Diagnostic accuracy of high adenosine deaminase level in pleural effusion

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A pleural effusion is excess fluid that accumulates in the pleural cavity. Pathophysiologically pleural effusion is divided into Transudate and Exudate. When a pleural effusion has been determined to be exudative, additional evaluation is needed to determine its cause. Tuberculosis (TB) continues to be a major global public health problem.[1] According to the World Health Organization, there was an incidence of 9.0 million cases of TB worldwide in 2014. Pleural extra pulmonary is the most frequent clinical presentation of human TB especially in developing world.

Diagnosis of pleural TB is difficult to confirm because of the paucibacillary nature of the pleural fluid.[2] Conventional tests such as microscopy and culture have relatively low sensitivity and a low negative predictive value for pleural TB.[3] Novel diagnostic modalities are necessary to simplify the analysis, reduce costs, and increase accuracy in developing countries. Percutaneous or closed (blind) needle pleural biopsy (CNPB) has historically been the gold standard procedure for the diagnosis of pleural TB.[4] However, this procedure can elicit several surgical complications and has limitations if performed in inexperienced hands. The British Thoracic Society guidelines report important hemorrhage related complications of pleural biopsies with an Abrams needle, including death.[3] Owing to these diagnostic difficulties, mis diagnosis of pleural TB is common.

The adenosine deaminase (ADA) enzyme test is a diagnostic biomarker assay for TB using pleural fluids. ADA is a nonspecific biomarker released from monocytes/macrophages and neutrophils during the immune response to Mycobacterium tuberculosis by live phagocytized micro-organisms.[5] It is a purine catabolic enzyme that catalyzes the conversion of adenosine to inosine and is particularly abundant in lymphoid tissue.[6] The total ADA assay has a higher sensitivity, specificity, positive likelihood ratio, and post-test positive predictive value for differentiating tuberculous from other causes of exudative pleural effusion especially malignant one.

Pleural fluid adenosine deaminase measurement is commonly used in countries with a moderate to high incidence of mycobacterium tuberculosis. It is often used routinely in the investigation of undiagnosed exudative pleural effusions in these areas. Also where a tuberculous effusion is suspected, it is used as a supplement standard pleural fluid analysis. It can be quickly analyzed and is relatively non-invasive to obtain with thoracocentesis as compared to other investigations. Direct visualization of acid fast bacilli in pleural fluid has low yield rates of between 5–10%[7,8] and culture results from pleural fluid and sputum only have a sensitivity of 50% and 30% respectively, as well as taking up to 8 weeks to perform.[9,10] In countries where the BCG was used nationally the Mantoux test has limited utility. Several diagnostic studies have concluded that an elevated P-ADA level allows for a diagnosis of tuberculous pleuritic with a sensitivity of 80% to 100% and a specificity of 89% to 100%.[11] The reported cut-off value for the P-ADA assay varies from 35.0 to 70.0 UI/L.[12] The high accuracy of a biochemical analysis for P-ADA can contribute to a diagnosis of pleural TB.

The gold standard for diagnosis of pleural TB is pleural biopsy.[13] The closed needle pleural biopsy (CNPB) procedure for the examination of pleural surfaces is still considered the “gold standard” for a definitive diagnosis of pleural TB. However, its main complication, pneumothorax, may occur in 3% to 20% of patients.[14,15] In experienced hands, the CNPB

procedure has no fatal complications, but the literature reports several potential complications such as fatal hemothorax and tension pneumothorax. Other complications include local pain, cough, obtaining no fluid, vasovagal reaction, re-expansion pulmonary edema, hypovolemia, subcutaneous hematoma, pleural infection, transient fever, and laceration of the diaphragm, heart, lung (bronchopleural fistula), liver, or spleen[15,16,] tumor seeding along the needle tract, tip of a pleural biopsy needle breaking in the pleural cavity17. In the medical literature, the sensitivity of the histopathology obtained by CNPB for the diagnosis of pleural TB ranges from 40.0% to 90.0%.[18] A study of nonspecific pleuritis by morphometric analysis showed that the presence of fibrin within the granulation tissue covering the submesothelial connective tissue had 100% specificity for the diagnosis of pleural TB.[19] This finding plus the presence of granuloma increases the yield of the histopathological diagnosis for pleural TB.

The nonparametric tetrachoric correlation can be used to evaluate the correlation between the P-ADA test and pleural histopathology. This is a very useful statistical test for describing the relationship between dichotomous variables (positive or negative, conclusive or inconclusive). According to Arnold et al.[20] in a population with a low incidence of TB, a P-ADA value greater than 35.0 IU/L in lymphocytic pleural effusions makes pleural TB the most likely diagnosis. However, it does not replace pleural biopsy as the gold standard investigation.

R F Behrsin et al.[21] Concludes that in regions with a high incidence of TB, the P-ADA activity assay is an accurate test for the diagnosis of tuberculous pleural effusions. The high diagnostic performance of the P-ADA could contribute to the diagnosis of pleural TB and render CNPB unnecessary. The P-ADA examination should be encouraged. Invasive diagnostic procedures with potential complications should be indicated after the evaluation of specific biomarkers with high accuracy, such as P-ADA. However, a biomarker should be used in conjunction with clinical and imaging manifestations, and the epidemiological profile of a disease.

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