ON THE BLOOD PROTEIN PATTERN IN PATIENTS SUFFERING FROM RHEUMATIC VALVULAR HEART DISEASE, WITH CONGESTIVE HEART FAILURE

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There exists no unanimity in the literature on the changes of blood protein components in rheumatic valvular heart disease in the stage of congestive heart failure. For example, while A. Nizov (after 6) assumes that cardiac insufficiency does not induce any changes, T. Zsoter and J. Pinter (after 6) report an uniform increase in the values of the globulin fractions also in the absence of active rheumocarditis. Other authors have established only an increase in gamma globulins or an increase in gamma and alpha 1 globulins (4), the increase of alpha 2 being ascribed to the active rheumatic process. In this country Todorov et al. (8) have found increased gamma globulins separately (more often) or in combination with increased alpha 2 globulins (more seldom) as a sign of activity of the rheumatic process with the advent of congestive heart failure. The same is established also by Trofimova (9). Tomov et al. (7) point out that the separate increase of alpha 1 or in combination with increase in the alpha 2 and gamma globulins represents a characteristic feature.

Based on these presumptions we set ourselves the task to follow up the changes in the blood protein components with regard to the degree of decompensation and the value of these changes for the diagnosis of active rheumocarditis.

Method and material

Our investigation covers 100 patients suffering from rheumatic valvular heart disease, of which 30 with congestive heart failure I grade, 30 with II grade and 40 with III grade. In the latter group are included 15 patients who later on died with severe congestive heart failure. The following examinations were performed: total protein, protein fractions, flocculation tests (Weltmann’s test, MacLagan’s thymol turbidity test, cadmium test of Wurmann-Wunderly, fibrinogen, C-reactive protein and ESR). The activity of the rheumatic process was evaluated by the ESR, the temperature, the leucocyte count and in deceased patients by the postmortem gros and microscopic findings. Total protein was determined after Kingsly, serum protein fractions by paper electrophoresis, using a bath for horizontal electrophoresis, veronal puffer and staining of the paper strips with bromphenolblau and 10% acetic acid. Five fractions are usually obtained after this technique. ESR was determined after Westergreen’s method, fibrinogen after the biuretic method, C-reactive
protein and flocculation tests after the standard methods. Normal values of the tests were admitted as follows: total protein — 6—8 gr%, albumin 48—65 relative percentage, alpha 1 globulin — 2,8—6,4%, alpha 2 — 4—13%, beta — 7—17%, gamma globulin — 14—26%, Weltmann — VI—VII test tubes, MacLagan's test — 0—40 U, fibrinogen — 400 mg%.

The patients were subjected to dynamic investigations during treatment, many of them repeatedly.

Elaboration and discussion of the material

The amount of total protein is shown on Table 1.

<table>
<thead>
<tr>
<th>Decompensation</th>
<th>Normalproteinemia</th>
<th>Hypoproteinemia</th>
<th>Hyperproteinemia</th>
<th>Mean values</th>
</tr>
</thead>
<tbody>
<tr>
<td>I grade</td>
<td>86,6%</td>
<td>10,5%</td>
<td>3,36%</td>
<td>7,3%</td>
</tr>
<tr>
<td>II grade</td>
<td>73,3%</td>
<td>23,3%</td>
<td>3,35%</td>
<td>6,8%</td>
</tr>
<tr>
<td>III grade</td>
<td>72,5%</td>
<td>25%</td>
<td>2,5%</td>
<td>6,6%</td>
</tr>
</tbody>
</table>

From the table it becomes evident that with the advance of congestive heart failure the number of hyperproteinemiac patients increases. In all patients with hyperproteinemia a strongly active rheumocarditis is present. Subsidence of rheumatic activity leads to the correction of hyperproteinemia.

The mean values of the protein fractions in the different groups are shown on Table 2.

<table>
<thead>
<tr>
<th>Decompensation</th>
<th>Albumins</th>
<th>Alpha 1 globulins</th>
<th>Alpha 2 globulins</th>
<th>Beta globulins</th>
<th>Gamma globulins</th>
</tr>
</thead>
<tbody>
<tr>
<td>I grade</td>
<td>45</td>
<td>8,9</td>
<td>12,9</td>
<td>12,4</td>
<td>21,8</td>
</tr>
<tr>
<td>II grade</td>
<td>43,5</td>
<td>8,6</td>
<td>11,7</td>
<td>14,4</td>
<td>21,8</td>
</tr>
<tr>
<td>III grade</td>
<td>42,2</td>
<td>7,3</td>
<td>11,5</td>
<td>14,6</td>
<td>24</td>
</tr>
<tr>
<td>Normal values</td>
<td>46—65</td>
<td>2,8—6,4</td>
<td>4—13</td>
<td>7—17</td>
<td>14—26</td>
</tr>
</tbody>
</table>

From the table a clear tendency is evident toward a gradual decrease of albumin values with the increase in the severity of congestive heart failure.

The mean values only for alpha 1 globulins among all the rest of the components of the electrophoregram increase above the upper limit of normal values even in patients with IIIrd grade congestive heart failure. Hyperalphaglobulinemia is established in patients with I grade congestive heart failure in 88%, with II grade — in 66,6% and with III grade — in 61%.

The same tendency is observed also in alpha 2 globulins although their mean values reach the upper limit of the normal only in the I group.
The reverse tendency is observed in the components of the right half of the electrophoregram. The mean values for the beta-globulins although entirely within normal limits display in all groups a clear tendency toward a mild increase. This is even more marked as regards gammaglobulins. Hypergammaglobulinemia is not so common — in 24% of the patients with I grade decompensation, in 29% — with II grade, in 31% — with III grade, and an increase as far as the mean values are concerned in 40% of the patients belonging to I and II groups and in 50% of those of the III group.

With the aggravation of congestive heart failure a clear tendency is also established for suppressing the ESR values in active rheumocarditis toward the mean of bordering values (5). High values for ESR and strongly positive electrophoretic fractions are associated more frequently with complications (bronchopneumonia, infarction etc.) rather than with marked activation of rheumocarditis.

The C-reactive protein values give also a diverse picture. In active rheumocarditis with or without congestive heart failure the values run parallel to those of alpha and of ESR. In severe congestive heart failure mild or accelerated positive values are established also in patients with negative necropsic findings for active rheumocarditis.

The mean values of Weltmann's, MacLagan's and fibrinogen tests are presented on Table 3.

<table>
<thead>
<tr>
<th>Decompensation</th>
<th>Weltmann</th>
<th>MacLagan</th>
<th>Fibrinogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>I grade</td>
<td>4,3</td>
<td>27,2</td>
<td>420</td>
</tr>
<tr>
<td>II grade</td>
<td>6</td>
<td>38</td>
<td>430</td>
</tr>
<tr>
<td>III grade</td>
<td>6</td>
<td>39</td>
<td>360</td>
</tr>
</tbody>
</table>

With the extension of the degree of decompensation the mean values of the flocculation tests are increased. The large interval of variations in Weltmann's test which in some patients from the I group ranges from 0—1—2 to 6—7 test tubes is replaced in patients with advanced decompensation by a considerably narrowed range — usually between 5 and 7½ test tubes.

As regards the values of MacLagan's test complex relations are also observed. With elevated ESR and Weltmann's test in most of the cases increased values are established. Elevated ESR, shortened Weltmann and normal or increased values for MacLagan's test in cases with advanced congestive heart failure are always associated with some kind of complication — infarction, bronchopneumonia etc. The high values therefore as well as the normal values of the test which are indicative of an active inflammatory process may be however of a different nature.

The cadmium test did not justify the expectations, created by the existing reports in literature (10). This test turned out to be a coarse and capricious one. It is positive only in 2 cases in the I group, in 7 of the II group and in 9 in the III group, mainly in patients who display a
markedly active rheumatic disease and increased values for alpha 1. It is positive also in patients with bordering values for the ESR.

The same relations were established also with regard to fibrinogen. It appeared positive only in the most acute phase of the inflammatory process (3). Its values normalize earlier as compared with the values of all the remaining indices.

No substantial relation was established between the values of the flocculation tests themselves and those of the electrophoretic components.

Conclusions

In general the results of our studies coincide with those reported in the literature, particularly in this country (19, 22). For that reason we shall discuss some problems on which controversy exists or no sufficient attention has been paid to.

The decrease of albumins and the increase of alpha 1 globulins independently or simultaneously with alpha 2 appear to be the most constant features of inflammatory activity in all grades of congestive heart failure; these changes are established also in the absence of rheumocardiitis.

With the aggravation of congestive heart failure an increase in beta and gamma globulins is added although not always, particularly of the gamma globulins and of the values of the flocculation tests. A continuous tendency is thus shaped up towards a decrease in the values of proteins, alpha globulins, fibrinogen and the ESR (the values of the components of the acute syndrome) and an increase in the values of gamma and partly of beta globulins and the flocculation tests (components of the chronic syndrome). This variation of the values surpasses the limits of the maximal normal values as regards the mean values of the albumins and the alpha 1 globulins.

The correlation which exists between the values of the individual components during a state of compensation are considerably disturbed with the aggravation of congestive heart failure.

With the occurrence of these changes in the blood protein picture of significance are not only the character and the degree of the inflammatory process as this is in compensated active rheumocardiitis. A new factor comes forth — the change, which occurs in the blood and in the internal organs under the influence of congestive heart failure: congestive albuminuria, formation of oedema, disorders in the protein synthesis, proliferative mesenchymmal activation in the visceral organs, particularly in the liver and the lungs — organs rich in RES elements. the occurrence of infarction, bronchopneumonia, thrombophlebitis etc.

With these changes may be explained the two basic types of clinical manifestations which we observe in patients with advanced congestive heart failure, owing to inconsistency between the values of the tests and the degree of activity of the rheumatic process.

On the one hand a picture of "apparently attenuated rheumocardiitis" with bordering or moderately increased values of the tests, particularly of ESR in the presence of severely active rheumocardiitis, even under the
form of pancarditis. This pattern is established mainly in patients with congestion, predominantly in the systemic blood circulation, associated with marked oedema and cyanosis.

In other cases a picture of “false rheumocarditis”, bordering and moderately positive values of the tests in the absence or insufficient pathologic data for rheumocarditis are present. This picture is established in some patients with exquisite mitral stenosis and severe congestion in the pulmonary circulation. The explanation should be searched for in the severe changes which occur in the lungs under the influence of the continuous congestion and in the conditions created for the appearance of clinically inapparent complications — microinfarctions, small broncho-pneumonic foci etc.

These observations give ground to assume that the changes in the blood protein picture in severe congestive heart failure are nonspecific by nature. They occur under the influence of the rheumatic process as well as the dysproteinemia due to the changes which take place in the organism as a result of severe congestive heart failure. For that reason, their evaluation as evidence of active rheumocarditis should be done with caution.

REFERENCES