LETTERS, BOOK REVIEWS, NOTICES

Letters

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IMMUNE COMPLEXES AND CLINICAL MANIFESTATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

To the Editor:

The value of detecting circulating immune complexes (CIC) in patients with rheumatoid arthritis (RA) remains to be established[1]. Recently McDougal, *et al* examined the validity of CIC determinations in the assessment of clinical activity in RA[2]. They concluded that associations between CIC and clinical variables were not strong enough to encourage their detection in RA.

We correlated CIC with clinical manifestations in 40 Hispanic patients with classical or definite RA. CIC were detected in serum and synovial fluid (SF) by our standardized Clq binding assay (Clq BA) Raji cell method[3]. Sera were obtained from venous blood samples after clotting at 37°C for 2 h and centrifuged at 1500 g for 10 min. SF was clotted at room temperature for 120 min and centrifuged at 3000 rpm. Samples were stored at −70°C. Clinical activity was evaluated by measuring morning stiffness, articular index and erythrocyte sedimentation rate. Extraarticular features (EAF) in eye, heart, lungs, skin, muscle and peripheral nerves were recorded. Statistical analysis was performed by 4-fold table and χ^2 analysis. Thirty of 37 patients (80%) had abnormal levels of serum Clq BA-CIC (40 ± 9% M ± SE, normal < 3.2%) and 16 cases (43%) showed serum Raji-CIC (218 ±154 μg ml M ± SE, normal < 25 μg). Sera from non-rheumatoid patients and healthy controls were always negative by both methods. Sixteen SF samples were all positive for Clq BA-CIC (32 ± 6 M ± SE) and 10 of 16 also revealed Raji-CIC (331 ± μg, M ± SE). We examined correlations between 13 different clinical or laboratory variables and presence of abnormal CIC levels.

Table 1 shows a significant correlation between articular index higher than 20 and abnormal levels of serum Raji cell-CIC (χ^2 =12, $p < 0.005$). Increased amounts of complexes in SF also correlated with the number of active joints ($\chi^2 = 4.06$, $p < 0.05$). We also observed a significant correlation between the number of EAF and serum Clq BA-CIC ($\chi^2 = 5.59$, $p < 0.002$). We found no correlation between rheumatoid factor titers and CIC levels. Hypocomplementemia was detected in 5 patients, but no correlation with CIC was observed since many patients with high levels of CIC had CH50 within normal limits. Other correlations did not reach statistical significance. There was a discrepancy between correlations of CIC and clinical manifestations. This may be due in part to the diversity of assays used for detecting CIC[6]. However, certain associations seem to be confirmed by this and previous studies. Thus, significant correlations between EAF and Clq BA-CIC were observed[4,5]. In our study, however,

Table 1. *Correlation between articular index and Raji cell-CIC and Clq-BA*

	Articular index (> 20)	Number of EAF
Serum Raji-CIC	$X^2 = 12$ ($p < 0.005$)	$X = 0.45$ (NS)
Synovial Raji-CIC	$X^2 = 4$ ($p < 0.05$)	$X = 0.57$ (NS)
Serum Clq BA	$X^2 = 1.13$ (NS)	$X = 5.5$ (< 0.02)

NS: not significant

serum and synovial Raji-CIC seemed to correlate better with the degree of clinical activity.

The correlation between CIC and certain measurements in RA suggest that certain types of complexes may be related to single clinical manifestations. This point deserves further research with better designed protocols and should be considered when looking for the presence of CIC in patients with RA.

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HYPERGASTRINEMIA IN RHEUMATOID ARTHRITIS RELATED TO SJÖGREN'S SYNDROME

To the Editor:

An increased prevalence of hypergastrinemia in rheumatoid arthritis (RA) has been reported[1-4]. No correlation with disease duration and activity nor with drug treatment has been found[2,4,5]. The exact frequency and significance of hypergastrinemia in RA are still disputed. Rooney[6] did not find an association with gastric acid secretion and suggested that biologically inert forms of gastrin were involved. However, Rowden, *et al*[7] and De Witte, *et al*[2] found a strong correlation and concluded that hypergastrinemia in these patients was due to achlorhydria or hypochlorhydria, probably as the result of chronic atrophic gastritis. We report the level of gastrinemia and its relation to Sjögren's syndrome (SS) in 80 consecutive patients admitted to our rheumatology ward for treatment of RA or ankylosing spondylitis (AS).

All patients were admitted because of disease exacerbation. There were 71 RA patients, 58 women and 13 men, mean age 56 ± 10 years; 9 AS cases, 7 men and 2 women, mean age 42 ± 9 years. The following data were recorded in all of them: weight and height, duration of disease, erythrocyte sedimentation rate and C-reactive protein (CRP), immunoglobulins, rheumatoid (RF) and antinuclear factors (ANF).

A Schirmer test was performed in 60 of the RA cases as a screening procedure for the presence of SS. The cut-off point was set at a combined wetting length of 2 filter paper strips of 15 mm in 5 min[8]. Serum gastrin concentration in basal condition was measured by radioimmunoassay using reagents obtained from IRE, Fleuris, Belgium, as described[11]. The mean normal gastrin level in our laboratory is 38 pg/ml, the upper limit of normal is 90 pg/ml. For statistical analysis the unpaired t test was used to compare gastrin levels between different patient groups and the χ^2 test to evaluate the association of hypergastrinemia with the presence of SS.

The results are summarized in Table 1. Mean serum gastrin concentration (± SD) in RA patients was 48 (± 38) pg/ml, as compared to 35 (± 7) pg/ml in AS patients. In RA patients with SS mean serum gastrin was 61 (± 53) pg/ml, as compared to 37 (± 19) pg/ml in those without, a significant difference ($p < 0.025$). In the whole group of RA patients there were 9 patients with basal hypergastrinemia (13%). A Schirmer test was performed in only 7 of them, and was positive in 6. The association of SS with hypergastrinemia was significant ($p < 0.025$).

Mean duration of disease was longer in RA patients with SS (16 vs 10 years: $p < 0.05$) and ANF was present more often (55% vs 37%). Immunoglobulin concentration and RF titer was the same for both groups. No correlation was found between serum gastrin concentration and duration of disease or activity of the inflammatory process as measured by ESR or CRP.

Although the results of our systemic survey agree with the prevalence of hypergastrinemia in RA reported elsewhere, some interesting observations were made. We confirmed that 13% of patients suffering from classical or definite RA show basal hypergastrinemia that was significantly associated with the presence of a SS. Mean serum gastrin level in RA patients as a whole was only slightly elevated. However, mean gastrinemia in RA patients with SS was significantly higher than in SS negative RA subjects or in AS patients, who had normal gastrin values.

The association in RA between SS and hypergastrinemia is new to us, but not surprising. Indeed, SS develops gradually in RA patients and in addition to the lacrimal and salivary glands, may also involve the gastric mucosa and its glands[8-10]. As SS is found more frequently in RA than in normal controls, this could explain the prevalence of hypergastrinemia in RA.

Finally, our data suggest that the presence of hypergastrinemia and atrophic gastritis in RA are secondary to SS, rather than being the result of the administration of antiinflammatory drugs or the effect of RA itself. The Schirmer test is only a screening procedure; therefore, to prove our hypothesis, a prospective study should be undertaken with SS confirmed by lip biopsy and assessing the degree of hypochlorhydria in all cases.

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