中文題目：感染性肋膜積水中的凝血酶與肋膜發炎及纖維化的相關性

英文題目：The Correlation Between Thrombin and Inflammation and Fibrosis in Infectious Pleural Effusions

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Rationale: Thrombin is important in the pathogenesis of lung inflammation and fibrosis. However, the role of thrombin in inflammatory pleural effusions and fibrosis has never been investigated. We aimed to determine whether thrombin has a pathogenic role in exudative effusions and its clinical implication.

Methods: Pleural fluid thrombin levels were measured in 86 consecutive patients presenting with undiagnosed pleural effusions and the levels were correlated with the etiology of effusions. Treatment outcome and pleural fibrosis, defined as radiological residual pleural thickening (RPT), were assessed at 6-month follow-up. Pleural mesothelial cells (PMCs) harvested from transudative pleural fluids were treated with or without (control) thrombin (0.2 U/ml), and the production of protein and mRNA of plasminogen activator inhibitor (PAI)-1, and phenotypic changes and expression of epithelial-mesenchymal transition (EMT) markers were assessed.

Results: The median thrombin levels were significantly higher in parapneumonic (PPE, n = 22), tubercuous (TBPE, n = 22) and malignant (MPE, n = 20) effusions than those in transudative effusions (n = 22) (5.3 U/ml, 5.2 U/ml, 5.4 U/ml, 0.6 U/ml, respectively, $p < 0.0001$). Both empyema (n = 3) and complicated PPE (CPPE, n = 10) patients had significantly higher pleural levels of thrombin than those with uncomplicated PPE (UPPE, n = 9) (6.5 U/ml, 5.4 U/ml vs. 4.9 U/ml, $p < 0.001$). Furthermore, the effusion thrombin levels were significantly higher in TBPE patients with (n = 10) RPT than those without (n = 14) (5.6 vs. 5.1 U/ml, $p < 0.0001$). As compared to control, thrombin time- and concentration-dependently up-regulated PAI-1 expression via PAR-1/JNK/AP-1 signaling, and induced EMT and collagen production in human PMCs.

Conclusions: Effusion thrombin correlates with pleural inflammation in PPE and pleural fibrosis in TBPE, and induces PAI-1 expression and EMT in human PMCs, implying an active role for thrombin in the pathologic process of pleural inflammation and fibrosis. Further studies are warranted to determine the clinical value of pleural thrombin as a biomarker or treatment target for infectious pleural effusions.