural fluid (Figure 1). The patient presented to our unit complaining of worsening dyspnea on exertion and respiratory failure development, therefore he was hospitalized.

An arterial blood sampling with gas analysis revealed hypoxemia with normocapnia, a venous sampling showed at chemistry, an increase in levels of indices of inflammation such as C reactive protein that was found to be 5 mg/dl, leukocytes were 15000/mm^3 with predominance of neutrophil granulocytes.

Subsequent echo-guided checks were performed, which showed the presence of loculated pleural effusion with fibrin septations located in the right lower lobe. A 12-gauge drainage tube was placed under echo- guidance, using the Seldinger method. The presence of yellow serous fluid was indicative of an exudate and infection of the pleural cavity. The recurrent effusion, combined with signs of inflammation, was interpreted as secondary infection of the pleural cavity

Then urokinase 100,000 units diluted with 100 ml of saline was introduced into the pleural cavity. Gentamicin 80 mg was also instilled into the pleural cavity. The drain was then clamped for 3 hours and then reopened. The following ultrasound- check showed a resolution and resorption of fibrin septa (Figure 2).

One hour after opening the drain, 1,500 mL of pleural fluid was drained, an ultrasound check with a convex probe showed the re-expansion of the lung base and a complete resorption of fluid (Figure 3).

The fluid was sent to the laboratory for physicochemical, microbiological and cytological characterization. The characteristics were those of an exudate. Indeed, the chemical and physical characteristics were as follows: mononucleated 63%, polymorphonucleated 36%, the proteins were 4.3 g/dl, glucose was 80 mg/dl, LDH 625 UI/l. cytological examination showed the presence of atypical cells and numerous neutrophilic granulocytes and monocytes indicative of ongoing infection and inflammation. On microbiological examination, there was no evidence of growth of specific microorganisms, probably also due to antimicrobial therapy given at home before admission. The patient underwent antibiotic therapy with third-generation cephalosporin.

Indices of inflammation had progressively improved as well as the respiratory clinical parameters. After radiographic and ultrasonographic examination that confirmed the absence of pleural effusion, the patient was discharged 10 days after removal of the drainage tube.

Subsequent radiographic checks at one month after the discharge showed no pleural effusion but only an inflammatory outcome on the pulmonary scissure (Figure 4). A subsequent radiographic check at three months continued to show the right lung re-expanded, as well as detecting. a mild obliteration of the left costophrenic sinus in conjunction with febrile symptomatology (Figure 5).

Discussion

This is an unusual clinical case with an innovative practical implication since intrapleural treatment with fibrinolytic and antibiotic through ultrasound-guided drainage tube was performed. This treatment was effective in allowing complete lung re-expansion after failure of chemical pleurodesis treatment that had resulted in a multiloculated effusion with

superimposed infection. Above all, the distinctive findings of the study lies in the fact that the fibrinolysis procedure was performed within the 30-day window after pleurodesis with talcum powder together with both local and systemic antibiotic therapy, leading to complete resolution of the saccal effusion and avoiding recurrence of the effusion. In fact, we know that the window period of effectiveness of talc pleurodesis is about 30 days from the procedure [4,5]. In addition, the echo-guided procedure was well tolerated. Lower pleural fluid pH and the glucose level in malignant pleural fluid is associated with poorer prognosis. They are predictive of extensive disease and lower chance of successful pleurodesis. Some clinical studies have shown that the effectiveness of pleurodesis overall is about 65 percent.

The presence of pleural tumor involvement is a frequent finding not only in lung cancer but also in many other solid tumors, such as breast tumors [4,5]. About 15% of lung cancer patients will develop malignant pleural effusion [5,6]. Pleurodesis is considered effective when the effusion does not relapse in the subsequent 30 days.

Dyspnea with chest pain is the most common symptom associated with pleural effusion.

Talc has been the preferred agent for pleurodesis, and introduction of talc by thoracoscopic route is the most commonly used technique. New clinical evidence shows that talc slurry by tube drainage is almost as effective as talc-poudrage [7]. The talc poudrage technique is safe and feasible but it is not always effective, as this clinical case demonstrates. Fibrinolysis performed at the same time or after pleurodesis can increase the chance of efficacy [8]. According to the literature intrapleural fibrinolytic instillation finds application in complex pleural effusions, the success rate increases after four weeks as well as surgery intervention [9]. In the present case the medical treatment was performed within 30 days of pleurodesis and new surgical approach was not necessary. Fibrinolytic along with antibiotics find indication whenever there is evidence of fibrin septa and infection in pleural effusion. The present case showed that the exudative pleural effusion had reabsorbed, the main symptoms and parameters were improved after treatment.

Lastly, we need to talk about the diagnostic approach to pleural effusion. Unequivocally, chest ultrasound enhances diagnostic efficacy and provides more information than CT scan. Exposure to ionizing radiation is low and the patient can be closely monitored quickly and accurately. The ultrasound technique also allows guided procedures to be performed, ensuring greater safety [10].

Conclusions

In case of failure of pleural talc procedure, the presence of infection of the pleural cavity must be taken into consideration, which promotes the formation of exudate and also fibrin bridges.

After a failure of chemical pleurodesis, ultrasound-guided intrapleural therapy with fibrinolytic and antibiotic should be taken into account and appropriately applied. Insertion of small-bore pleural drainage is very useful in the case of effusions sepimented by fibrin shoots, facilitating fluid reabsorption, lung re-expansion and better distribution of therapeutic agents.

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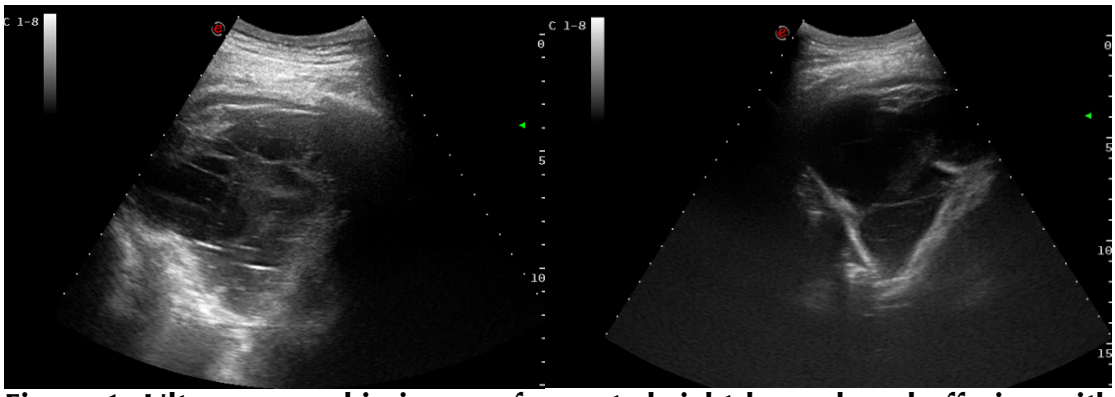

Figure 1. Ultrasonographic image of saccated right lung pleural effusion with presence of fibrin shoots.

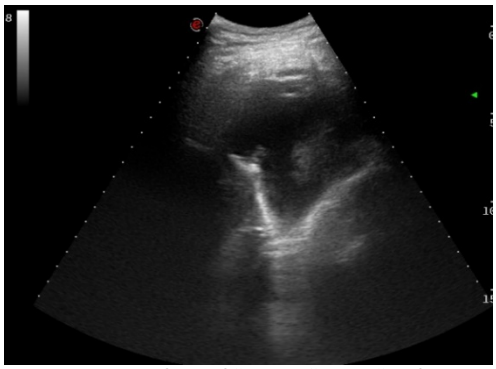

Figure 2. After fibrinolysis before opening drainage tube, resorption of fibrin bridges.

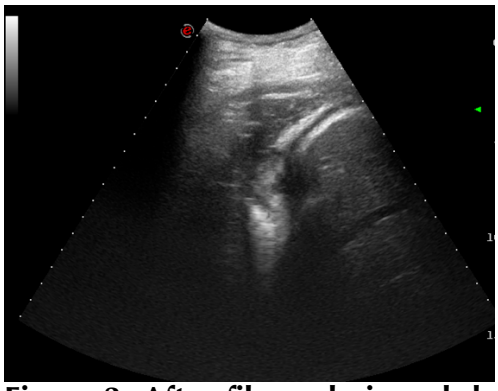

Figure 3. After fibronolysis and drainage tube opening: acoustic impedance between liver and pleural cavity, showing complete reabsorption of liquid portion.

Figure 4. Follow-up at one month after discharge: no pleural effusion on the right lung.

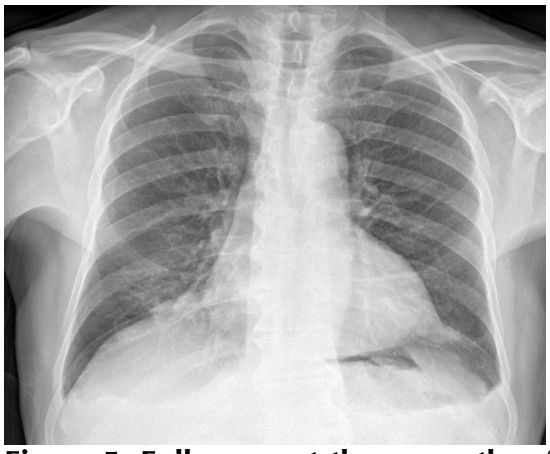

Figure 5. Follow-up at three months after discharge: mild pleural effusion on the left lung, basal site.