False-positive test results for syphilis in relatives of a patient with systemic lupus erythematosus

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SUMMARY In a family of nine members, two had systemic lupus erythematosus and seven positive serological test results for syphilis. None of the affected subjects had a history or physical signs of syphilis, but two had positive results to the Treponema pallidum immobilisation test. The explanation for these findings is not known, but possibly they were all false-positive reactions.

Introduction

Familial aggregation of systemic lupus erythematosus (SLE) is widely reported and has been reviewed by Masi (1968), who found an incidence of 1-2% in first-degree relatives of patients with SLE. The reason for this finding is not clear, but it is probable that both genetic and environmental factors play a role. Humoral abnormalities are found in about 10% of first-degree relatives, the most common being hypergammaglobulinaemia, rheumatoid factor, antinuclear antibody, and false-positive lipid test results for syphilis (Morteo et al., 1961.)

We report a family in which two members had SLE and seven of the other eight had positive results to serological tests for syphilis, including the fluorescent treponemal antibody test (FTA-ABS) and the Treponema pallidum haemagglutination (TPHA) test.

Material and methods

SEROLOGY

The Venereal Disease Research Laboratory (VDRL) test followed a standard method (Communicable Disease Center, 1969). The FTA-ABS test was performed as described by Hunter et al. (1964) and the TPHA test as described by Johnston (1972).

PATIENTS

Case 1

A 50-year-old woman presented in 1974 with a large leg ulcer of 27 years' duration. She was found to have thinning of the scalp hair, discoid lupus erythematosus, polyarthritis, and mouth ulcers. On investigation her haemoglobin was 11·2 g/dl, white cell count 2·7 × 10⁹/l, with normal hepatic and renal function. The LE-cell test gave a positive result, the antinuclear antibody was present at a titre of 1/500, the VDRL test gave a positive result at a titre of 1/2, and the FTA-ABS test gave a positive result with a homogeneous pattern. Her symptoms improved with rest in bed and the administration of salicylates. She remained well until May 1977, when she was admitted in a stuporous state and died, probably of cerebral lupus.

Case 2

The 29-year-old daughter of Case 1 presented in 1977 with severe haemolytic anaemia, positive results to the LE-cell test, and antinuclear antibody at a titre of 1/100.

Because of our interest in familial aggregation of lupus, we then examined the siblings of Case 2. Our findings are summarised in the Table. None of the subjects had a history or physical signs suggesting a connective tissue disease or syphilis, but seven of the eight tested showed some abnormality in the serological test results for syphilis. Two subjects had a positive result to the Treponema pallidum immobilisation (TPI) test. None had received recent antibiotic therapy.

Discussion

The family which we describe is not unusual in having two members with SLE. The occurrence of false-positive reactions in family groups is less well known and has been reviewed by Putkonen and Lassus (1965), who reported two families with an
aggregation of false-positive reactors, one of the
affected subjects having rheumatoid arthritis.
Kostant (1972) later described a further two families,
including one in which three generations were
affected. Tuffanelli (1968) examined 103 false-
positive reactors and their 199 relatives and found a
high incidence of antinuclear antibody, rheumatoid
factor, and hypergammaglobulinaemia. He
suggested that this implied an inherited defect in
immunoglobulin control mechanisms, and this could
help to explain the familial aggregation of both false-
positive reactors and SLE.

It seems possible that the family we describe has a
hereditary abnormality associated with false-positive
serology and a predisposition to develop SLE, the
abnormal serology being a marker of the 'lupus
diathesis'. A study (Lowenstein and Rothfield, 1977)
of related and unrelated household members showed a
higher incidence of antinuclear antibody in related
persons but more household members with positive
immunofluorescent findings on skin biopsy. This
supports the view that both genetic and environmental
factors could be concerned in the pathogenesis of SLE.

The serological tests for syphilis (Jaffe, 1975) fall
into two groups, the treponemal and the non-
treponemal. The latter, including the VDRL test, use
non-specific cardiolipin as antigen and may give a
positive result in a wide range of conditions,
including viral illnesses, malaria, leprosy, and the
connective tissue disorders. In a study of 110 chronic
false-positive reactors, Johansson (1971) found that
30 had probable or definite SLE and 25 were
completely normal. It was initially thought that the
treponemal tests were specific for syphilis, but this has
not proved to be the case, 15-23% of patients
with SLE having a false-positive result to the FTA-
ABS test (Shore, 1976). In SLE this reaction may
take the form of a beaded (Kraus et al., 1970) or a
homogeneous fluorescence, the latter being
indistinguishable from the true positive (Shore and
Faricelli, 1977). The atypical, beaded pattern appears
to be due to the presence of anti-DNA antibody in
the serum (Kraus et al., 1971) but the factor
responsible for the homogeneous FTA-ABS test has
not been identified. The TPHA test may be even less
specific in some laboratories. Garner et al., (1973)
applied the test to 274 subjects with false-positive
reaginic test results but negative FTA-ABS test
results, and found 11.3% to give positive results to the
TPHA test.

The TPI test is thought to be highly specific for
syphilis, although its results may become negative if
the patient is treated early in the disease (Lassus,
1968). Moore and Mohr (1952), examining a group of
people thought to be false-positive reactors, found
16% to have positive results to the TPI test. They
concluded that clinical judgement was probably at
fault rather than the test, but they were, of course,
unable to prove this.

The positive results to the TPI test in two of our
subjects raise the question of possible false-positive
results to this test. The only recognised false-positive
reaction is that seen when the patient is taking an
antibiotic, but this was not the case in our subjects.
Another possibility, which cannot be completely
excluded, is that two members of the family had had
syphilis and four others had false-positive results to
serology. Both venereal and endemic syphilis
commonly occur in the small rural communities of
South Africa (Du Toit, 1969). Du Toit found,
however, that nasopharyngeal ulceration, mucous
patches, condylomata lata, gummatas, and bone
lesions were common in endemic syphilis, and our
subjects had none of these.

The most likely explanation for our findings is that
the members of the family described above had a
variety of serological abnormalities which gave rise to

<table>
<thead>
<tr>
<th>Sibling</th>
<th>Year of birth</th>
<th>ANA</th>
<th>CH50</th>
<th>VDRL</th>
<th>FTA-ABS</th>
<th>TPI</th>
<th>TPHA</th>
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<tbody>
<tr>
<td>1</td>
<td>1925</td>
<td>1/500</td>
<td>119</td>
<td>1/1</td>
<td>ND</td>
<td>ND</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>1947</td>
<td>—</td>
<td>149</td>
<td>—</td>
<td>B</td>
<td>ND</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>1948</td>
<td>1/100</td>
<td>70</td>
<td>—</td>
<td>—</td>
<td>6%</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>1949</td>
<td>—</td>
<td>137</td>
<td>—</td>
<td>B</td>
<td>ND</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>1950</td>
<td>—</td>
<td>172</td>
<td>1/1</td>
<td>B</td>
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<td>+</td>
</tr>
<tr>
<td>6</td>
<td>1954</td>
<td>—</td>
<td>175</td>
<td>—</td>
<td>—</td>
<td>ND</td>
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<td>+</td>
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<tr>
<td>8</td>
<td>1959</td>
<td>—</td>
<td>154</td>
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<td>B</td>
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<tr>
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<td>1961</td>
<td>—</td>
<td>172</td>
<td>1/8</td>
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<tr>
<td>10</td>
<td>1966</td>
<td>—</td>
<td>161</td>
<td>1/1</td>
<td>+</td>
<td>8%</td>
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+ positive — negative
ANA = antinuclear antibody
CH50 = total haemolytic complement (normal 160-210)
ND = not done
B = borderline
false-positive results to the VDRL, FTA-ABS, TPHA, and TPI tests in certain members and to SLE in two cases.

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References


