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ORIGINAL ARTICLE

C-reactive protein and serum amyloid A levels in discriminating malignant from non-malignant pleural effusion

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KEYWORDS

Pleural effusion;
C-reactive protein;
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Non-malignant

Abstract *Introduction:* Distinction between malignant and non-malignant pleural effusion is of great importance in the patient management.

The aim: We examined the diagnostic value of C-reactive protein (CRP) and serum amyloid A (SAA) in distinguishing different etiologies of pleural effusion and if they could discriminate between malignant and non-malignant pleural effusions.

Subject and methods: CRP and SAA levels in both serum and pleural fluid were measured in 92 patients with pleural effusion. Of the 92 patients included in our study; 44 were diagnosed with malignant pleural effusions (group I) [with male to female ratio (M/F) 23/21 and mean age 57.7 ± 11.5 years in the form of mean ± 2SD] and 48 were diagnosed with non-malignant pleural effusion (group II) [with M/F ratio 33/15 and mean age 54.7 ± 10.4 years in the form of mean ± 2SD].

Results: CRP and SAA values were significantly higher in both serum and pleural effusion of malignant vs. non-malignant group ($P < 0.003$), but there was no statistical significant difference as regards pleural/serum CRP and pleural/serum SAA ratios between the two groups ($P = 0.148$ and $P = 0.453$ respectively). A statistically significant positive correlation between pleural fluid CRP and pleural fluid SAA in malignant and non-malignant effusions was detected ($r = 0.315$ and $P = 0.002$ respectively). Diagnostic performance of pleural fluid CRP and pleural fluid SAA in both infectious and malignant pleural effusions showed that at a cutoff value of 96.15 μg/ml for CRP; diagnostic sensitivity was 61% and specificity was 45%, while for pleural fluid SAA, a cutoff value of 137.5 μg/ml was associated with 41% sensitivity and 93% specificity.

Conclusion: Measurement of SAA and CRP levels in pleural fluid has good diagnostic utility in differentiation between malignant and non-malignant pleural effusion and pleural SAA has a better diagnostic performance than CRP.

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Introduction

Pleural effusion is an accumulation of fluid in the pleural space that exceeds the physiological amount of 10–20 ml. Pleural effusion develops either when the formation of pleural fluid is excessive and/or when the fluid resorption is disturbed [1].

Diagnosis and management of pleural effusion remain a clinical challenge due to significant cost both to patients and to the health care system. In everyday clinical practice a variety of laboratory tests are used for the differential diagnosis of pleural effusions; however, a significant proportion remains undiagnosed [2].

A major problem remains the differentiation between malignant and benign effusions, as they have different outcome and management. Cytological examination of pleural fluid is a convenient and relatively efficient method for establishing the diagnosis of pleural malignancy. However, pleural fluid cytology is positive in only 50% of cases [3]; therefore, there is an increasing demand for markers that may help in this differentiation.

Serum amyloid A (SAA) and C-reactive protein (CRP) are acute-phase proteins predominantly produced and secreted by hepatocytes [4]. Other cells including lymphocytes, monocytes, and macrophages can also produce these proteins. The induction of SAA and CRP synthesis is triggered by a number of cytokines, chiefly IL-6, which is released from a variety of cell types, but mainly from macrophages and monocytes at inflammatory sites [4].

Increased serum CRP and SAA levels have been found in a number of pulmonary disorders, including bacterial infections, malignancies, and pulmonary thromboembolism. However, only a few studies have focused on their role in pleural effusions [5].

Aim

The aim of this study was to assess the diagnostic value of C-reactive protein (CRP) and serum amyloid A (SAA) in distinguishing different etiologies of pleural effusion and if they could discriminate between malignant and non-malignant pleural effusions.

Patients and methods

Study subjects

We investigated 92 patients with pleural effusion. Patients were divided into 2 groups:

Group I: (malignant pleural effusion), included 44 patients, [with male to female ratio (M/F)of 23/21 and a mean age of 57.7 ± 11.5 years in the form of mean ± 2SD].

Group II: (non- malignant or benign pleural effusion), included 48 patients, [with M/F ratio 33/15 and a mean age of 54.7 ± 10.4 years in the form of mean ± 2SD]. This group included tuberculous, parapneumonic and transudative pleural effusions.

Study design

Patients were subjected to:

1. History taking.
2. Clinical examination.
3. Chest radiography.
4. Thoracic ultrasound.
5. Tuberculin skin test: using 5 units P.P.D in 0.1 ml intradermal injection.
6. Laboratory investigations including: serum protein, LDH, liver and kidney function tests.
7. Aspiration of pleural fluid was done and was sent immediately for the following:
   a. Biochemical examination including: protein, LDH, C-reactive protein and serum amyloid A (SAA) levels.
   b. Cytological examination.
   c. Bacteriologic examination: Gram-staining, Ziehl–Neelsen stain and culture.
8. Tissue biopsy: One of the following was done according to case:
   a. Abram's needle pleural biopsy.
   b. Thoracoscopic biopsy; if the closed pleural biopsy is non diagnostic.

- Classification of pleural fluid into transudative or exudative is based upon Light's criteria (2002) [6]
- Transudative pleural effusion fulfills the following criteria:
  (1) Total fluid protein is less than half of that of the total serum protein level.
  (2) Fluid Lactate Dehydrogenase (LDH) is less than 0.6 of that of the serum LDH.
  (3) Pleural fluid LDH is less than two thirds the upper limit of the normal of that of the serum level.

- Effusions were considered malignant if malignant cells were found on the cytology examination of pleural fluid or in the pleural biopsy specimens,
- The diagnosis of tuberculous pleurisy was based upon high tuberculin positivity, lymphocytic pleural fluid, few mesothelial cells, elevated ADA level in the pleural fluid or pleural biopsy showing caseating granuloma.
- Criteria for parapneumonic effusion were; clinical, biochemical and radiological signs of suspected pneumonia, positive Gram staining, positive culture for bacteria or neutrophil predominance in pleural effusion.

Methods

*Serum and pleural SAA concentrations were determined using Enzyme-linked immunosorbent assay (ELISA) kit supplied by Assaypro (3400 Harry S Truman BlvdSt. Charles, MO 63301USA).

*Serum and pleural CRP concentrations were determined using ELISA kit supplied by ChemuxBioScience (South San Francisco, CA 94080, USA).