Elevated Levels of Serum β-Acetylglucosaminidase in Some Patients with Rheumatoid Arthritis[1] (37031)

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In an earlier report from this laboratory (1) we have shown that the activities of β-acetylglucosaminidase and arylsulfatase A are often increased in the serum of patients with various inflammatory disorders of muscle and connective tissue. It has been found in active polymyositis and dermatomyositis, in systemic lupus erythematosus and in a few patients with certain other systemic collagen diseases. In the present study we have extended our previous observations and found elevated serum levels of these lysosomal enzymes particularly β-acetylglucosaminidase in some patients with rheumatoid arthritis.

Materials and Methods. The blood specimens were obtained from 83 normal individuals and 65 patients with rheumatoid arthritis, 5 with osteoarthritis, 4 with psoriatic arthritis and 10 with various other rheumatoid disorders. Information was obtained about the duration of the disease, drug therapy and the extent and activity of disease. The patients were under treatment with the usual antirheumatic drugs including corticosteroids. Routine laboratory data including erythrocyte sedimentation rate (ESR), total leukocyte count and serum levels of rheumatoid factor, albumin, globulin, bilirubin and also of alkaline phosphatase were obtained in all cases.

β-Acetylglucosaminidase, arylsulfatase A and creatine kinase were assayed as described previously (1).

Results. In normal controls serum β-acetylglucosaminidase activity was found to be 11.0 ± 0.23 μmoles/l/min (Table I). In 65 patients with rheumatoid arthritis the enzyme activity was 12.2 ± 0.52 μmoles/liter/min and the difference was significant ($p < 0.02$). In 13 instances (20%), the enzyme activity was higher than normal limit. Five patients with osteoarthritis, 4 with psoriatic arthritis, 4 with Reiter's disease and 6 with other related disorders showed values in the normal range.

The activity of arylsulfatase A in normal sera was 16.5 ± 0.53 μmoles/liter/hr. In 65 patients with rheumatoid arthritis the enzyme activity was found to be 16.7 ± 1.11 μmoles/liter/hr. The mean difference was, however, not significant. In 10 instances (15%) the enzyme activity was above normal limit. The enzyme activity was within the range of normal in osteoarthritis, psoriatic arthritis and in a few other related disorders.

Serum creatine kinase level was slightly decreased in the patients with rheumatoid arthritis. Only one patient with muscle weakness showed elevated serum activity (236 μmoles/liter/min).

Discussion. The present study has shown that serum levels of certain lysosomal enzymes especially β-acetylglucosaminidase are moderately elevated in 20% of the patients with rheumatoid arthritis. Some correlation was found between the increased serum β-acetylglucosaminidase activity and the severity of disease. No direct correlation was found between high serum β-acetylglucosaminidase and the ESR, the level of rheumatoid factor or the total leukocyte count.

The pathogenesis of joint inflammation in rheumatoid arthritis is not known. However, it has been suggested that at one stage of inflammation, a disruption of lysosomes occurs in the synovial lining cells and in inflammatory cells in the synovial membrane

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TABLE I. Serum Enzyme Levels in Patients with Rheumatoid Arthritis.[a]

Diagnosis	No. of cases	β-Acetylglucosaminidase (μmoles/liter/min)	Arylsulfatase A (μmoles/liter/hr)	Creatine kinase (μmoles/liter/min)
Normal[b]	83	11.0 ± 0.23	16.5 ± 0.53	43 ± 1.32
Rheumatoid arthritis	65	12.2 ± 0.52[c]	16.7 ± 1.11[d]	26 ± 3.63[c]
Osteoarthritis	5	11.4 ± 0.78	12.5 ± 1.15	36 ± 0.75
Psoriatic arthritis	4	9.3 ± 0.92	15.5 ± 2.01	20 ± 2.29
Miscellaneous disorders[e]	10	12.9 ± 0.70	14.2 ± 1.68	34 ± 4.75

[a] All results are expressed as mean ± standard error.

[b] Normal range of values were established in a previous study (1).

[c] Significantly different from normal by the t test ($p < .02$ and $p < .001$, respectively).

[d] Not significant.

[e] Includes these patients: Reiter's disease, 4; gout, 2; myalgias of unknown cause, 2; idiopathic asthma, 1; arthralgias, 1.

and synovial cavity resulting in the release of lysosomal acid hydrolases and the subsequent degradation of joint cartilage (2, 3). Lysosomes from various sources are shown to contain a number of glycosidases which have the ability to degrade hyaluronic acid by releasing *N*-acetylglucosamine (4). Increased activity of β-acetylglucosaminidase has been observed in inflamed synovium (5) as well as in the synovial fluid (6) of patients with rheumatoid arthritis. Raised levels of collagenase (7, 8), acid cathepsin (9) and acid phosphatase (10) in rheumatoid synovium have also been reported. It appears, therefore, that elevated levels of serum β-acetylglucosaminidase probably reflect increased release or abnormal fragility of lysosomes present in the inflamed tissues.

Increased activity of a number of lysosomal hydrolases in the serum of patients with rheumatoid arthritis has been observed by various investigators. Pruzanski, Saito and Ogryzlo (11) found high lysozyme activity in about 35% of patients. Caygill and Pitkeathly (6) observed elevated acid phosphatase in a similar percentage of patients. These authors also measured β-acetylglucosaminidase in the serum of 19 patients and found normal values in all but one. The reason for this discrepancy is not clear.

The levels of commonly studied serum enzymes like the transaminases, aldolase and lactic dehydrogenase are usually normal in rheumatoid arthritis. However, one or more enzymes may be moderately elevated if a particular visceral organ is severely or acutely affected (12). In the present study serum creatine kinase has been found to be slightly decreased in this disorder. The 13 patients with high serum β-acetylglucosaminidase had no liver disease. In 3 out of 13 patients serum alkaline phosphatase was slightly above normal. High serum alkaline phosphatase in rheumatoid arthritis has been attributed to subtle liver involvement (13). Since serum β-acetylglucosaminidase has been found to be elevated in patients with liver disease, particularly acute or chronic hepatitis (14), liver involvement in rheumatoid arthritis could complicate this test. However, we did not find any correlation between the increased activity of serum alkaline phosphatase and that of β-acetylglucosaminidase. There were 6 patients in this series who had slightly elevated serum alkaline phosphatase and had normal β-acetylglucosaminidase.

It is known that the broad group of collagen-vascular disorders includes several distinguishable disease entities in which there is considerable overlap in clinical, immunological or pathological features. The results of this study and our previous findings (1) demonstrate that an elevated level of certain serum lysosomal hydrolases especially of β-acetylglucosaminidase is one biochemical feature which is common to several diseases of this group. These results showing elevated serum β-acetylglucosaminidase in a number of inflammatory disorders suggest that similar biochemical degradative processes are operative in this group of disorders.

Summary. Serum β-acetylglucosaminidase,

arylsulfase A and creatine kinase activities were measured in 65 patients with rheumatoid arthritis and 10 patients with related disorders. β-Acetylglucosaminidase and arylsulfatase A were increased in 20% and 15%, respectively, in serum samples from patients with rheumatoid arthritis. The increase in arylsulfatase A was, however, not significant. Serum creatine kinase was slightly decreased in rheumatoid arthritis. This study suggests a correlation between lysosomal enzymes in the inflamed tissues and serum β-acetylglucosaminidase activity.

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