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Tuberculous empyema: combined intrapleural therapy might be an alternative

Philippe de Figueiredo Braga Colares[1], Jennifer Kiara Delgado Rivas[1], Amanda dos Santos Sciortino[1], Roberta Karla Barbosa de Sales[1], Lisete Ribeiro Teixeira[1]

TO THE EDITOR,

Tuberculous empyema (TE) is characterized by the presence of pus in the pleural cavity as a consequence of chronic active infection of the pleura by *Mycobacterium tuberculosis*, resulting in an influx of neutrophils and subsequent development of purulent effusion, thickening, and eventually, pleural calcification.[1] Nevertheless, the pathophysiology of TE is not yet completely understood. It is postulated that infection of the pleural cavity by mycobacteria may occur through several mechanisms, including the progression of improperly treated tuberculous pleural effusions; direct dissemination of the infection from a ruptured thoracic lymph node, rupture of the pulmonary cavity, or a subdiaphragmatic focus; hematogenous spread from a distant focus; or even contamination of the pleural cavity after pulmonary surgery/pneumonectomy.[1,2]

The treatment of pleural involvement by tuberculosis is similar to that of pulmonary disease; however, when it comes to TE, there are no extensive recommendations in the literature for pleural management, and evidence of the treatment of bacterial empyema is usually extrapolated.[1] Despite being the initial recommendation, one-third of patients with TE have failed pleural drainage.[2] Invasive procedures, such as open thoracotomy with pleural decortication and, more recently, video-assisted thoracoscopic surgery (VATS), may be necessary to resolve the infectious process and prevent progression to fibrothorax. Still, the risks and costs are not negligible.[3,4] As in bacterial empyema, the use of combined intrapleural therapy with fibrinolytics and deoxyribonuclease (DNase), in synergy with oral medication, could be part of the therapeutic arsenal for patients with initial failure of chest drainage.[5]

A 36-year-old male with no known comorbidities and a history of fever and productive cough for 12 months was subjected to several treatments for community-acquired pneumonia, without success and with recurrence of symptoms, associated with a weight loss of 12 kg in that period. Three sputum samples were tested for acid-fast bacilli (AFB) smears, nucleic acid amplification tests (Xpert MTB/RIF Ultra), and mycobacterial cultures, and all results were negative. Initial chest radiography revealed an opacity in the left apex associated with moderate ipsilateral pleural effusion. Due to the high prevalence of pleural tuberculosis in Brazil, a standard regimen with rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE) was started for 2 months, followed by maintenance therapy with RI. Four months after the start of treatment, despite the clinical resolution of the fever, the patient maintained weight loss, dyspnea, and hyporexia, in addition to the persistence of a large left pleural effusion. The patient was then forwarded to a tertiary service for investigation.

Bedside point-of-care ultrasound showed a moderate amount of pleural effusion, with homogeneous echogenicity, internal septations, and swirling echoes, in addition to significant pleural thickening (complex pleural effusion). Computed tomography (CT) of the chest confirmed the presence of moderate left loculated pleural effusion associated with pleural thickening and enhancement, as well as bilateral centrilobular pulmonary micronodules with a "tree-in-bud" aspect that were sometimes confluent in areas of pulmonary consolidation. The presence of left upper lobe fibroatelectasis was also observed. Diagnostic thoracentesis was performed, with drainage of 60 mL of purulent fluid. Pleural fluid analysis showed an exudate (Light's criteria) with pH 7.12, 4,774 U/L of lactic dehydrogenase, 5.8 mg/dL of protein, 321 U/L of adenosine deaminase (ADA), and cytology of 115,200 cells, 98% of which were leukocytes (100% polymorphonuclear). In addition, the Xpert MTB/RIF Ultra assay was positive. Thoracic drainage with a small 14F pigtail catheter was indicated, with an immediate output of 200 mL of purulent fluid, despite a significant reduction in output on the second day and persistence of pleural effusion in a control radiograph. The patient was provided intrapleural therapy with 10 mg of tissue plasminogen activator (Actilyse®) and 5 mg of DNase (Pulmozyme®), injected through the chest tube, associated with pleural lavage with 250 mL of 0.9% saline solution, for 3 days. The patient progressed with a significant increase in pleural output (1,130 mL in 5 days) and rapid clinical and radiological improvement without complications associated with local therapy. The chest tube was removed after the fifth day of treatment, and the patient was discharged after 7 days of hospitalization without the need for additional interventions, with maintenance of oral therapy (RI).

Although its pathophysiology is not well understood, TE is a serious condition that, aside from high mortality, can result in severe pleural sequelae.[1,2] Despite its high efficacy in the treatment of pleural tuberculosis, drug therapy (RIPE) may be insufficient for the management of TE. Recent studies have confirmed the effectiveness of VATS as a therapeutic option in cases of chest drainage failure;[1,2] however, this therapy is reserved for patients with low surgical risk, in addition to being an inaccessible and expensive option for the vast majority of the Brazilian population.[2,4] Although well-established for the management of infected pleural effusion

1. Divisão de Pneumologia, Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo (SP), Brasil.

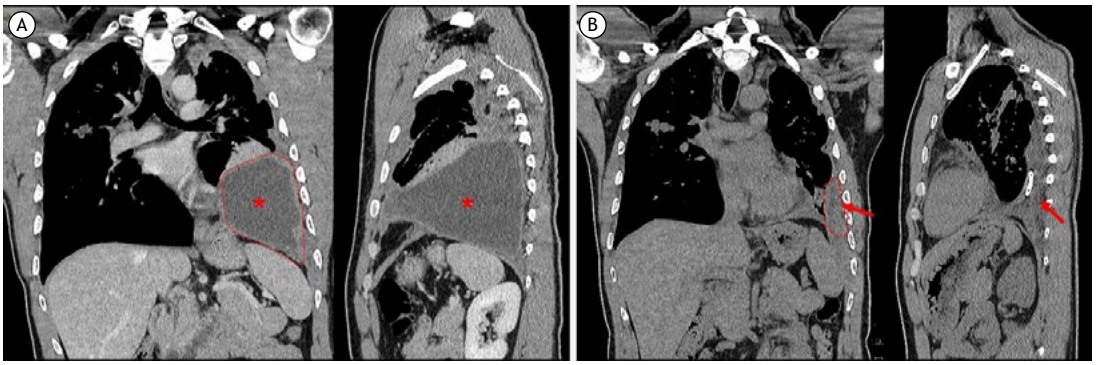

Figure 1. Chest CT (coronal and sagittal) before intrapleural therapy, showing the presence of moderate left loculated pleural effusion (red asterisk and dotted line) (A). Chest CT (coronal and sagittal) after intrapleural therapy, showing the pigtail catheter and a significant reduction in pleural effusion (red arrow and dashed line) (B).

(parapneumonic),[3-7] few studies have evaluated the efficacy of intrapleural therapy for patients diagnosed with TE, either with fibrinolysis alone or in association with DNase, limited to a few case series.[5]

Here, we report the case of a patient diagnosed with TE with persistent symptoms and pleural effusion, despite Directly Observed Therapy (DOT). As a first step, the insertion of a chest tube was indicated but was insufficient for the complete resolution of the condition. In this case, some surgical procedures, such as VATS, could be necessary to resolve this pleural infection. However, the adjuvant intrapleural therapy with alteplase and DNase for 3 days resulted in clinical, laboratory, and radiological improvement associated with a short hospital stay, without the need for a more invasive surgical procedure and without adverse effects.

There is no consensus on the intrapleural dose that should be used.[3,6] Thus, larger studies need to be carried out to assess the efficacy and safety of the intrapleural use of alteplase-DNase in TE as an alternative therapy to surgical interventions.

AUTHOR CONTRIBUTIONS

PFBC: study design, data collection, writing, and manuscript review. JKDR and ASS: data collection and writing the manuscript. RKBS and LRT: study design and manuscript review.

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