

Diagnosis and treatment of the asymptomatic newborn child of a mother with syphilis case report

Abstract

Syphilitic infection in newborn could be a devastating disease with upward trend in incidence. The prevalence rate of this disease is around 5 to 100,000 neonates and 60% of them are asymptomatic. There is two clinical forms: early and late. Infected infants may suffer severe sequelae, including cerebral palsy, hydrocephalus, sensorineural hearing loss and musculoskeletal deformity, all of which may be prevented with timely treatment during pregnancy. Questions about the prevention and management of congenital syphilis persist because the diagnosis of suspected cases and management may be confusing, and the potential for severe disability is high when cases are missed. The case here presented is an early case with any lesions in the newborn. The treatment was a successful and after there was not any complications.

Keywords: newborn, syphilis, treponema pallidum, neonatal sepsis

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Introduction

Congenital syphilis is a multisystem infection caused by *Treponema pallidum* and transmitted to the fetus through the placenta.¹ This disease is still a global problem, with an estimated incidence of 12 million infections per year. Infected pregnant women can transmit the infection, which can be associated with serious adverse events for pregnancy in up to 80% of cases. However, there are options to detect it in time and start its management avoiding complications in both the pregnant mother and the product. Such tests as well as treatment are relatively cheap and very effective and contribute positively to global efforts to eliminate congenital Syphilis.²

Despite global efforts to eliminate, we still have cases, the incidence of the problem can be reduced through relatively simple and proven interventions. But as long as their prevalence is high in adults, the risk of congenital transmission is high.^{3,4}

When this pathology is not treated, it produces a wide range of adverse results on fetuses. These consequences can occur in up to 80% of women with active Syphilis and involve fetal deaths (17-40%).^{5,6}

What could be the case of our patient to present his Mother in his first feat with unknown death a month of life. Perinatal death (20-23%) and neonatal infections (20%) [Schulz 1987, Scmid 2007].⁶

The WHO has estimated approximately 130 million births per year worldwide, of which 8 million infants die before their first year of life and of these 3 million die before the first week of life. In addition, 3.3 million are fetal deaths.1 Many of which have been associated with treponema infections, the vast majority of which are in developing countries. [Goldenberg 2003].⁷

In Latin America and the Caribbean, coverage in terms of prenatal care is acceptable, greater than 50%, but we continue to have deficiencies in both the detection and care of Maternal Syphilis and consequently in areas of limited access, rural areas, communities far from urban areas.

Therefore, considering the deficiency that our country (Mexico) continues to face and considering that there is a large population of pregnant women who are positive serology for Syphilis without diagnosis in hard-to-reach areas and who therefore do not receive treatment during their prenatal check-up. Of these pregnant women, one third of newborns will have congenital Syphilis and a similar number will end up in Miscarriage. Returning to the definition that fetal death will be considered as the one that occurs at the 20th week or more of pregnancy. And it will be divided into 3 categories a) early, less than 28 weeks or 1000gr as a cutoff point; b) late preterm of week 28-36 and c) term, of week 37 and more.[Goldenberg and Thompson 2003].⁸

Despite how alarming these aforementioned figures sound, there are no precise estimates about the real magnitude of the condition and we continue to have a high underreporting of cases of Maternal Syphilis and congenital Syphilis in Mexico, there are epidemiological notification studies in the units of the entire national health system in case of congenital Syphilis (Figure 1) which must be reported, but sometimes this continues to be ignored by many levels of care.⁹

Epidemiological situation of congenital syphilis

From the year 2000 in Mexico to date, a total of 2,622 cases of Congenital Syphilis have been recorded, with a significant increase observed in 2008 with 168 confirmed cases; with a decrease until 2013, however, from 2014 the cases show an upward trend, registering 372

confirmed cases in 2019 with an incidence of 16.9 cases per 100,000 inhabitants under one year of age.⁹

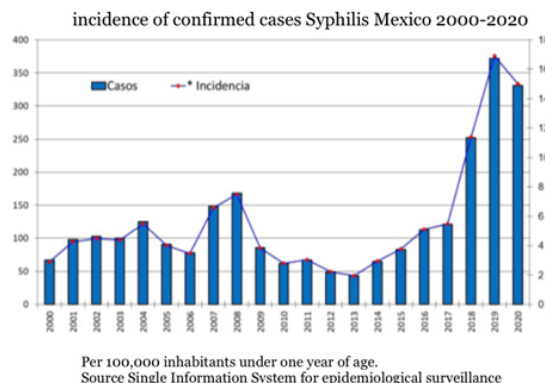


Figure 1 Source single information system for epidemiological surveillance.

For the year 2020, 331 confirmed cases of congenital syphilis were recorded, representing a reduction of 11% compared to the previous year (Table 1).⁹

Table 1 Confirmed cases and incidence of congenital syphilis by federal entity Mexico 2019-2020

State	2019		2020	
	Cases	Incidence	Cases	Incidence
Aguascalientes	16	62	38	147.7
Bma California	79	129	63	102
Baja California Sur	9	64	5	34.9
Coahuila	11	20.3	3	5.5
Colima	6	45	13	97.6
Chihuahua	4	3.6	5	7.2
Cilidaid De Mexico	3	2.5	0	
Durango	11	33.6	4	12.2
Guanajuato	6	3.6	4	3.6
Guerrero	4	8.6	2	2.9
Hidalgo	2	3.7	1	1.9
Jalisco	57	38.6	73	49.5
Michoacan	6	6.9	5	5.8
Morelos	1	2.9	1	2.9
Nayarit	12	51.3	5	21.2
Nuevo Leon	13	14.9	9	10.3
Puebla	5	4.1	5	4.1
Ouere Taro	2	5.3	2	5.3
Quintana Roo	2	6.3	5	15.5
San Luis Potosi	8	15.4	0	0
Sinaloa	29	55.0	22	41.9
Sonora	29	54.0	33	61.2
Tabasco	10	22.6	2	4.5
Tamaulipas	20	32.6	21	34.2
Veracruz	15	10.8	5	4.5
Yucatan	5	12.6	3	7.6
Zacatecas	2	6.7	2	6.7
Total	372	16.9	331	15.0

In the case of congenital Syphilis, abortions and stillbirth fetuses are not included in almost any country, therefore the case definitions for the diagnosis of Syphilis in pregnant women are not homogeneous.

Therefore, it remains the importance, and relevance of this manuscript to standardize the procedures of medical care and epidemiological surveillance as well as the early diagnosis and

treatment of maternal Syphilis and congenital Syphilis that are offered in the different units that conforms the national health system by state.

Starting with that, we will leave a definition according to terms;

Case of gestational syphilis

It is understood as almost gestational syphilis to be any pregnant woman, postpartum or woman with recent abortion, who has at least one positive non-treponemic test (VDRL or RPR) with titers equal to or greater than 1:8 dilutions or in fewer dilutions (1:2 or 1:4) as long as she has a positive treponemic test (FTA-abs or TPH).¹⁰

Compatible case of congenital syphilis

Any product of the gestation (Abortion, morinate or live birth) of a mother with gestational Syphilis without inadequate treatment or treatment, regardless of whether or not the product shows signs of disease and the result of non-treponemic tests. Case confirmed by epidemiological nexus.^{11,12}

Probable case of congenital syphilis

Any newborn with a positive non-treponemic (VDRL or RPR) or treponemic (ELISA, TPPA) test regardless of the maternal history and/or with clinical manifestations suggestive of congenital syphilis (Table 2).

Table 2 Syphilis serological tests

Non treponemal (VDRL or RPR)	Treponemal (TPHA or FTA-abs)	Interpretation
Negative	Negative	Healthy or very recent infection (<15 days)
Negative	Positive	Very recent or very old treated syphilis
Positive	Positive	Syphilis untreated or recently treated
Positive	Negative	False positive

Confirmed case of congenital syphilis

Children with a positive non-treponemic or treponemic test VDRL and FTA and/or MHA-TP positive and/or with clinical manifestations of congenital Syphilis and who tested positive for FTA IgM or Treponema Palidum was identified by dark field and/or IF of umbilical cord placenta lesions and autopsy.

Annulled case Congenital syphilis

Children without specific clinical manifestations of congenital syphilis and with negative laboratory tests (FTA-ABS or TPH).¹²

Diagnostic

Non-treponemic tests

They include flocculation tests such as those of Khan, Mazzini, Kline, the rapid reagin test and the most commonly used is VDRL, in which the presence of reagin is demonstrated, making dilutions until observing the last sample in which there is visible flocculation, the interpretation of VDRL can give false positives, especially in the face of This test is performed in the blood but can also be performed on cerebrospinal fluid (CSF), denoting neurosyphilis if it is reactive, particularly if the titration is greater than or equal to 1:8.¹³

Non-treponemic tests detect IgG and IgM antibodies against cardiolipins, cholesterol and lecithin produced in tissues damaged by treponema or other diseases. For this reason, they are not specific

tests for *Treponema pallidum*. The most used in our environment are VDRL And RPR, which have been shown to be very useful for early diagnosis and due to their relatively easy execution and low cost, it is convenient to be used as screening tests at the first level of care.¹⁴

Treponaemic tests

Those that detect specific antibodies directed against *Treponema pallidum* antigens. These tests require a reference laboratory, trained personnel and their performance is complex. They are known as confirmatory tests and the most common in our environment are FTA-AB's and TPHA, ELISA.¹⁵

FTA-AB's IgM is a more specific test, it uses indirect immunofluorescence to detect serum antibodies against spirochaete, it is performed in serum in primary and secondary syphilis and in CSF for tertiary sy, it is not recommended to evaluate the response to treatment, it can be false positive in individuals with systemic lupus erythematosus, genital herpes, frambesia, pinto disease and Lyme disease, etc.^{16,17}

Finally, cabinet studies should be carried out in all cases of suspicion or confirmation where osteochondritis and periostitis are documented in the metaphysis of long bones in early syphilis, during fetal life and the first postnatal stage, sometimes the lesions extend to the diaphysis being characteristic of the epiphysis being respected, it is rare that Affects cranial vault and late Syphilis affects ribs, flat bones and spine.¹⁷

The initial gestational diagnosis is made by VDRL or RPR. In our environment, it is necessary to request a non-treponaemic test from every pregnant woman when she begins her prenatal check-up, regardless of gestational age. If the initial test is negative, it must be repeated at 28 weeks or at the beginning of the third trimester. During this period, maternal treatment can still be effective in preventing congenital syphilis. At the time of delivery, another serology should always be performed and the hospital discharge of the mother and child binomial should not be authorized without knowing this result, (Official Mexican Standard NOM-039).

It is highly recommended that in the event of abortion or fetal death, a non-treponemic examination of the mother and the product also be performed. Unfortunately, this practice is rarely done in most public institutions of our health system.

It is important that a complete physical examination is also carried out in the face of clinical suspicion, this because the skin manifestations due to syphilis can be varied and unspecific; for this reason it is called "the great simulator".¹⁸

Treatment/Management

Treatment for congenital syphilis when the disease is confirmed or likely to be present is:

- Infants up to 4 weeks of age: Aqueous crystalline penicillin G, 50,000 units/kg per dose intravenously every 12 hours in the first seven days of life. After 7 days of life, 50,000 units/kg per dose intravenously (IV) every 8 hours for 10 to 14 days. Alternatively, procaine penicillin G, 50,000 units/kg/day intramuscularly for 10 to 14 days.¹⁸⁻²⁰
- Infants older than 4 weeks and older children: Aqueous penicillin G, 50,000 units/kg per dose every 6 hours intravenously for 10 to 14 days.¹⁸⁻²⁰

The management of an asymptomatic infant potentially exposed to syphilis but unlikely to have the disease is controversial. These are

infants of mothers who received adequate treatment more than 4 weeks before delivery. However, most experts and the CDC recommends benzathine penicillin G 50,000 units/kg per dose intramuscularly (IM) in a single dose in these asymptomatic children.^{18–20}

Differential diagnosis

Congenital syphilis may present similarly to other disease processes which should also be considered by the clinician. These include neonatal sepsis especially given the pneumonia-like chest x-ray findings in CS. Other considerations include TORCH infections including Toxoplasmosis, Rubella, Cytomegalovirus, herpes simplex virus. Neonatal hepatitis should also be considered given hepatomegaly and elevated LFTs. Co-infections with HIV should also be considered.

Table 3 Clinical findings related to congenital syphilis

System	Findings
Gestational	<ul style="list-style-type: none"> •Stillbirth •Prematurity •Small stature for gestational age •Nonimmune hydrops
Reticuloendothelial	<ul style="list-style-type: none"> •Generalized, nontender lymphadenopathy •Anemia (hemolytic and non) •Leukopenia or leukocytosis •Thrombocytopenia •Hepatosplenomegaly (extramedullary hematopoiesis)
Mucocutaneous	<ul style="list-style-type: none"> •Snuffles •Laryngitis •Maculopapular rash (coppery-brown) •Mucous patches (palate, perineum) •Condyloma lata (perioral and perianal)
Skeletal	<ul style="list-style-type: none"> •Symmetrical longbone lesions (lower>upper extremities) •Metaphyseal osteochondritis with mild to destructive lesions (5 weeks of infection) •Wimberger's sign: desmineralization and destruction of the proximal tibial metaphyses •Diaphyseal periostitis with periosteal new bone formation after 16 weeks of infection) •Osteitis ("celery stick" appearance)
Neurological	<ul style="list-style-type: none"> •Dactylitis with involvement of the metacarpals, metatarsals and proximal phalanges •Cerebrospinal fluid abnormalities (pleiocytosis, elevated protein, low glucose) •VDRL reactive in cerebrospinal fluid •Signs and symptoms of meningitis •Chronic meningovascular syphilis with hydrocephalus cerebral infarction and cranial nerves palsies
Ocular	<ul style="list-style-type: none"> •Salt and pepper chorioretinitis, glaucoma, uveitis
Other organ involvement	<ul style="list-style-type: none"> •Renal involvement: nephrotic syndrome •Pulmonary: pneumonia alba •Myocarditis •Pancreatitis •Gastrointestinal inflammation and fibrosis



Normal X-ray in an asymptomatic newborn son of a mother with syphilis.

Figure 2 Normal X-ray in an asymptomatic newborn son of a mother with syphilis.

Prognosis

Excellent prognosis if diagnosed and treated appropriately in a timely fashion. Syphilis is easily treated with penicillin. However, there is an increased risk for worse outcomes and possible death in:

- Premature infants
- Those who have a delay or do not receive proper treatment
- Patients who display an extensive spread of the disease with multiple organ failure
- Infants with a severe Jarisch-Herxheimer reaction upon treatment (Table 3) (Figure 2).

Complications

Delayed diagnosis and treatment can lead to late, persistent clinical features of intellectual disability, skin gummas, scarring, hearing deficits and skeletal abnormalities. Initiation of treatment in some infants can lead to a Jarisch–Herxheimer reaction leading to fevers, chills, hypotension, and possibly fetal death as a result of an inflammatory response to the dying spirochetes.

Clinical case

23-year-old mother, Original from Chihuahua, Mexico, social alcoholism, Elementary education, married, Started sexual life 15 years, sexual partners 3 gestations 3 Vaginal Delivery 0 cesarean 2 Abortion 0 death at one month of life of the newborn ;unknown cause 7 years ago probable sepsis. Prenatal control from week 7.5sdg adequate intake of Multivitamin and folic acid and ferrous sulfate diagnosis of Syphilis 3 years ago management with Penicillin G

Benzathine as well as during pregnancy from the beginning with Penicillin G Benzathine 2.4 million single dose at week 30.1 by US with VDRL (+) 1:56 other sexually transmitted diseases HIV and HEPATITIS B were negative. The Mother goes to evaluation where a cesarean section is scheduled. Obtaining a single female product of 37 weeks of gestation with vigorous crying, weight 7.45pounds, height 20.07 inches, head circumference 35cm, normal physical examination. No added data, control studies from the newborn with VDRL 1:10.28(+) are requested, for which a single dose of 50,000IU Crystalline Penicillin Aquosa is indicated. Before discharge with an appointment in 1 week and after this each month to see a decrease in titers.

Discussion

Neonates with congenital syphilis are infected in utero, or by contact with active genital lesions at the time of passage through the birth canal at birth. The primary mode of horizontal transmission is by sexual contact.¹

About 60% of infected neonates are asymptomatic at birth and develop the first clinical manifestations of the disease in the first weeks, particularly in the second to sixth week of life, classifying it as early or late. The early congenital presentation is polymorphic, characterized by persistent rhinitis in 4% to 22% of cases; hepatosplenomegaly, generalized lymphadenopathy, vesicular-bullous or maculo-papular exanthema, associated with scaling of the palms of the hands and soles of the feet, presenting erythema multiforme and interstitial keratitis.¹⁻⁵ Holler⁶ points out that in 88% of cases with congenital syphilis they have elevated liver transaminases, 35% have thrombocytopenia and 26% anemia; positive VDRL is reported in 80% of cases. The presence of glomerulonephritis is also reported in them and in premature infants there is a high frequency of intrauterine death or in the perinatal stage. Radiographic abnormalities are reported in 20% of these children: they affect the tibia, tubular bones of the hands and feet, clavicles, and cranial bones. Osteochondritis (also known as pseudo-Parrot's palsy) are the most common and earliest lesions: they are characterized by asymmetric pain and flaccid paralysis of the upper extremities. Diaphyseal periostitis is asymptomatic and radiographic changes are usually seen after three months of age.

As for cutaneous-mucosal lesions, they present in the neonatal period and include: rhinitis, condylomas planes, mucous membranes, erosions, scaly violaceous papules and hemorrhagic blisters. These can be present at birth or appear in the first weeks of life. Hemorrhagic vesicles and blisters on the palms and soles of the feet are considered pathognomonic of congenital syphilis and papulosquamous lesions are the most frequent lesions, and are the same as those that occur in secondary syphilis of the foot. adult.⁷

When congenital syphilis develops after 2 years of age, it is characterized by chronic granulomatous inflammation,^{3,4} and with regard to neonatal neurosyphilis (usually asymptomatic), it is difficult to diagnose. suspicion, it is recommended to perform histochemical studies and VDRL of the CSF, which usually has low sensitivity, but is associated with histochemical alterations: such as increased cellularity and proteins; it also correlates with the identification of *T. pallidum*.⁶⁻¹⁰ Beta 2 microglobulin is a low molecular weight protein (11,800 Daltons); it constitutes the light chain of class 1 HLA antigens and is present on the surface of all nucleated cells; of this, a high concentration is observed in inflammatory states that generally decreases after treatment with antibiotics, but is not specific for syphilis.⁹ The diagnosis of congenital syphilis is difficult to confirm and there is still no rapid, sensitive and specific method available to confirm the diagnosis in children who are born asymptomatic. *Treponema*

pallidum cannot be cultured and identification of spirochetes in body fluid samples (using darkfield microscopy) has low sensitivity in newborns.¹¹ The serological tests used in the diagnosis of syphilis, such as VDRL, RPR (Rapid Plasma Reagin) and tests confirming the presence of *treponema*: as FTA-ABS (Indirect immunofluorescence with absorption and double staining) and MHA-TP, detect IgG and IgM immunoglobulins. In this regard, during pregnancy, especially in the last trimester, IgG passes through the placenta, so positive serology in a newborn does not allow to differentiate the passive transfer of maternal antibodies and the infection of the newborn by syphilis.¹¹⁻¹³ False positive reactions can be secondary to some viral infections such as: infectious mononucleosis, hepatitis, chicken pox or rubella; or by tuberculosis, malaria, lymphoma, endocarditis, connective tissue disease. For a false-positive non-treponemal test result, confirmatory studies of the presence of *treponema* may be necessary: by detection of fluorescent treponemal antibodies by absorption (FTA-ABS) or by agglutination of *Treponema pallidum* (TPPA). Antibody titers remain reactive throughout life, even after treatment, and their presence correlates poorly with clinical disease activity and may not be used to assess therapeutic response.¹¹⁻¹³

The use of treponemal and non-treponemal tests have been replaced by enzyme tests known as immunoassays, which recognize the presence of IgG and IgM to treponemal; A quantitative non-treponemal test and specific serology for antitreponemal IgM are also used to monitor the effect of the instituted treatment. It is worth mentioning that it is not possible to detect IgM between 3 and 9 months of life, when early syphilis has been successfully treated; change in late syphilis it is possible that IgM may be positive up to 18 months after treatment. The diagnosis of congenital syphilis by polymerase chain reaction (PCR) has a sensitivity of 94% in serum or blood, while its sensitivity in CSF is 65%; however, it is a technique that ordinarily not available.¹¹⁻¹³

As far as treatment is concerned, parenteral penicillin G continues to be the drug of first choice, in newborns the recommended dose of crystalline aqueous penicillin is 100,000-150,000 U/kg/day, administering as 50,000 U/kg /dose every 12 hours in the first seven days of life and in intervals of eight hours up to a total of 10 days. The treated neonates are followed up at 3, 6 and 12 months, until serological laboratory studies are negative.^{11,13}

Conclusion

It is convenient to incorporate a prenatal screening program for the diagnosis and prevention of congenital syphilis, between weeks 11 to 20 of the season, and it is recommended to repeat this study in the third trimester of pregnancy. The US Center for Disease Control (CDC) recommends using VDRL at the first visit of the pregnant woman and at 28 weeks it is suggested to do an additional test and scrutiny of the woman's sexual history, since the treatment in pregnant women before 20 weeks of gestation prevents this disease in the fetus but not when it is treated after this period. The early prevention of congenital syphilis in newborns is possible by diagnosing this disease in pregnant women and early diagnosis and correct treatment of newborns with syphilis is effective, so it falls on obstetricians and pediatricians to avoid the neurological consequences of syphilis congenital.

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Conflicts of interest

No potential conflict of interest was reported by the authors.

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