Value of serological diagnosis in congenital syphilis
Report of nine cases

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SUMMARY  The diagnosis of congenital syphilis is difficult since it depends mainly on the results of serological tests. The results of five serological tests (three specific and two non-specific) in nine neonates with congenital syphilis are compared with those obtained in three with passively acquired antibodies. It appears that the serological diagnosis of congenital syphilis must be based on the finding of specific neonatal antibodies in cord serum, which give positive results to the fluorescent treponemal antibody absorption test for immunoglobulin M, together with high titres of total IgM and negative results to latex tests. The non-specific tests are useful for confirming the efficacy of treatment.

The mean number of cases of congenital syphilis in Seville is 0·81/1000 live births.

Introduction

Congenital syphilis reached a low level during the late 1950s. With the increase in infectious syphilis in the adult population during the 1960s, however, the incidence of early congenital syphilis in infants under 1 year of age increased in many parts of the world. In the United States 132 cases were reported in 1969 and 144 in 19771; the number then seemed to have stabilised, with 107 cases in 1978. During the period from January to March 1979 the number of cases fell by 16% from that reported in the same period the previous year.2 The evolution in England has been similar. Cases of syphilis are rare in Sweden.3 In Spain there are no statistics on the incidence of this disease.

The diagnosis of congenital syphilis presents a considerable problem, since it depends mainly on the results of serological tests and also because most syphilitic neonates are asymptomatic at birth.

All the standard serological tests for syphilis depend on responses involving IgG and IgM antibodies.4 This makes their interpretation in neonates extremely difficult as the IgG antibody found in the serum of neonates is largely passively acquired through the placenta5 and does not represent the infant's own response. In 1968 Scotti and Logan4 described the fluorescent treponemal antibody absorption test for antitreponemal IgM antibodies (IgM-FTA-ABS). In theory, any antitreponemal IgM found in the serum of the neonate would be expected to have been produced by the baby in response to the T pallidum present in its tissues.

The aims of this work were: (a) to determine the incidence of congenital syphilis in the population of Seville; and (b) to evaluate the different serological tests in the diagnosis of congenital syphilis.

Over a period of three years we have studied nine cases of either symptomatic or asymptomatic early congenital syphilis using the IgM-FTA-ABS test together with three other specific and two non-specific tests for syphilis. We have compared these results with those obtained in three neonates with passively acquired antibodies. We have followed most cases for several months and have monitored the treatment and evolution of the disease.

Patients and methods

STUDY POPULATION
The sera of all antenatal patients attending the hospital were screened by the Venereal Disease Research Laboratory (VDRL) test; sera giving positive results were confirmed by the FTA-ABS test. Most women arriving to give birth in our hospital have never attended this hospital for antenatal care. Over a period of three years 4000 VDRL tests were performed and 6% gave positive results. Of these 6% (240) only 0·3% (12) gave positive results by the FTA-ABS-IgG and FTA-ABS-IgM tests, a further eight gave positive results by the FTA-ABS-IgG test but negative results by the FTA-ABS-IgM test.
The 12 cases reported here were detected by routine screening of the infants’ mothers. Nine babies had congenital syphilis and three had passively acquired antibodies. All were followed for 5-6 months. The parents and siblings were also studied.

SEROLOGICAL TESTS
Non-specific and specific serological tests were carried out.

Non-specific. These included: estimation of total IgM in serum; the latex test (the serum was tested at a dilution of 1/25); the VDRL qualitative and quantitative test; and the qualitative and quantitative reagin screen test (RST).

Specific. These included: the FTA-ABS test; the FTA-ABS-IgM test; the T pallidum haemagglutination assay (TPHA); (qualitative and quantitative determinations using microtitre plates); and the T pallidum immobilisation (TPI) test.

Three standard sera giving positive, weakly positive, and negative results were included in each batch of tests as controls.

TREATMENT
Pregnant women were treated according to the Willcox schedule using procaine penicillin 0.6 megaunits/day for eight days (total dose 4.8 megaunits).

Syphilitic neonates were treated with procaine penicillin G 50 000-100 000 units/kg body weight daily for at least 15 days.

RESULTS
The results of the serological tests are shown in the table.

CASE 1
This was a twin birth, in which only the boy had clinical evidence of congenital syphilis. He was born at term following an uncomplicated twin delivery. Height and weight were below the tenth percentile. The infant was pale; the liver was palpable at 4 cm and the spleen at 1 cm below the costal margins. A roentgenogram showed periosteal new bone forma-

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TABLE Results of serological tests in nine infants with congenital syphilis (cases 1-9) and in three with passively acquired antibodies (cases 10-12)

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<tr>
<th>Case Nos</th>
<th>Sex</th>
<th>Age (days)</th>
<th>Total IgM (g/l)*</th>
<th>VDRL (titre)</th>
<th>RST (titre)</th>
<th>Latex (1/125 dilution)</th>
<th>TPI†</th>
<th>TPHA (titre)</th>
<th>FTA-ABS‡</th>
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*Normal values of IgM in neonates are between 0.16 and 0.2 g/l
†TPI test: + = 100% immobilisation
‡FTA-ABS test: 1+, 2+, 3+, 4+ = increasing intensity of fluorescence
+ Positive − negative
Conversion: SI to traditional units — immunoglobulin concentration 1 g/l ≈ 100 mg/100 ml
tion on several of the ribs and on the proximal area of
the humerus. Additional films showed thickened
periostal new bone in the extremities. His total IgM
was 2·05 g/l (205 mg/100 ml) and all serological test
results were strongly positive. The tests were repeated
three and five months later. Only the FTA-ABS-IgM
and VDRL-RST tests were modified after treatment,
and at the fifth month the first gave negative results
while the total IgM was normal.

The girl showed no clinical evidence of congenital
syphilis and all serological tests gave negative results
except the TPI; total IgM concentration was raised.
The discrepancy between the serological results of
the girl and that of her twin was because the boy was
affected through the placenta and the girl was not as
she had a different placenta.

CASE 2
This was a girl, who had clinical evidence of con-
genital syphilis at birth. At eight hours after birth she
had a swollen, tender, crepitant left elbow and
limited abduction of the left hip. Roentgenograms
showed that the left hip was dislocated with evidence
of destruction in the proximal metaphysis and
periostal reaction. All the tests performed gave
positive results with high values of total IgM. Four
months later the tests produced similar results except
for total IgM, which fell from 3 g/l to 1·55 g/l
(300 mg/100 ml to 155 mg/100 ml).

CASE 3
This was a girl, who showed no clinical evidence of
congenital syphilis at birth. The results of the non-
specific tests were negative and those of the specific
tests were positive with raised total IgM. Six months
later the total IgM concentration was normal and the
FTA-ABS-IgM test gave a negative result.

CASE 4
This was neonate, who did not show clinical evidence
of congenital syphilis. The tests all gave positive
results with high concentrations of total IgM.

CASE 5
This was a 5-month-old girl, in whom the only
clinical symptom was a slight tibial osteitis. All tests
gave strongly positive results, which remained
positive until six months later.

CASE 6
This was a 2-week-old infant, who was admitted to
hospital because of anaemia. He had a hypo-
pigmented rash on the back and neck, which later
spread over the body to the hands and feet. The
lesions included blisters, vesicles, and wrinkled
peeled areas. His haemoglobin was 6·6 g/dl.

Roentgenograms showed a solitary abnormality of
the right tibia with resorption of the cortex. The
parents were diagnosed as having syphilis and were
treated at the beginning of the mother’s pregnancy.

CASES 7 AND 8
These were two polymalformed neonates, who died
during the first month of life. The second child had
some perianal condylomata which harboured
numerous treponemes.

CASE 9
This was a neonate, whose mother had been
diagnosed as having syphilis late in pregnancy.
Latex tests gave negative results in all the nine
cases studied. Serological tests were carried out on
samples of cerebrospinal fluid from cases 1, 3, 4, and
9, and all of them gave negative results.

PASSIVE ANTIBODY TRANSFER
Three cases of passive antibody transfer through the
placenta are summarised in the table. The results of
all the tests measuring IgG were positive and those of
tests measuring IgM were negative while total IgM
values were normal.

BIRTH STATISTICS
An analysis of the birth statistics at the University
Hospital of Seville over a three-year period showed
that out of 11 110 live births nine babies had
neonatal syphilis, an incidence of 0·81/1000 live
births.

Discussion
Since its original description in 1968, the usefulness
and accuracy of the nonspecific FTA-ABS-IgM
test for congenital syphilis has been assessed by
several workers. Some have found doubtful or
negative results in syphilitic babies. False-positive
results have also been reported.

The nine cases of congenital syphilis we studied
had positive results to the FTA-ABS-IgM tests and
these remained positive as long as the total serum
IgM was higher than normal. Furthermore, we were
unable to detect IgM specific antibodies in the three
patients with passively acquired antibodies who
showed normal values of total IgM. These findings
indicate that we did not encounter either false-
negative or false-positive results for the FTA-ABS-
IgM test.

Recent studies suggest that the FTA-ABS-IgM test
can detect IgM directed against maternal IgG rather
than against T pallidum. This anti-antibody
appears to be similar to the rheumatoid factor found
in many adults. Some workers have reported false-
positive tests due to adult rheumatoid factors. Because of the possibility that this rheumatoid factor might lead to an apparently positive FTA-ABS-IgM test, the latex test must be carried out to exclude false-positive results; this test gave negative results for all of the nine babies with congenital syphilis we studied.

When the cases of congenital syphilis are compared with those of passively acquired antibodies, we did not find any differences in the results of the FTA-ABS test, TPHA, and TPI test because these tests depend only on maternal antibody titres. Differences were found in the total IgM titres—which are normal in cases of passive transfer and very high in syphilitic babies—and in the FTA-ABS-IgM test, which gave positive results only for the syphilitic babies. In the non-specific tests higher titres were obtained in the syphilitic babies than in their mothers and lower titres in the babies with passive transfer than in their mothers.

We conclude that serological diagnosis of congenital syphilis must be based on the demonstration of specific neonatal antibodies in the cord serum. As these antibodies belong to the IgM fraction, high titres of total IgM—together with positive FTA-ABS-IgM test results and negative latex test results—are the findings needed to make a serological diagnosis of congenital syphilis.

The results of non-specific tests are useful during follow-up after treatment to confirm its efficacy.

References

Value of serological diagnosis in congenital syphilis. Report of nine cases.
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doi: 10.1136/sti.56.6.377

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