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Title: Diagnostic value of quantitative measurement of pleural fluid interferon-gamma (IFN-gamma) versus QuantiFERON-TB Gold in tube assays (QFT-IT) in blood, pleural fluid and isolated pleural fluid cells in tuberculous pleural effusion

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Body: Background: Noninvasive diagnosis of pleural tuberculosis (TB) remains a challenge. Indirect detection of Mycobacterium tuberculosis-specific T cells can be useful. Objectives: Evaluation of pleural fluid IFN-gamma levels versus QFT-IT in blood and its adapted variants, using pleural fluid or isolated pleural fluid cells in the diagnosis of pleural TB. Methods: Blood and pleural fluid were collected from 38 patients at presentation for IFN-gamma assays. Ex vivo pleural fluid IFN-gamma levels, QFT-IT in blood and its adapted variants were compared with final diagnosis as confirmed by blind and/or thoracoscopic pleural biopsy. Results: The final clinical diagnosis was TB in 20 (53%), malignancy in 10 (26%), and effusion due to other causes in 8 patients (21%). Ex vivo pleural fluid IFN-gamma levels accurately identified TB in all patients and were superior to the QFT-IT assays using blood or pleural fluid (70 and 78% sensitivity, with 60 and 83% specificity, respectively). QFT-IT assay applied to isolated pleural fluid cells had 100% sensitivity and 72% specificity. The optimal cut-off obtained with ROC analysis was 0.73 for TB Gold in blood assay, 0.82 IU/ml for pleural fluid assay, and 0.94 for isolated pleural cells assay. Conclusion: The ex vivo pleural fluid IFN-gamma level is an accurate marker for the diagnosis of pleural TB. QFT-IT assay in peripheral blood or its adapted versions using pleural fluid and/ or washed pleural fluid cells had no diagnostic advantage over pleural fluid IFN-gamma in the diagnosis of pleural TB.