Seromucoid in lupus erythematosus and scleroderma

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SYNOPSIS Seromucoid levels in blood of 50 normal men and in 63 cases of cutaneous collagen diseases were studied. There was a marked rise in the seromucoid level in cases of systemic lupus erythematosus and also a significant rise in scleroderma. This rise in seromucoid level may be a reflection of the degenerative connective tissue.

Seromucoid comprises a heterogenous fraction of the serum that is left in solution by perchloric acid and precipitated by phosphotungstic acid. This is identical with the plasma 'mucoprotein' of Winzler (1955) but distinct from the 'mucoprotein' of Meyer (1953), which is a hexosamine-rich protein-carbohydrate complex. The principal component is acidic L-l-glycoprotein, orosomucoid, which can be readily demonstrated by electrophoresis at pH 4.5. In addition, there is another acidic component with an isoelectric point below pH 4.5. These components are designated as M_1 and M_2 when separated by paper electrophoresis (Markham, Jacobs, and Fletcher, 1956). The importance of orosomucoid is further strengthened by the observation of Gross, Highberger, and Schmitt (1952) that long, spaced collagen fibrils could be precipitated by the addition of orosomucoid to the soluble collagen fraction from the rat tail tendon. This observation may indicate a possible inter-relationship between seromucoid and collagen fibrils. Dische, Danilczenko, and Zelmenis (1958) isolated a neutral mucopolysaccharide from the subcutaneous tissue and believe it to be related to the seromucoid fraction of the blood plasma.

In lupus erythematosus and scleroderma, the collagen content is constantly being diminished with a reciprocal rise in the hexosamine level (Panja, 1961). The close similarity of these hexosamine-containing substances (seromucoid) with those of the mucopolysaccharides of the ground substance may indicate a possibly significant alteration in the two cutaneous collagen diseases lupus erythematosus and scleroderma.

MATERIALS AND METHODS

Sera were collected from 63 cases of different cutaneous collagen disorders. The control samples were drawn from 50 blood donors.

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The quantitative estimation of seromucoid was performed by the turbidimetric method of De la Hueraga, Dubin, Kushner, Dyniewicz, and Popper (1956). Electrophoresis of the serum mucoprotein was carried out by the method of Markham *et al.* (1956) in citric acid phosphate buffer at pH 4.5. The strips were stained for protein with a solution of 0.1% bromophenol blue and 10% mercuric chloride in 95% alcohol (Wintrobe, 1956). The papers were stained differentially for polysaccharide component by the method of Köi and Grönwall (1952).

RESULTS

Quantitative estimations showed that the seromucoid level was significantly altered from the normal in all the disease groups (Table I). The alteration was most marked in systemic lupus erythematosus. The rise in the seromucoid level is significant in the other groups also.

TABLE I
SEROMUCOID LEVEL IN THE DIFFERENT GROUPS

	No. of Cases	Seromucoid Level (mg. %)
Normal	50	43.8 ± 17.1
Systemic lupus erythematosus	6	130.8 ± 40.6
Generalized discoid lupus erythematosus	24	73.5 ± 20.6
Localized discoid lupus erythematosus	18	70.5 ± 26.2
Scleroderma		
Morphoea	7	79.3 ± 25.6
Generalized	8	88.6 ± 24.6

The quantitative estimation was further corroborated by a paper electrophoretic study (Fig. 1). The seromucoids, due to the isoelectric point at pH 4.5, shows considerable migration towards the anode; albumin remained stationary and the globulins moved towards the cathode. The principal M_1 fraction (orosomucoid) was increased as was the minor M_2 component.

DISCUSSION

The seromucoid level was found to be remarkably

FIG. 1. Results of electrophoretic study in the groups described in Table I

constant (Stary 1957). Shetlar, Payne, Bullock, Patrick, Hellbaum, and Ishmael (1953), from the histochemical findings and seromuroid level, suggested a possible relationship between serum and tissue polysaccharide in rheumatic fever, rheumatoid arthritis, and systemic lupus erythematosus. They postulated that the mechanism was a result of tissue injury, tissue proliferation, or both. Winzler (1955) believed that this rise might be due to local synthesis and liberation of glycoproteins from the inflamed tissue in the plasma.

A rise in circulating serum hexosamine in all cases of lupus erythematosus was observed by Boas and Rerner (1951) and by Boas and Soffer (1951). Greenspan (1955), however, found a rise in 50% of lupus cases only.

The correlated rise in hexosamine-containing substance in serum and tissues may be interpreted as a reflection of the destructive process in the tissues (Seibert, Pfaff, and Seibert 1948), whose hypothesis was supported by the observations in different inflammatory, neoplastic, and degenerative diseases by Kelley, Good, and McQuarrie (1950), Fahey, McCoy, and Horbett (1958), and by Giles *et al.* (1958). The higher levels of seromucoids in cases

of systemic lupus erythematosus and in lesions with pronounced degenerative changes showed that it apparently furnished objective evidence of the state of activity of the disease process.

Thus rises in the circulating hexosamine-containing serum constituents are related to the destructive and/or proliferative changes occurring in the connective tissue ground substance. Panja (1961) observed a significant rise in the tissue hexosamine content in the cutaneous lesions of lupus and scleroderma. The seromuroid concentration in the plasma may be an indication of the tissue changes involved in these pathological entities involving similar components of the connective tissue. In the absence of a proliferative process histologically (Panja, 1961), the rise in seromuroid level in these cutaneous collagen diseases may be attributed to the destructive process of the connective tissue observed in these cases.

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