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Serum histidine in rheumatoid arthritis: a family study

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SUMMARY We have compared free serum histidine in patients with rheumatoid arthritis, their blood relatives, and their non-blood relatives. The hypohistidinaemia of rheumatoid arthritis is acquired with the disease and does not provide a biochemical marker of those at risk.

Free serum histidine levels are low in rheumatoid arthritis, a finding that appears to be unique to this disease.[1] Genetic factors, mediated by histocompatibility antigens, have been shown to be important in rheumatoid arthritis,[2] and since amino acid levels in the blood may also be determined genetically[3] it remains a possibility that a low serum histidine might be of value as a marker for determining those persons at risk of developing rheumatoid arthritis. The significantly lower serum histidine found in normal females[4] than in normal males supports this hypothesis, since rheumatoid arthritis is also more common in females.

We have therefore compared free serum histidine in patients with rheumatoid arthritis, their blood relatives, and their non-blood relatives, who acted as a control group. We have also examined the relationship of serum histidine to seropositivity for rheumatoid factor.

Subjects and methods

There were 28 patients with classical or definite rheumatoid arthritis (ARA criteria) and 29 blood relatives of whom 2 were sisters, 2 brothers, 9 daughters, 10 sons, 1 a mother, 2 nieces, 1 a nephew, and 2 grand-daughters. Seventeen non-blood relatives formed a control group of whom 13 were spouses, 1 a sister-in-law, 2 daughters-in-law, and 1 a son-in-law. A medical history was taken from each subject and rheumatoid factor (latex slide test and sheep cell agglutination test) measured. A clotted blood sample was taken and serum separated within 4 hours and frozen to −20°C. Histidine levels were measured by a spectrofluorometric method.[5] Student's *t* test was applied to the results.

In a further study of 79 patients with peripheral polyarthritis of rheumatoid type as defined by the criteria of the American Rheumatism Association the relationship between serum histidine and rheumatoid factor was investigated.

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Results

The mean free serum histidine was significantly lower in the rheumatoid patients than in their non-blood relatives who acted as controls (Table 1).

The mean free serum histidine of the blood relatives of rheumatoid patients did not differ significantly from that of the non-blood relatives. All blood relatives and non-blood relatives were seronegative for rheumatoid factor, and none gave a history of rheumatoid arthritis.

In the subsequent study in which the mean serum histidine was measured in 79 patients with peripheral polyarthritis 49 patients positive for circulating rheumatoid factor had a mean histidine of 1·18 (SD = 0·26), while 30 patients with seronegative polyarthritis had a mean histidine of 1·32 (SD = 0·30).

Discussion

We found no significant degree of hypohistidinaemia

Table 1 *Free serum histidine levels in 3 groups of subjects*

	Rheumatoid arthritis	*Blood relatives*	*Non-blood relatives (control group)*
No. of subjects	28 M/F= 10/18	29 M/F= 13/16	17 M/F= 8/9
Serum histidine (mgms/100 ml); mean±standard deviation	1·23 (±0·19) M/F=1·17/ 1·33	1·45 (±0·20) M/F=1·48/ 1·41	1·47 (±0·22) M/F=1·56/ 1·39
Latex fixation test	All positive	All negative	All negative
Level of significance compared with control	$p<0·001$	$p>0·5$	—

in the fit blood relatives of patients suffering from rheumatoid arthritis. The hypohistidinaemia is a direct consequence of acquired rheumatoid arthritis rather than an inherited trait that might act as a marker for susceptible individuals. The subsequent finding that the hypohistidinaemia is less marked in patients with seronegative polyarthritis than in seropositive patients confirms that the abnormality is a consequence of the disease, apparently associated with seropositivity rather than mere inflammation of the synovium.

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