Letters to the Editors

Antinuclear antibodies seroconversion in 100 patients with lupus

Sirs,

In a recent drug trial using the monoclonal antibody Benlysta it was noted that 29.5% of patients with systemic lupus erythematosus (SLE), were ANA-negative. The literature contains relatively little information about what happens to the serological abnormalities in patients with SLE over long periods of time. We have audited the results on 97 SLE patients followed for a minimum of 10 years to determine how many were no longer ANA positive.

The cohort consisted initially of 100 randomly selected patients from a total cohort of 650 SLE (all of whom were under follow-up and met the revised American College of Rheumatology criteria for SLE) and on whom ANA, ENA and anti-dsDNA results were available from the time of diagnosis and at follow-up ten years later. Full demographic, clinical and laboratory data were available in all except 3 patients who were excluded from the final analysis. The SLE patients were followed up in the Lupus Clinic at The Centre for Rheumatology Research University College Hospital London. Disease activity was assessed using the 'classic' BILAG (British Isles Lupus Assessment Group) system. Disease remission was defined as no BILAG A or B score at follow-up ten years later.

The antinuclear antibody results were obtained by immunofluorescence (IF) using a Hep2 substrate (positive = 1/80 or greater). The anti-dsDNA and anti-ENA antibody profiles were determined by ELISA (Eurodiagnostica) at diagnosis and ten years later (positive = >50). The IF assessments throughout the study (the samples assessed were spread over a period of about 15 years) were undertaken by the same experienced senior technician.

There were 83 female (85.5%) and 14 male (14.4%) patients of whom 62 were Caucasian, 8 Chinese, 18 Afro-Carribean, 8 Asian and one was of mixed ethnicity (Caucasian, Phillipino). Thus 96 patients out of 97 (98.9%) were ANA positive at diagnosis. However 17 patients (17.57%) became ANA-negative ten years later. Of these ANA-negative patients, 15 (88%) are Caucasian. Caucasian patients are more likely to become ANA-negative over ten years (p=0.0021).

Thirty-two patients (33%) had a negative anti-dsDNA test at diagnosis of whom eighteen became positive after ten years. Sixty-five patients (67%) were anti-dsDNA positive at the beginning and twelve became negative ten years later.

Anti-ENA testing showed that there were thirty-seven (38.1%) Ro+ and ten (10.3%) La+ at diagnosis. Among those initially Ro+, 94.4% remained positive 10 years later and among those historically Ro-, 83% were still negative. Those patients Ro+ at the beginning are more likely to be persis-tently ANA-positive (p=0.012).

No relationship was found between patients whose ANA became negative with respect to treatment or disease remission.

Although an immunofluorescence test for ANA is the most sensitive test for SLE, being positive in about 95% of cases, it is not specific. A positive ANA is relatively common, even in the healthy population (1).

In the present study of 97 SLE patients we found that ANA positivity disappeared over time in 17.5% of SLE patients.

In a study of 50 SLE patients, a positive result for ANA occurred in 76% of the SLE patients that had previously been ANA-positive (2), as well as in a multicenter phase II trial of belimumab in 449 SLE patients in which 71.3% of SLE patients at entry were positive for ANA at baseline, although 98% were historically positive (3).

Our results emphasise the importance of recognising that in patients with SLE, approximately 1 in 6 patients initially ANA positive will become ANA-negative during the decade after diagnosis. In order to ensure homogeneity in clinical trials it is important to check ANA at entry into the trial and not rely upon historical data. A positive ANA, even if only historical, is important not at least for Lupus classification purposes. Certain antibody profiles are also important clinically, being particularly linked to particular clinical features thus anti dsDNA are strongly linked to renal disease and anti-Ro with photosensitivity and neonatal lupus syndrome.

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