Brain natriuretic peptide and tumour markers in the diagnosis of non-malignant pericardial effusion

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A R T I C L E   I N F O

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Pericardial effusion (PE) is a potentially life-threatening condition that occurs in a wide variety of diseases [1–5]. Any infection, neoplasm, autoimmune or inflammatory process that can cause pericarditis can cause PE. However, idiopathic PE is the most common diagnosis [1–5].

Several markers may be used for the differential diagnosis of PE [6–9]. Tumour markers were also measured in suspected malignant disease [9,10] and B-type natriuretic peptide (BNP) in those with heart failure [11]. The aim of this study was to evaluate the levels of BNP and tumour markers in patients with non-malignant PE and to evaluate their relations to the amount of the fluid.

A total of 163 patients with PE were included in the study between January 2003 and November 2007. Etiological evaluation included complete blood count, measurement of troponin I, erythrocyte sedimentation rate, evaluation for viral etiology, thyroid stimulating hormone, rheumatological markers and computerized tomography of thorax in all patients. Diagnostic and therapeutic pericardiocentesis was performed in 44 patients. Pericardial fluid samples were sent for biochemical, microbiological and cytological analyses. The patients with constrictive pericarditis, heart failure and malignancy were excluded from the study.

Forty-five healthy people were selected as the control group for the comparison of the marker levels.

All the patients were informed about the protocol of the study and a written informed consent was obtained from all subjects. The study was approved by the Local Ethical Committee.

Echocardiographic examinations were performed on admission before medical and/or interventional management. They were performed with a standard protocol and a standard device. An anterior–posterior echo-free space at end-diastole under 10 mm is considered as small, 10–20 mm as moderate and over 20 mm is considered as large PE.

Mitral flow velocities were obtained as previously described [12]. The ratio of early-to-late peak velocities (E/A) was calculated and diastolic filling were defined as: normal (EDT 160–240 ms, IVRT 70–90 ms, E/A 1–2, PVs/PVd ≥ 1), abnormal (EDT > 240 ms, IVRT > 90 ms, E/A < 1, PVs/PVd ≥ 1), pseudonormal pattern (EDT 160–200 ms, IVRT < 90 ms, E/A 1–1.5, PVs/PVd < 1) and restrictive pattern (EDT < 160 ms, IVRT < 70 ms, E/A > 1.5, PVs/PVd < 1) [13].

BNP was measured with immunoassay method. CEA, AFP, CA 15–3 and CA 19–9 were measured with electrochemiluminescence immunoassay on Roche Modular E170. CA-125 was measured with quantitative immunoassay technology.

Comparisons of tumour markers and BNP between the study groups were performed by analysis of variance (ANOVA). Correlation between quantitative variables was assessed by Spearman’s correlation coefficient. Change in BNP and tumour markers after the follow-
Table 1
Characteristics of the patients according to the amount of fluid.

<table>
<thead>
<tr>
<th></th>
<th>Small</th>
<th>Moderate</th>
<th>Large</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>44 (23/21)</td>
<td>51 (24/27)</td>
<td>53 (28/25)</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.5±19.5</td>
<td>55.1±13.9</td>
<td>59.1±15.7</td>
<td>NS</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (%)</td>
<td>65.2±32.4</td>
<td>83.6±37.9</td>
<td>98.7±64.7</td>
<td>NS</td>
</tr>
<tr>
<td>WBC ×1000 (×/mm³)</td>
<td>17.4±18.3</td>
<td>23.6±21.6</td>
<td>20.5±19.7</td>
<td>NS</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>9.5±9.4</td>
<td>10.5±9.5</td>
<td>9.2±6.9</td>
<td>NS</td>
</tr>
<tr>
<td>LDH (u/l)</td>
<td>247.3±79.9</td>
<td>354.1±193.6</td>
<td>351.3±180.4</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of hospitalization (days)</td>
<td>14.3±9.4</td>
<td>21.5±11.3</td>
<td>19.7±7.4</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2
The distribution of BNP and tumour markers according to the fluid level.

<table>
<thead>
<tr>
<th></th>
<th>Small</th>
<th>Moderate</th>
<th>Large</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA (ng/ml)</td>
<td>4.3±6.1</td>
<td>2.3±2.1</td>
<td>3.1±4.6</td>
<td>3.7±3.2</td>
<td>NS</td>
</tr>
<tr>
<td>AFP (IU/ml)</td>
<td>1.3±0.6</td>
<td>1.8±0.8</td>
<td>1.9±1.4</td>
<td>1.7±1.2</td>
<td>NS</td>
</tr>
<tr>
<td>CA 15-3 (U/ml)</td>
<td>21.9±12</td>
<td>26.5±25.7</td>
<td>19.7±25.1</td>
<td>22±15.2</td>
<td>NS</td>
</tr>
<tr>
<td>CA 19-9 (U/ml)</td>
<td>25.2±29.1</td>
<td>22.7±27.4</td>
<td>20.9±25.8</td>
<td>23.5±17.3</td>
<td>NS</td>
</tr>
<tr>
<td>CA-125 (U/ml)*</td>
<td>55.4±42.6</td>
<td>54.1±41.4</td>
<td>97.6±70.2</td>
<td>32.7±16.7</td>
<td>0.005</td>
</tr>
<tr>
<td>BNP (pg/ml)*</td>
<td>17.5±9.4</td>
<td>22.7±11.4</td>
<td>179.6±89.3</td>
<td>17.1±15.3</td>
<td>0.038</td>
</tr>
</tbody>
</table>

NSAI; non-streoidal anti-inflammatory drug, RA; right atrium, RV; right ventricule, EF; left ventricular ejection fraction, E; mitral valve diastolic E wave, A; mitral valve diastolic A wave, LVDD; left ventricule end diastolic dimention, WBC; white blood cell, CRP; C-reactive protein, LDH; lactate dehydrogenase enzyme.

There was statistical difference between large PE and other groups.

The distribution of BNP and CA-125 levels to the fluid amount.

![Fig. 1. The distribution of BNP and CA-125 levels to the fluid amount.](image)

Levels of BNP according to presence tamponade.

![Fig. 2. Levels of BNP according to presence tamponade.](image)

Changes of CA-125, BNP percentage of the patients during the follow-up period.

![Fig. 3. Changes of CA-125, BNP percentage of the patients during the follow-up period.](image)
125 is primarily used for detection and follow-up of ovarian tumours [14,15]. However, it may also be raised in a wide variety of non-malignant diseases [16,17]. In our study the level of CA-125 was elevated only in patients with large amount of fluid. Although mean CA-125 levels were similar among small and moderate PE groups, Spearman analysis revealed a significant positive correlation between CA-125 and size of fluid. However, presence of right atrial chamber collapse was not a determinant of increased CA-125 level. This study shows that CA-125 level is not a good predictor of the hemodynamic impact of non-malignant pericardial fluid. However, high levels of CA-125 can be predictive of high amount of fluid. Also, significant decline in CA-125 levels can suggest decrease in the amount of the fluid in the follow-up.

Our study also identified BNP as a marker for large fluid collection and hemodynamic compromise. In a study, increased NT-proBNP levels in patients with cardiac tamponade were detected compared to patients without this finding [18]. It is well known that pericardial diseases lead to diastolic dysfunction [19]. Fernandes et al. reported that NT-proBNP was increased in pericardial diseases and was associated with diastolic dysfunction. However, in this study, the relation between NT-proBNP levels and PE severity was not shown [20]. In our study, in some patients with hemodynamic compromise BNP levels were very low. Also low BNP levels can be detected in patients with heart failure. This could be due to many factors such as age, gender, obesity, extracardiac secretion of natriuretic peptides, and decreased clearance of natriuretic peptides due to impaired kidney function [21,22].

In conclusion, both CA-125 and BNP levels correlate with the amount of pericardial fluid and decrease after resolution of pericardial fluid. High CA-125 level does not indicate hemodynamic compromise whereas a high level of BNP may indicate tamponade.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [23].

References