ABSTRACT

Background. Pleural effusion (PF) is a common clinical presentation in several diseases. Various parameters from pleural fluid have been studied to identify the cause. The diagnostic value of these parameters varies. The present study was carried out to evaluate the value of alkaline phosphatase concentration in the pleural effusions as a diagnostic tool.

Methods. One hundred and one patients with pleural effusion admitted over a period of two years were studied. The diagnosis was confirmed by pleural biopsy and cytology for malignant cells.

Results. Pleural fluid alkaline phosphatase levels of more than 75 mg/dl was found in exudative effusions and less than 75 mg/dl in transudative ones. But it did not differentiate tubercular pleural effusions from other exudative ones.

Conclusion. Pleural fluid alkaline phosphatase of > 75 mg/dl is a useful biochemical marker to suggest exudative effusions.

Key words: Pleural fluid (PF), Alkaline phosphatase (ALP), Thoracocentesis, Pleural biopsy.

INTRODUCTION

Diagnosing the etiology of pleural effusions clinically with certainty is a challenging task for physicians. Various pleural fluid parameters have been used to identify the cause. Light et al. have classified pleural effusions into transudates and exudates using pleural fluid protein and LDH concentrations. Other parameters studied include pleural fluid cholesterol, PF bilirubin, PF amylase, PF adenosine deaminase (ADA), PF lysozyme and PF gamma interferon. Attempts to differentiate tuberculous pleural effusions from non-tuberculous effusions using biochemical markers such as ADA, lysozyme and gamma interferon, have been carried out. These are reported to be elevated in tuberculous pleural effusions. Alkaline phosphatase concentration has been shown to be elevated in tuberculous pleural effusions as compared to transudates of congestive heart failure.

We assessed the usefulness of pleural fluid alkaline phosphatase levels in differentiating transudates from exudates and further in separating tuberculous pleural effusions from other causes of exudative effusions (malignant and parapneumonic pleural effusions).

MATERIAL AND METHODS

This study included 101 adult patients of pleural effusion admitted in the Department of Internal Medicine, Institute of Medical Sciences, Srinagar, Kashmir over a period of two years. Besides routine investigations of haemogram with ESR, urine analysis, and serum chemistry, all the patients were subjected to chest
radiography (PA view), pleural fluid analysis for total and differential leucocytic count, red cell count, malignant cells, mesothelial cells, 48-hour culture and sensitivity, Ziehl-Neelsen’s stain for acid-fast bacilli (AFB) and AFB culture in LJ medium.

Pleural fluid and venous blood were simultaneously drawn for biochemical parameters of protein, sugar, lactic dehydrogenase and alkaline phosphatase. Biochemical analysis was done by multi-channel analyser (Hitachi-704, Japan). Pleural fluid pH estimation was done on arterial blood gas machine. Pleural biopsy was done by Abrahams’ pleural biopsy needle on all patients with lymphocytic exudative effusion excluding the ones where pleural fluid for malignant cells was positive. Twenty-four-hour urinary protein with serum protein, albumin and cholesterol were estimated on all clinically suspected cases of nephrotic syndrome. Bronchoscopy was done on patients, if necessary and biopsy for histopathology taken wherever indicated. Lights’ criteria was used to differentiate transudative from exudative pleural effusions. The results were interpreted by odds ratio analysis.

RESULTS

The age and sex distribution of this study revealed that 47% of patients were from 41 to 60 years of age. There were 63 males and 38 females. The distribution of patients according to the etiology of effusions included 45 patients of tuberculosis, 30 patients of malignancy, nine patients of congestive heart failure (CHF), eight patients of nephrotic syndrome, six patients of parapneumonic effusions and three unclassified exudative effusions.

By Lights’ criteria, 84 effusions were classified as exudates.

Alkaline phosphatase (ALP) levels greater than 75 mg/dl were observed in 72 out of 84 exudates but none in the 17 transudates (Table 1). All the transudates had levels less than 75 mg/dl. Thus, the sensitivity of ALP estimation for diagnosis of exudates was 100% and specificity was 85.71 percent. The positive predictive value was 58.62%, while the negative predictive value was 100 percent. However, the ability of ALP levels to differentiate tuberculous effusions from other causes of exudates was limited. Data are shown in table 2.

Table 1. Alkaline phosphatase (ALP) levels in transudates and exudates

<table>
<thead>
<tr>
<th>ALP (mg/dl)</th>
<th>Pleural effusion</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Transudate</td>
<td>Exudate</td>
</tr>
<tr>
<td>≤75</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>&gt;75</td>
<td>0</td>
<td>72</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>84</td>
</tr>
</tbody>
</table>

Table 2. Alkaline phosphatase (ALP) levels in different exudative subgroups

<table>
<thead>
<tr>
<th>ALP (mg/dl)</th>
<th>Exudative pleural effusions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tuberculous</td>
</tr>
<tr>
<td>&gt;75</td>
<td>41</td>
</tr>
<tr>
<td>≤75</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
</tr>
</tbody>
</table>

Specificity 91.11% 86.66% 33.33% 100%
Sensitivity 20.51% 14.81% 10.25% 14.81%
Positive predicted value 56.94% 36.11% 2.7% 4.16%
Negative predicted value 66.66% 66.67% 66.67% 100%
Odds ratio (OR) 2.64 1.13 0.057 1.04
95% of CI or OR -0.3169 to -1.1707 to -4.7130 to -3.0168
Significance Not significant Not significant Not significant

*Non-specific : wherein no cause was found.
DISCUSSION

The present study shows that estimation of ALP in pleural fluid is a useful marker to differentiate exudates from transudates. However, it has limited utility in separating tubercular from non-tubercular exudates. Alkaline phosphatase is one of the biochemical markers found in pleural effusion. It is a plasma membrane derived enzyme of uncertain physiologic function, that hydrolyses synthetic phosphate esters at pH 9. It is present in serum in several forms, i.e., ALP-1 alpha 2, ALP-2 beta 1 and ALP-3 beta 2. These activities arise from bone, liver, intestine and placenta also.

The only study available to our knowledge on pleural fluid alkaline phosphatase was by Syabbalo9 carried out in 1991. He studied 55 tuberculosis pleural effusions and 10 patients of CHF. He suggested that a high level of ALP may be useful to differentiate tuberculous effusions from transudates. Whether this helps to differentiate tubercular from other non-tuberculous exudative effusions, has not been studied before.

In the present study, we found that levels of ALP (>75 mg/dl) was highly suggestive of exudates with a sensitivity of 100% and a specificity of 85.71 percent. On comparing the different exudative groups among themselves, the odds ratio of ALP did not differentiate reliably tubercular effusions from other causes of effusion, including malignancy, parapneumonic effusion (PNE) and non-specific.

To conclude, alkaline phosphatase is a useful biochemical marker to differentiate exudates from transudates with cut off level of greater than 75 mg/dl favouring exudates and less than 75 mg/dl suggestive of transudates. Alkaline phosphatase concentration does not help to differentiate the etiology of exudative effusions.

REFERENCES