

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.

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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)

		Results of serological tests								
Case Nos	Sex	Age (days)	Total IgM (g/l)*	VDRL (titre)	RST (titre)	Latex (1/125 dilution)	TPI†	TPHA (titre)	FTA-ABS‡	
									IgG	IgM
1	M	1	2.05	1/128	1/128	-	+	1/1640	2+	2+
		30	1.15	1/128	1/128	-	+	1/640	2+	2+
		90	1.06	1/16	1/16	-	+	1/640	2+	2+
1	F	150	1.00	1/4	1/4	-	+	1/640	2+	-
		1	2.15	-	-	-	+	-	-	-
		30	1.84	-	-	-	+	-	-	-
2	F	150	1.05	-	-	-	+	-	-	-
		1	3.00	1/64	1/64	-	+	1/640	2+	2+
		120	1.55	1/64	1/64	-	+	1/640	2+	2+
3	F	1	2.15	-	-	-	+	1/2560	4+	4+
		120	1.06	-	-	-	+	1/2560	4+	-
4	M	1	3.50	1/256	1/256	-	+	1/2560	4+	3+
		30	2	1/32	1/32	-	+	1/2560	4+	3+
		60	1	1/8	1/8	-	+	1/2560	4+	3+
5	F	150	1.4	1/16	1/16	-	+	1/640	2+	2+
		180	1.9	1/16	1/16	-	+	1/640	2+	2+
		990	1.4	1/8	1/8	-	+	1/640	2+	1+
6	M	1	3.2	1/2	1/2	-	+	1/320	3+	2+
		90	2.4	-	-	-	+	1/80	2+	2+
7	M	1	0.3	1/4	1/4	-	+	1/320	3+	2+
8	F	5	4.7	1/2	1/2	-	+	1/1280	4+	4+
9	M	1	2.06	1/64	1/32	-	+	1/1200	4+	3+
10	M	1	0.7	-	-	-	+	1/320	2+	-
		74	0.7	-	-	-	+	1/320	2+	-
		88	0.66	-	-	-	+	1/320	2+	-
11	F	1	0.66	+	+	-	+	1/320	+	-
		97	0.6	-	-	-	+	1/160	+	-
12	F	1	0.32	-	-	-	+	1/160	+	-

*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 \approx 100 mg/100 ml

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 serum⁶; the latex test (the serum was tested at a dilution of 1/25)⁷; the VDRL qualitative and quantitative test⁸; and the qualitative and quantitative reagin screen test (RST).⁹

Specific. These included: the FTA-ABS test¹⁰; the FTA-ABS-IgM test⁴; the *T pallidum* haemagglutination assay (TPHA)^{11,12} (qualitative and quantitative determinations using microtitre plates); and the *T pallidum* immobilisation (TPI) test.¹³

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 schedule¹⁴ 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.¹⁵

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-

tion on several of the ribs and on the proximal area of the humerus. Additional films showed thickened periosteal 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 congenital 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 periosteal 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 hypopigmented 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 monospecific FTA-ABS-IgM test for congenital syphilis has been assessed by several workers.¹⁶ Some have found doubtful or negative results in syphilitic babies.^{17 18} False-positive results have also been reported.¹⁹

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 may detect IgM directed against maternal IgG rather than against *T pallidum*.^{21 22} 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.^{12 20 22 23} 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^{7 24}; 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.

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