COMPARATIVE STUDY BETWEEN INTERFERON GAMMA AND ADENOSINE DEAMINASE FOR DIAGNOSIS OF TUBERCULOUS PLEURAL EFFUSION

Thesis

Submitted for Partial Fulfillment of M.D. Degree in Chest Diseases

Presented By

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Introduction

Pleural effusion is a manifestation of a variety of pulmonary and nonpulmonary conditions; however, consensus as to the tests that should be conducted in its diagnosis is not unanimous. Chest radiography and complete analysis of pleural fluid are performed in most patients, and a pleural biopsy is recommended in cases with no diagnosis ***(Sokolowsky et al., 1989).***

Nevertheless, 20% of patients with pleural effusion undergoing pleural fluid analysis and closed-needle pleural biopsy remain undiagnosed ***(Light, 2002).***

Lymphocytic pleural effusions are common in clinical practice. Tuberculosis (TB) is an important cause of lymphocytic effusions, along with malignancies, lymphoma, collagen vascular diseases, chylothorax***(Light, 1995).***

Malignant pleural effusion is one of the leading causes of exudative effusion; studies have demonstrated that 42 to 77% of exudative effusions are secondary to malignancy ***(Valdes et al., 1996).***

Malignant pleural effusions are a common clinical problem in patients with neoplastic disease. In one postmortem series, malignant effusions were found in 15% of patients who died with malignancies ***(Rodriguez-Panadero et al ., 1989).***

Currently, lung cancer is the most common metastatic tumour to the pleura in men and breast cancer in women ***(DiBonito L et al., 1992).***Together, both malignancies account for approximately 50–65% of all malignant effusions. Lymphomas, tumours of the genitourinary tract and gastrointestinal tract as a group account for a further 25% ***(Abbruzzese et al., 1994).***

Pleural effusions from an unknown primary are responsible for 7–15% of all malignant pleural effusions ***(Molengraft van de FJJM & Vooijs GP, 1989).***

TB is one of the major causes of pleural effusion; and TB pleurisy is the second most frequent form of extrapulmonary TB (23%) after TB lymphadenitis. According to World Health Organisation (WHO), in the next decade, incidence of TB pleurisy is estimated to be 18.2–62 / 100.000 ***(Frank, 2002).***

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 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.

(Yew et al., 1991).

Conventional methods for the diagnosis of pleural TB have proven inefficient. Direct examination of pleural fluid and Ziehl–Neelsen staining requires bacillary concentrations of 10,000/mL and, therefore, has a low sensitivity (0 to 1%).

Although a culture is more sensitive (11 to 50%), it requires 2 to 6 weeks to grow Mycobacterium tuberculosis and a minimum of 10 to 100 viable bacilli.

The sensitivity of pleural biopsy specimens is reportedly higher whether by culture (39 to 79%) or histologic evaluation (71 to 80%). However, this procedure requires greater expertise, is more invasive, and is subject to sampling error.

(Escudero–Bueno et al., 1990).

More invasive diagnostic procedures like thoracoscopy may be needed for differential diagnosis and repeatitive invasive procedures to achieve the diagnosis increase the risk of complications and they also increase the cost.

Potential risks of failure to diagnose TB pleurisy and delay in treatment and also overdiagnosing by clinical suspicion rather than microbiological diagnosis mandate quicker and less invasive procedures.

Thus, some biological markers like adenosine deaminase (ADA), gamma interferon (γ–IFN), soluble interleukin 2 (IL–2) receptors are studied for TB pleurisy diagnosis.

Increase in ADA activity is the result of a local inflammatory response and it is mainly produced by monocytes and macrophages. Also γ–IFN is a cytokine produced by CD_{4+} lymphocytes which increases the

phagocytic activity for mycobacteria and local production of γ –IFN is increased in TB pleurisy.

(Light, 2001).

IFN-γ also called Type II interferon, is a homodimeric glycoprotein containing approximately 21 to 24 kD subunits. The human IFN-γ gene, situated on chromosome 12, contains three introns; the four exons code for a polypeptide of 166 amino acids, 20 of which constitute the signal peptide ***(Naylor et al., 1983).***

IFN-γ values in pleural fluid are significantly higher in tuberculous pleuritis patients than those in nontuberculous pleuritis patients, with a sensitivity and a specificity of 100% ***(Aoki et al., 1994).***

Aim of the work

The aim of this work is to compare between interferon gamma and adenosine deaminase for diagnosis of tuberculous pleural effusion.

Subjects and Methods

- The present study will be conducted upon forty patients.
- The present study will be conducted at Ain shams University Hospitals.
- The forty patients in the present study will be classified into four groups :

Group A :

Consists of ten patients diagnosed of having tuberculous pleural effusions based on histopathological and/or bacteriological examination.

Group B :

Consists of ten patients diagnosed of having malignant pleural effusions based on histopathological and/or cytological examination.

Group C :

Consists of ten patients having pleural effusions secondary to infectious causes (e.g. pneumonia, lung abscess & empyema) diagnosed by both clinical presentation, bacteriological examination and radiological findings.

Group D :

Consists of ten patients diagnosed of having transudative pleural effusions based on chemical examination (as a control group).

- The diagnosis of all the patients in the present study will be established by one of the following procedures :
    1. Pleural aspiration.
    2. Pleural biopsy by Abram's needle.
    3. Thoracoscopic guided biopsy.

- All patients in this study will be subjected to :
    1. Detailed medical history taking.
    2. Thorough clinical examination.
    3. Routine laboratory investigations.
    4. Plain chest X– ray postero–anterior view.
    5. Computed tomography (CT) scan of the chest when needed.
    6. Measurement of interferon gamma and adenosine deaminase in both pleural samples and blood serum samples using ELIZA (Enzyme-linked immunosorbent assay) technique.

- All data will be collected and statistically analyzed.

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