Egyptian Journal of Chest Diseases and Tuberculosis (2012) **61**, 371–375

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

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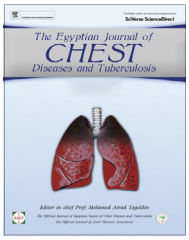

ORIGINAL ARTICLE

Clinical utility of interferon-γ compared to ADA in tuberculous pleural effusion

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Received 30 August 2012; accepted 10 September 2012
Available online 24 January 2013

KEYWORDS

Adenosine deaminase;
Interferon-γ;
Pleural fluid;
Tuberculous pleuritis

Abstract *Introduction:* Tuberculosis (TB), the single most frequent infectious cause of death worldwide, also is a major cause of pleural effusion, which in TB usually has lymphocytic and exudative characteristics. Differential diagnosis between TB and nontuberculous pleural effusion can be sometimes difficult, representing a critically important clinical problem.

Aim of the work: To evaluate the clinical utility of pleural IFN-γ level in pleural fluid for diagnosing tuberculous pleuritis.

Subject and methods: The study was conducted in kasr El-Aini hospital, Cairo University in the period from January 2011 to January 2012. It was carried on 40 patients. The patients included in the study were classified into group (included 20 cases with tuberculous pleural effusion) and group II (included 20 cases with non tuberculous pleural effusion). All patients were subjected for complete history taking and clinical examination, chest X-rays PA and lateral views, pleural fluid aspiration and analysis.

Result: Our results demonstrate that the pleural fluid concentrations of ADA, INF-γ in patients with tuberculous pleural effusions are significantly higher than in other effusions. Most importantly, ROC analysis clearly demonstrated ADA to be more sensitive and specific than INF-γ for diagnosis of tuberculous pleuritis.

Abbreviations: ADA, adenosine deaminase; INF, interferon; ROC, receiver operating characteristic; TB, tuberculosis.

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

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Introduction

Worldwide, tuberculosis (TB) is the single most frequent cause of death by an infectious agent [1]. TB also is a major cause of pleural effusion; tuberculous effusions usually are lymphocytic and exudative. The diagnosis of tuberculous pleuritis should be considered in any patient with an exudative pleural effusion. Management of patients with tuberculous pleuritis who have

0422-7638 http://dx.doi.org/10.1016/j.ejcdt.2012.09.003

acquired pleural effusion requires an effective treatment plan based on timely and accurate diagnostic information.

The diagnosis of tuberculous pleuritis commonly is made from observation of granulomas in pleural biopsy specimens or a culture finding positive for Mycobacterium tuberculosis from pleural tissue or pleural fluid. However, sensitivity of these methods is sufficiently low that even when histopathology and culture are combined, the diagnosis can be uncertain or missed in "negative" cases [2,3]. While repeating invasive diagnostic procedures ultimately may yield positive results, such an approach places patients at increased risk of complications and also increases costs. A reliable clinical marker providing physicians with rapid and accurate diagnosis of tuberculous pleuritis is greatly needed.

A variety of biological markers have been proposed to aid in the diagnosis of tuberculous pleuritis, including increased pleural fluid concentrations of adenosine deaminase (ADA), [4–6] interferon (INF)-γ, [7–13]. However, which of these markers is most useful for diagnosis of tuberculous pleuritis has not been determined. Here we studied 40 patients with pleural effusion to determine whether ADA, INF-γ concentrations in pleural fluid shows associations with the cause of pleural effusion.

Materials and methods

Patients

Forty inpatients presenting with pleural effusions who were admitted to Kasr El-Aini Hospital between January 2011 and January 2012 were studied. Informed consent was obtained from the patients. Clinical signs and symptoms, demographic data, and radiologic results were recorded. Of these 18 men and 22 women ranging age from 21 to 70 years old, 19 patients had tuberculous pleurisy, 11 patients had malignant pleuritis, 5 patients had parapneumonic pleural effusions and 5 patients had pleural effusion with various nontuberculous, nonmalignant etiologies (liver cell failure in 1 patient, metastatic adenocarcinoma in 1 patient and undetermined etiology in 3 patients).

Specimen collection and processing

For each subject, at least 40 mL of pleural fluid was collected in a syringe during thoracentesis. A portion of the sample was submitted for acid-fast staining, bacteriologic examination, cytologic examination, and measurement of protein, lactate dehydrogenase (LDH), and glucose. Another part of the sample was centrifuged at 2000 rpm for 10 min. The supernatant was frozen at $-20\,^{\circ}$ until assays for markers.

Diagnosis of tuberculous, malignant, and miscellaneous pleural effusions

Patients were classified into one of following diagnostic groups:

A. Tuberculous pleural effusion: These patients were subcategorized into two groups to the diagnostic tests for tuberculosis: (i) patients with granulomas in the pleural biopsy specimen in the absence of other pleural granulomatous diseases; (ii) patients aged 40 years or younger, with a constitutional manifestation with either a positive purified protein derivative test or at least 95% lymphocytes in the pleural fluid. Patients were classified according to the highest group for criteria met.
B. Neoplastic pleural effusions: These patients had a cytologic or histologic diagnosis of neoplasm of the pleural space or a histologic diagnosis of a tumor in another organ, and no other cause of pleural effusion.
C. Parapneumonic effusions: These patients presented with cough, fever, and a radiographic pulmonary infiltrate that resolved with antibiotic treatment. Patients with empyema, defined as pus in the pleural cavity, were included in this group.
D. Pleural effusions of unknown (nontuberculous) etiology: Patients with no known cause of pleural effusion who had nonspecific pleuritis by pleural biopsy, thoracoscopy.

Determination of pleural fluid levels of ADA, INF-γ

ADA activity was measured by auto analyzer using commercially available kits. INF-γ was measured using commercially available enzyme-linked immunosorbent assay kits.

Statistical analysis

Quantitative data were presented as mean and standard deviation (SD) values. For parametric data, Student's *t*-test was used for comparisons between mean values of two groups. One way ANOVA (Analysis of Variance) was used to compare between mean values of more than two groups. Tukey's post hoc test was used for pair-wise comparisons between mean values when ANOVA test is significant.

For non-parametric data, Mann–Whitney U test was used to compare between two groups. This test is the non-parametric alternative to Student's *t*-test. Kruskal–Wallis test was used to compare between more than two groups. This test is the non-parametric alternative to one-way ANOVA. Mann–Whitney U test was used for pair-wise comparisons between the groups when Kruskal–Wallis test is significant.

Qualitative data were presented as frequencies and percentages. Chi-square (×2) test was used for studying the comparisons between different qualitative variables.

Spearman's correlation coefficient was used to determine significant correlations between the different variables.

Receiver operating characteristic (ROC) curve was constructed to establish the optimal cut-off points and the likelihood ratios (LRs) of ADA and interferon.

Results

Diagnostic accuracy of ADA

At cut-off point of 30 IU/L, the sensitivity of ADA was (84.2%), specificity was (71.4%) and the diagnostic accuracy was 77.5%.

ROC curve analysis

Interferon

ROC curve analysis of interferon values for the diagnosis of TB in the present study showed that the optimal cut-off point was determined at 0.25. The likelihood ratios (LRs) were 1.88 and 0.20 for values above or below this cut-off point.

Diagnostic accuracy of interferon

The sensitivity of interferon was (84.2%), specificity was (57.1%) and the diagnostic accuracy was 70%. (see Table 1–5).