arthritis which does not fulfill the RA criteria. If some subtle changes are present in HTLV-I infected arthritic patients, further analysis using functional assays of lymphocytes may be useful for detecting these changes.

SHINJI IJICHI
IKURO MARUYAMA
YOSHIKAZU MARUYAMA
MITSUHIRO OSAME
Third Department of Internal Medicine
Faculty of Medicine
Kagoshima University
Kagoshima, Japan

TAKEMASA MATSUDA
TATSURO NINOMI
Center of Rheumatic Diseases
Kagoshima Red Cross Hospital
Kagoshima, Japan

SHUNRO SONODA
Department of Virology
Faculty of Medicine
Kagoshima University
Kagoshima, Japan

Correspondence to: Dr Shinji Ijichi, Third Department of Internal Medicine, Faculty of Medicine, Kagoshima University, 8–35–1 Sakuragaoka, Kagoshima 890, Japan.


False negative results of anticardiolipin antibody test

Sirs: It has been reported that certain anticardiolipin antibodies (ACAs) react against the cardiolipin-β2-glycoprotein I (β2-GPI) complex and that the binding of ACA is enhanced by adding β2-GPI to the conventional enzyme linked immunosorbent assay (ELISA) system. Possibly, therefore, false negative results of ACA are determined and recorded unless β2-GPI is added to the ELISA system in some patients with antiphospholipid syndrome.

We present the case of a 30 year old woman who was diagnosed for systemic lupus erythematosus in 1980. She had previously had two fetal losses. In 1985 her first pregnancy resulted in intrauterine fetal death during the 20th week of gestation. During her second pregnancy in 1988 retardation of fetal growth and oligohydraminosis progressed during the 20th week of gestation and resulted in fetal death during the 22nd week of gestation. Small multiple infarctions in the placenta were recognised.

In 1989 she was admitted to our hospital during the fourth week of gestation. She had no special physical signs. Laboratory findings were white blood cell count 4.5×10⁹/l, haemoglobin 104 g/l, platelets 16.8×10⁹/l, erythrocyte sedimentation rate, 4 mm/h and low concentrations of complements were recorded; C3 460 mg/l (normal 700–1300), C4 230 mg/l (normal 300–500), and CH50 21.4 U/ml (normal 32–36). The antinuclear antibody titre was 1/32 and SS-B antibodies were absent. No antibodies to Sm or RNP were detected. Latex agglutination test for rheumatoid factor was 1/40. Cryoglobulin and circulating immune complexes (Clq binding assay) were not detected. Anticardiolipin antibodies of IgG and IgM were negative by the conventional ACA assay performed without β2-GPI. The activated partial thromboplastin time was 31.4 s (control 30.2). Lupus anticoagulant and Venerale Disease Research Laboratory tests were negative. No abnormal findings of blood urea, creatinine, and urine analysis were noted. A raised concentration of the thrombin-antithrombin III complex (TAT), which has been reported as a marker for thrombosis, was recorded as 101 ng/ml. Prednisolone 10 mg/day and aspirin 75 mg/day were given. For prophylactic treatment double filtration plasmapheresis was carried out once a week from the 10th week of gestation.

Clinical status and laboratory findings of the patient stabilised by the 19th week of gestation. During the 20th week of gestation circulating immune complexes and TAT increased to 15.9 ng/ml (normal 10–30) and 21.8 ng/ml (normal <8–3) respectively. Retardation of placental growth was recognised by echography. Therefore, prednisolone was increased to 30 mg/day and plasmapheresis was carried out three times during the next two weeks. The TAT concentration, however, increased beyond 60 ng/ml and retardation of fetal growth was again detected during the 23rd week of gestation. Fetal distress was recognised during the 26th week of gestation, and therefore caesarean section was performed; a
baby girl was delivered (650 g; small for date: Apgar 4). Examination of the placenta disclosed focal decidual infarctions. The mother progressed well after birth, but although the baby was intensively treated, she died within a month owing to complications associated with rupture of the intestine.

Anticardiolipin antibody (IgG) was retrospectively determined by ELISA with or without the addition of β2-GPI to the ELISA system. The concentration of ACA with β2-GPI increased from the 20th week of gestation when retardation of placental growth was noticed and the TAT concentration showed an extraordinary increase, whereas the level of ACA without β2-GPI remained within the normal range (figure). Furthermore, the level of thrombomodulin, which has been reported as a marker for endothelial cell injury, increased from the 24th week of gestation. There were no remarkable changes in other serological data, except circulating immune complexes, which increased transiently during the 20th week of gestation.

Thus ACA can be determined with the addition of β2-GPI. Furthermore, serial examination of TAT or thrombomodulin concentrations, or both, will provide additional information as to whether subclinical thrombotic conditions exist or not because ACA is not always associated with a pathological role andnor does a marked increase of ACA always induce thrombosis.10

KOBAYASHI M. TANAKA H. TSUDA H. HASHIMOTO S. HIROSE Department of Rheumatology, Juntendo University School of Medicine, Hongo, Bunkyo-ku, Tokyo 113, Japan

Correspondence to: Dr Shigeto Kobayashi, Department of Rheumatology, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113, Japan.

Sulphoxidation status in rheumatoid arthritis

Str: In a recent issue of this journal Emery et al found an increased prevalence of poor sulphoxidation in patients with rheumatoid arthritis (RA). Using the same methods as Emery’s group, we have found similar results. Sulphoxidation status was assessed in 116 of 200 patients enrolled in a comparative study of sulphalazine and β-penicillamine as second line drugs in RA (table). Follow up data are available on these patients for between 5 to 7 years from entry into the trial. Surprisingly, no increase in toxicity from either drug was observed in the poor sulphoxidisers group (figure).

Previous studies have suggested that toxicity from intramuscular gold2 and β-penicillamine3 is related to sulphoxidation status. In contrast, with gold and β-penicillamine, however, sulphalazine is metabolised predominantly by acetylation rather than sulphoxidation, and one would therefore have predicted that toxicity from sulphasalazine would not be influenced by sulphoxidation status. In this study we failed to find any association between toxicity from β-penicillamine and sulphoxidation status. Although the period of follow up in this study is longer than in previous studies, this finding cannot be explained by an excess of late toxicity in the good sulphoxidisers group.

A second possible explanation is that the group in whom sulphoxidation status was measured was not representative of the group as a whole. To consider this point we noted toxicity in those patients in whom sulphoxidation status was not assessed. Of the patients receiving sulphalazine in whom sulphoxidation status was known, 35% developed toxicity compared with 30% of those in whom sulphoxidation status was not known. In those receiving β-penicillamine the figures were 34% and 38% respectively. Thus although there was a small excess in toxicity in those receiving β-penicillamine who did not have sulphoxidation status assayed, this was not statistically significant (χ²). We cannot rule out the possibility that the ratio of good and poor sulphoxidisers might have been different in those who were not assayed. There were 12 deaths (five sulphalazine, seven β-penicillamine) in the group where sulphoxidation status could not be evaluated compared with two in the group where sulphoxidation status was assayed (one sulphalazine, one β-penicillamine). None of these deaths was directly attributable to drug toxicity.

The consistent finding that poor sulphoxidisers are overrepresented in RA compared with the normal population is of great interest, and the effect of sulphoxidation status on susceptibility to RA or disease expression, or both, merits further study.

Correspondence to: Dr Elizabeth Murphy, University Department of Medicine, Glasgow Royal Infirmary, Glasgow G31 2ER, United Kingdom.

Numbers (percentages) of patients receiving sulphalazine or β-penicillamine who were good or poor sulphoxidisers

<table>
<thead>
<tr>
<th></th>
<th>Poor</th>
<th>Good</th>
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<tbody>
<tr>
<td>Sulphalazine (n=63)</td>
<td>49 (78)</td>
<td>14 (22)</td>
</tr>
<tr>
<td>β-penicillamine (n=53)</td>
<td>36 (68)</td>
<td>17 (32)</td>
</tr>
<tr>
<td>Expected</td>
<td>26 (22)</td>
<td>90 (78)</td>
</tr>
</tbody>
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False negative results of anticardiolipin antibody test.

S Kobayashi, M Tanaka, H Tsuda, H Hashimoto, S Hirose, T Saikawa and K Yoshida

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