Paper Electrophoretic Studies of Glycoproteins in Rheumatic Fever

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The classic report by Longworth et al. (1) in 1939 on serum protein fractionation by free electrophoresis included rheumatic fever as one of the febrile diseases that had been studied. Employing the same medium, Rutstein et al. (2) followed this work with a more detailed study of serum proteins in rheumatic fever and noted changes in total protein and gamma globulin concentrations.

Shetlar and co-workers (3–5) employed chemical analytic technics in studies of serum polysaccharides in rheumatoid diseases and found significant changes in these conditions.

In the comprehensive study of Kuhns and Crittenden (6), involving paper electrophoretic fractionation of serum proteins, glycoproteins, and lipoproteins in rheumatoid arthritis and associated rheumatoid diseases, a similarity was noted in the serum-glycoprotein patterns of rheumatoid arthritis and rheumatic fever.

Subsequent work by Salt (7), Sunderman and Sunderman (8), and Stidworthy et al. (9) with serum protein and glycoprotein fractionation has resulted in the consensus that, in rheumatoid arthritis, serum proteins show decreased albumin with increased alpha-2 and gamma globulin fractions. Glycoprotein changes in rheumatoid arthritis and rheumatic fever were most marked by increased alpha-1 and alpha-2 globulins (9).

A review of the studies to date shows that most investigations have been focused on serum-protein changes encountered in rheumatoid arthritis and allied diseases. Consequently, it was felt that a study of serum glycoproteins in individuals diagnosed as having rheumatic fever might supply additional information of interest on the subject.

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This presentation concerns itself with a paper electrophoretic study of serum-glycoprotein patterns in patients with rheumatic fever.

MATERIALS AND METHODS

Studies of glycoprotein patterns in patients with rheumatic fever were made on individuals who had been clinically diagnosed as having this disease, or who gave evidence of having carditis, as determined by their clinicians.

Normal individuals, including laboratory personnel, were utilized in procurement of statistical data for the normal control group.

The glycoproteins were fractionated by paper electrophoresis at 24°C with the use of a barbital buffer at pH 8.6 with ionic strength of 0.075. Serum samples of 0.030 ml. were applied by a striper and run at 6.8 ma. for 16-18 hours in a Durrum-type cell.

Integration of paper strips, after staining by the method of Kiöw and Gronwall (10), was accomplished on the Spinco Analytrol, using the B-3 cam with green and neutral filters (11).

Total glycoproteins were determined by visual comparison of the strips with a control strip of normal concentration of glycoprotein fractionated concurrently and graded as normal or increased. All specimens were run in duplicate, and reproduction was within 1.5 per cent limits.

Antistreptolysin-O titers were determined by the method of Rantz and Randall (12). Mucoproteins were determined by the method of de la Huerga (13) and C-reactive protein by the method of Anderson and McCarty (14).

RESULTS

Table 1 and Fig. 1 illustrate the comparison of glycoprotein studies in normal subjects and in patients having rheumatic fever.

The mean values of the normal group correlate well with the following mean values compiled from 9 references by Ehrmantraut (15): albumin, 11.6; alpha-1, 17.4; alpha-2, 29.0; beta, 25.1; and gamma, 17.0 per cent, respectively.

Comparison of the means of the normal and rheumatic fever groups (Table 1) shows a significant increase in the alpha-2 glycoprotein fraction, whereas alpha-1 and beta components show moderate decrease in concentration. The increase in the alpha-2 fraction in the patients with rheumatic fever generally exceeds the standard deviation of the normal group with a range of 5-20 per cent from the normal mean.
Table 1. Tabulation of Studies Conducted on Individuals with Clinical Diagnosis of Rheumatic Fever

<table>
<thead>
<tr>
<th>No.</th>
<th>Age—Sex</th>
<th>Albumin</th>
<th>α1</th>
<th>α2</th>
<th>β</th>
<th>γ</th>
<th>AS-O titer</th>
<th>Muco-protein in mg./100 ml.</th>
<th>CRP</th>
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<tbody>
<tr>
<td>1</td>
<td>A-10-F</td>
<td>3.5</td>
<td>16.0</td>
<td>44.0</td>
<td>23.0</td>
<td>13.5</td>
<td>166</td>
<td>130</td>
<td>+2</td>
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<tr>
<td>2</td>
<td>B-7-F</td>
<td>8.5</td>
<td>11.5</td>
<td>35.5</td>
<td>25.0</td>
<td>19.5</td>
<td>333</td>
<td>170</td>
<td>+2</td>
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<tr>
<td>3</td>
<td>C-8-F-1</td>
<td>24.5</td>
<td>10.0</td>
<td>24.5</td>
<td>17.5</td>
<td>21.0</td>
<td>833</td>
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<td>+1</td>
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<tr>
<td>4</td>
<td>D-10-M</td>
<td>7.5</td>
<td>14.5</td>
<td>48.0</td>
<td>13.5</td>
<td>16.5</td>
<td>833</td>
<td>180</td>
<td>+3</td>
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<tr>
<td>5</td>
<td>E-8-M</td>
<td>9.0</td>
<td>13.0</td>
<td>40.0</td>
<td>21.0</td>
<td>12.0</td>
<td>833</td>
<td></td>
<td>+3</td>
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<tr>
<td>6</td>
<td>F-10-M-1</td>
<td>9.5</td>
<td>15.5</td>
<td>35.5</td>
<td>25.0</td>
<td>15.0</td>
<td>1250</td>
<td>100</td>
<td>+1</td>
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<tr>
<td>7</td>
<td>G-10-F</td>
<td>11.0</td>
<td>16.0</td>
<td>35.5</td>
<td>27.5</td>
<td>11.0</td>
<td>1250</td>
<td>110</td>
<td>+1</td>
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<tr>
<td>Arith. mean of B.F. group</td>
<td>9.4</td>
<td>13.5</td>
<td>40.7</td>
<td>21.8</td>
<td>14.7</td>
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<tr>
<td>S.D. in % G.P.</td>
<td>± 3.7</td>
<td>± 3.4</td>
<td>± 5.7</td>
<td>± 6.8</td>
<td>± 3.0</td>
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<tr>
<td>Arith. mean of normals (31)</td>
<td>11.0</td>
<td>17.0</td>
<td>30.5</td>
<td>25.5</td>
<td>16.0</td>
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<td>S.D. in % G.P.</td>
<td>± 3.1</td>
<td>± 1.4</td>
<td>± 3.2</td>
<td>± 2.7</td>
<td>± 2.3</td>
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<tr>
<td>Diff. between means in %</td>
<td>− 1.6</td>
<td>− 3.5</td>
<td>+10.2</td>
<td>− 2.7</td>
<td>− 1.3</td>
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*C-8-F-1 diagnosed glomerulonephritis; not included in tabulations.

Total glycoprotein concentration was rated as increased in all cases of rheumatic fever by the method previously noted. The amount of increase can be seen by comparison of the tracings in Fig. 1.

DISCUSSION

Figure 1 shows densitometer tracings of 4 representative glycoprotein fractionations. The patient with rheumatoid arthritis had a latex fixation titer of 1:80 and a serum-protein distribution as follows: albumin, 48.0; alpha-1, 5.0; alpha-2, 9.5; beta, 13.5; and gamma, 24.0 per cent, respectively. The total glycoprotein and glycoprotein components did not show any significant elevations.

The general pattern encountered in patients with rheumatic fever showed increased total glycoproteins and a marked increase in the alpha-2 component.

Alpha-1 and beta fractions generally showed a decrease in con-
Fig. 1. Comparison of glycoprotein patterns of normal subjects and patients with arthritis and rheumatic fever.
centration, which differs somewhat from the increase in alpha-1 and alpha-2 glycoprotein correlated with rheumatoid arthritis (9).

Although not pertinent to this study, mucoprotein and C-reactive protein results are noted. A good correlation was noted between the increase in alpha-2 glycoprotein and generally increased levels in both tests.

The distribution of Antistreptolysin-O titers encountered in the cases of rheumatic fever ranged from 166–1250 Todd units, emphasizing the fact that all titers may be significant in consideration of the potentialities of rheumatic fever.

A study covering the correlation of glycoprotein patterns with Antistreptolysin-O titers is in preparation for publication.

In tabulations C-8-F-1 and C-8-F-2, two varying glycoprotein patterns were encountered. The patient originally had been diagnosed and treated for acute glomerulonephritis. A repeat study 45 days later showed a change in the glycoprotein patterns, and the patient was hospitalized with carditis. It is not known whether the original glycoprotein pattern was indicative of the glomerulonephritis syndrome, because the number of available cases was insufficient.

SUMMARY

Studies of serum glycoproteins by paper electrophoresis in rheumatic fever showed the following: Total glycoproteins were generally increased in concentration, the alpha-2 glycoprotein fraction showed moderate to marked increases in value, and alpha-1 and beta glycoprotein components generally showed moderately decreased concentrations.

REFERENCES