Prognostic significance of specific proteins and immunoglobulins in sero positive Rheumatoid Arthritis patients.

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Abstract:

Background: Increased levels of specific proteins and Immunoglobulines have been detected in serum from patient with rheumatoid arthritis (RA).

Objective: To clarify the clinical significance of specific serum proteins and Immunoglobulin in RA.

Methods: Forty- two patients with sero-positive rheumatoid factor (group 1 and 2 according to disease activity progresses) and twenty age- matched healthy subjects were included in the study. Serum total proteins, Protein electrophoresis and Immunoglobulin level were evaluated.

Results: Acute phase reactants in RA patients showed a significant increase in comparison to healthy subjects ($P < 0.001$). There was a significant difference in the levels of α- globulins, γ-Nglobulins, IgG and IgM in group 1 as compared to group 2.

Conclusion: The prognostic value of serum specific proteins and Immunoglobulin in patients with RA is high, and can provide some help in predicting the outcome of joint inflammation.

Key words: rheumatoid arthritis, specific proteins immunoglobulin.

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Introduction:

Rheumatoid arthritis (RA) is a chronic, system disease characterized by recurrent inflammations of the diarthrodial joints and related structures. (1) There are often a variety of non- articular features, including subcutaneous nodules, radiographic articular erosions, and circulating antiglobulins (rheumatoid factor). (2) RA is characterized by periods of remission and exacerbation of disease activity. Mortality rates are higher with severe disease. The cause of RA is unknown.

However, it is thought that particularly in predisposed individuals, several etiologies are possible; infections such as Epstein-Barr, some environmental antigenic trigger probably a virus leads to the formations of an abnormal immunoglobulin G (IgG).

RA is characterized by the presence of autoantibodies against this abnormal IgG. The autoantibodies to this altered IgG are termed rheumatoid factors, and they combine with IgG to form immune complexes that deposit in the joints, blood vessels and pleura. Complement is activated and an inflammatory response results. (3) Metabolic and biochemical abnormalities may play a part in the cause or expression of the disease, but their contribution is entirely speculative. (4) This prospective study aimed to evaluate the prognostic significance of specific proteins and Immunoglobulin in serum in the radiologically detected knee joint destruction in patients with (RA).

Materials and Methods:

Blood specimens were obtained from 42 patients who met the American Rheumatism Association criteria for Classical or definite RA. (5) Of these patients, 27 (64 %) were females and 15 (36 %) were males, their ages ranged from 30 to 60 (mean 45) years.

The patients had been afflicted with RA for an average of 3 years. All patients were latex Fixation test positive, and regarded as seropositive if Waaler-Rose reading in the serum was 32 or more. The specimens were drawn in plain glass tubes and allowed to clot for 30 minutes followed by centrifugation and serum stored frozen until required for analysis. Hemolysed samples were discarded. A matching group of 20 healthy subjects, 12 females and 8 males whose ages ranged from 30 – 60 (mean 45) years.

Laboratory analyses were carried out using Beckman Microzone electrophoresis and scanning densitometer (Beckman Instruments Inc.Fullerton CA 92643) for protein electrophoresis. Estimation of serum Immunoglobulin levels was carried out by single radial immunodiffussion method of Mancini. (6) Supplied by Immunodiagnostika, Vienna/ Austria. Samples were assayed in duplicate. Inter-assay variance ranged from 5-7% and intra-assay variance was less than 5%. The stage of radiological joint destruction was evaluated by Larsen's method. (7)

The patients were divided into two groups: Group 1 with progress of radiologically detected destruction in the knee joints: n= 17. Group 2 without progress of radiologically detected destruction in the knee joints: n= 25. All results were expressed as mean ± SD, Student's test was used in statistical analysis

Results

Data of serum total proteins, protein electrophoresis and Immunoglobulin of 42 patients with RA were compared with healthy subjects in Table 1. Serum protein electrophoresis showed an increase in acute phase reactants (α- globulins and γ- globulins in RA patients in respect to controls ($P < 0.001$). No significant abnormality was observed in the remaining fractions.

The levels of IgG and Ig M showed a significant increase in RA patients ($P < 0.001$). No significant difference in the level of IgA was noted between the patients and controls.

In Table 2, group 1 presented with a significant increase in α- globulins, γ- globulins IgG and IgM as compared with healthy subjects, ($P < 0.005$, $P < 0.005$, $P < 0.001$ and $P < 0.002$) respectively.

The level of albumin was decreased as compared with healthy subjects ($P < 0.005$). In group 2 no significant difference was observed in the levels of serum protein electrophoresis and Immunoglobulin as compared to controls. There was a significant difference in the levels of α- globulins, γ- globulins, IgG and IgM in group 1 as compared with group 2, ($P < 0.001$, $P < 0.002$, $P < 0.001$ and $P < 0.005$) respectively.

Table 1: serum total protein, protein electrophoresis and immunoglobulin levels of rheumatoid arthritis patients

	Healthy subjects N = 20	**Patients N = 42**
Total proteins (g %)	7.3 + 0.2	7.6 + 0.4
Albumin (g %)	4.0 + 0.1	3.5 + 0.4
Globulin (g %)	3.3 + 0.3	4.1 + 0.5
Alpha-1 (g %)	0.32 + 0.3	0.4 + 0.3
Alpha-2 (g %)	0.7 + 0.2	0.9 + 0.3
Beta (g %)	0.98 + 0.2	1.0 + 0.3
Gamma (g %)	1.3 + 0.2	1.8 + 0.5
Immunoglobulin	1700 + 90	2259 + 127*
IgG (mg %)	187 + 28	205 + 82
IgA (mg %)	124 + 10	186 + 34
IgM (mg %)		

* As compared to the control group: $p<0.001$.

Table 2: serum total protein, protein electrophoresis and immunoglobulin levels in the two groups of patients and in the healthy subjects group

	Healthy subjects N = 20	Group 1 N = 17	Group 2 N = 25
Total proteins (g %)	7.3 + 0.2	7.7 + 0.3	7.5 + 0.2
Albumin (g %)	4.0 + 0.1	3.3 + 0.4	3.8 + 0.3
Globulin (g %)	3.3 + 0.3	4.5 + 0.4	3.8 + 0.4
Alpha-1 (g %)	0.32 + 0.3	0.46 + 0.5	0.38 + 0.2
Alpha-2 (g %)	0.7 + 0.2	1.0 + 0.3	0.8 + 0.3
Beta (g %)	0.98 + 0.2	1.05 + 0.3	0.97 + 0.1
Gamma (g %)	1.3 + 0.2	2.05 + 0.2	1.2 + 0.2
Immunoglobulin			
IgG (mg %)	1700 + 90	2712 + 110*	1810 + 90
IgA (mg %)	187 + 28	218 + 33	192 + 71
IgM (mg %)	124 + 10	226 + 19*	144 + 31

* As compared to the control group: $p<0.001$.

Discussion:

Although no single laboratory test is conclusive, several findings are helpful in diagnosing (RA) in conjunction with the history and physical examination.

Serum protein electrophoresis and immunoglobulin analysis are common, but little is known about the prognostic significance of these in radiologically detectable destruction of joints. [8, 9]

Abnormalities in the elecrtophoretic patterns of serum proteins in RA have been described by various workers. [10, 11]

An increase in the relative concentration of α- globulins, γ- globulins and lowering of albumin have been observed and have associated consistently with the activity of the disease. [12]

The changes in the protein fractions were correlated with the clinical and laboratory indications of the degree of severity of arthritis. It is worth noting that a significant difference was observed in the mean levels of α- globulins, γ- globulins, IgM and IgG in group 1 as compared with healthy subjects. Acute phase response may indicate severe joint inflammation which may lead to joint destruction. [4, 13]

Monocytes isolated from patients with RA have different capabilities for inducing alteration of acute phase proteins in vitro. [14]

Some workers reported that increase levels of IgG and IgM in rheumatoid arthritis patients was due to the presence of a persistent antigenic stimulation and associated with higher incidence of severe radiological changes. [15] The purpose of this study was however, to elucidate whether the parameters of protein and immunoglobulin can provide some help in predicting the outcome of joint inflammation and may help to explain the different effects of different drugs on the evolution of x-ray changes. [16]

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