Autoantibodies in the sicca syndrome (primary Sjögren’s syndrome)

KEITH B. ELKON, AZZUDIN E. GHARAVI, GRAHAM R. V. HUGHES, AND HARALAMPOS M. MOUTSOPOULOS

From the Rheumatology Unit, Hammersmith Hospital and Royal Postgraduate Medical School, Du Cane Road, London W12, and the School of Medicine, University of Ioannina, Greece

SUMMARY IgA and IgM rheumatoid factors as well as antibodies to Ro and La were measured in 37 patients with the sicca syndrome and 9 patients with Sjögren’s syndrome secondary to rheumatoid arthritis. Positive results were found in 84% (IgA rheumatoid factor), 76% (IgM rheumatoid factor), 62% (Ro), and 50% (La) of patients with the sicca syndrome. There was no significant difference in the frequency of positive results in patients with glandular versus extraglandular disease. Antibodies to La invariably occurred in patients with antibodies to Ro. In addition, patients who were anti-Ro positive also had significantly higher IgA (p<0.05) and IgM (p<0.01) rheumatoid factor activity. Since 81% of the sicca patients were concordant for 3 of the 4 antibodies tested, production of these autoantibodies appears to be related.

A broad range of autoantibodies are detected in the serum of patients with the sicca syndrome (primary Sjögren’s syndrome). We measured serum IgA and IgM rheumatoid factors as well as antibodies to Ro (SSA) and La (SSB) in a large series of sicca syndrome (SS) patients to determine the following: (1) the frequency with which these antibodies could be detected in the serum; (2) whether differences exist in autoantibody frequency in patients with disease confined to the exocrine glands (glandular or local SS) compared with patients with systemic features (extraglandular or systemic SS); (3) whether the elevation of each antibody occurs in isolation or is accompanied by increases in other antibodies. In a smaller group of patients with Sjögren’s syndrome secondary to rheumatoid arthritis (RA) we compared the frequency of detection of the same autoantibodies.

Materials and methods

Patients. Thirty-seven patients were diagnosed as having primary SS at the National Institute of Health on the basis of a positive lip biopsy with keratoconjunctivitis sicca, xerostomia, and recurrent salivary gland enlargement. The following were classified as extraglandular features of SS: Raynaud’s phenomenon, arthritis, purpura, nephropathy, mononucleosis, vasculitis, myositis, and pseudolymphoma. Nine patients with definite or classical RA and the sicca complex (histologically confirmed) were included as a separate group.

Rheumatoid factor radioimmunoassay. IgA and IgM rheumatoid factor activity were measured by a solid-phase radioimmunoassay as described previously. The assay was modified in that human rather than rabbit IgG was used as antigen. Incubations were performed at room temperature, and affinity-purified 125I-labelled F(ab’), anti-μ or anti-α were used to detect IgM and IgA rheumatoid factors respectively. The results were expressed as percentage F(ab’), anti-μ or anti-α bound. Binding greater than 2 standard deviations above the mean obtained in 20 normal controls was considered positive.

Assay for Ro and La. These antigens were prepared from human spleen and rabbit thymus extract (Pel-Freeze, Arkansas, USA) according to published methods. Counterimmunoelectrophoresis was performed by the method of Kurata and Tan with minor modifications.

Results

IgA and IgM rheumatoid factors. IgA and IgM
rheumatoid factor activity in patients with SS and Sjögren's syndrome (RA) are shown in Fig. 1A and B. Thus 31/37 (84%) of SS patients were positive for IgA rheumatoid factor and 28/37 (76%) positive for IgM rheumatoid factor. The mean rheumatoid factor activity (expressed as % F(ab')₂ bound) for glandular (G) and extraglandular patients (EG) was similar, namely, IgA rheumatoid factor 4-2 (G) and 4-6 (EG), IgM rheumatoid factor 15·1 (G) and 15·6 (EG). The corresponding mean percentage binding for Sjögren's syndrome (RA) was 3·9 (IgA rheumatoid factor) and 18·0 (IgM factor). These values did not differ significantly from the results obtained in the sicca syndrome (Student's t test).

While no correlation between IgA and IgM rheumatoid factor was found in SS (EG) (r=0·43, p>0·1), a weak correlation was found in SS (G) (r=0·52, p<0·05).

Antibodies to Ro and La. Antibodies to Ro were found in 23/37 (62%) and antibodies to La in 16/37 (43%) of patients with SS. Both antibodies were present in slightly higher frequency in patients with extraglandular features (Ro 69%, La 50%) compared than in patients with glandular disease (Ro 57% and La 38%). None of the patients with Sjögren's syndrome (RA) had antibodies to either antigen detected.

All SS patients with antibodies to La also had antibodies to Ro and 16 of 23 (70%) anti-Ro positive patients had antibodies to La. Patients with SS who were anti-Ro positive had significantly higher IgA (p<0·05) and IgM rheumatoid factor activity (p<0·001) than patients who were anti-Ro negative. Sixteen of 17 (94%) patients with IgM rheumatoid factor activity above 15% binding had anti-Ro antibodies (Fig. 1) compared with only 7/20 (35%) patients with low IgM rheumatoid factor activity (<15% binding) (p<0·01). Thirty patients (81%) had concordant results for three of the 4 autoantibodies measured.

Discussion

The sicca syndrome is a disease characterised by infiltration of exocrine and mucosal glands. We recently demonstrated high levels of IgA rheumatoid factor in the serum of SS patients and showed that these antibodies were predominantly polymeric in nature, suggesting a possible mucosal origin. In the current study of a larger number of SS patients, we confirmed the high frequency (84%) of serum IgA rheumatoid factors but found no significant difference in activity in glandular versus extraglandular disease (Fig. 1). IgM rheumatoid factors were detected in 76% of SS patients, and, although the correlations between IgA and IgM rheumatoid factors were weak, the results were concordant in 32/37 (86%) of patients.

The frequency of detection of antibodies to the
We gratefully acknowledge technical assistance from C. C. Bunn and B. M. Patel.
Autoantibodies in the sicca syndrome (primary Sjögren's syndrome).
K B Elkon, A E Gharavi, G R Hughes and H M Moutsoupoulos

Ann Rheum Dis 1984 43: 243-245
doi: 10.1136/ard.43.2.243

Updated information and services can be found at:
http://ard.bmj.com/content/43/2/243

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/