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RESEARCH ARTICLE

Congenital Syphilis

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Abstract

The risk of transmission of syphilis to the fetus depends on the stage of syphilis, primary at 100%, secondary at 70%, early latent at 40%, the risk of transmission increases with the progression of pregnancy. Congenital syphilis is defined by the presence of:

- a child born to a mother who is not or badly treated
- a child with clinical or biological signs of congenital syphilis.

Early congenital syphilis (before 2 years) may be asymptomatic in 2/3 of cases or result in a disseminated fulminant infection, mucocutaneous lesions, osteochondritis, anemia, hepato-splenomegaly, neurosyphilis. Late congenital syphilis (> 2 years after birth) can manifest as interstitial keratitis, lymphadenopathy, hepato-splenomegaly, bone lesions, anemia, dental malformations (Hutchinson's teeth), neurosyphilis.

Screening carried out during the first trimester and between the 28th and 32nd week of pregnancy aims to prevent the transmission of syphilis to the fetus. Screening performed shortly before the end of pregnancy or at the time of delivery is mainly used to detect cases.

Samples of placenta, cord, amniotic fluid, gastric fluid, nasal and oral discharge, CSF, newborn skin lesions can be analyzed by PCR to detect T. pallidum DNA. Any suspected case of congenital syphilis must be assessed by the CNR IST Bacterial Syphilis expertise (sending sample(s) for confirmation by PCR and serological tests).

Serological tests on the child's blood sample (1 ml) with the determination of specific IgM (note that cord blood is not suitable) and maternal serum (2 ml) taken at birth. Interpretation of serodiagnosis should take into consideration maternal history, including stage of syphilis, maternal treatment, and maternal serologic results. Infected infants are often asymptomatic at birth and may be HIV-negative if the mother was infected late in gestation.

Maternal treatment is based on the early administration of penicillin. Child care is based on diagnosis and early treatment with parenteral penicillin. Infants should be treated at birth 1) if symptomatic, 2) if the TNT non-treponemal test titer is four times (two dilutions) or more that of the mother, 3) if the mother's treatment was not not adequate, did not contain penicillin, is unknown, occurred in the last month of pregnancy or 4) if the mother's serological response to treatment is inadequate, 5) if follow-up of the infant cannot be guaranteed.

Keywords: Syphilis; Pregnancy; Screening; Newborn

Introduction

Syphilis is a sexually transmitted infection (STI), caused by the strictly human spirochete Treponema pallidum pallidum (TPP). TPP is a highly invasive bacterium that is able to cross the placental barrier leading to congenital syphilis. Congenital syphilis represents a major public health problem in developing countries but also in Western countries in populations where monitoring of pregnant women is weak, or even non-existent. It is estimated that the incidence of syphilis represents 150,000 new cases per year worldwide and that syphilis is responsible for more than 210,000 miscarriages or premature deliveries. It can be associated with fetal loss, early neonatal death (50%), prematurity (25%), severe neonatal infection with deformative and/or neurological sequelae in surviving children (20%). Prevention of infection is based on systematic screening at the start of pregnancy, to be repeated in the event of a high risk of exposure by a treponemal test TT (TPPA or Elisa) coupled with a non-treponemal test TNT (VDRL or RPR).

It is recent infections (primary, secondary, early latent syphilis < 1 year) that confer the highest risk of mother-to-child transmission. In these situations, the precocity of the treatment determines the obstetrical prognosis.

Child care is based on diagnosis and early treatment with parenteral penicillin. Maternal management is based on the early administration of penicillin.

Congenital syphilis remains a major cause of fetal morbidity and mortality worldwide.

Epidemiology

General Notions

Treponema pallidum pallidum is the agent of syphilis. It is a spirochete bacterium: spiral Gram-negative bacillus, whose only reservoir is man.

Other subspecies are associated with non-venereal treponemal infections responsible for benign skin lesions:

- T. pallidum endemicum is responsible for Bejel in dry and desert areas of Africa, the Middle East, Iran, Afghanistan
- T. pallidum pertenue is responsible for yaws in hot and humid subtropical regions,
- T. pallidum carateum is responsible for the Pinta in Latin America.

Impact

The incidence of congenital syphilis has been rising since 2005 in Europe, the United States and China, where a 70% rise has been reported in 15 years. [1]

The number of pregnancies complicated by syphilis is estimated at around 1 to 1.3 million per year worldwide, with 50% miscarriages/perinatal deaths, 25% IUGR/prematurity and 25% patent congenital syphilis. [1, 2]

Congenital syphilis is responsible for 1.3% of deaths of children < 5 years old, and more children are currently born with congenital syphilis than children with congenital HIV. [3]

Transmission [4]

Transmission of syphilis is either direct or vertical from an infected mother to her child.

direct transmission

Direct transmission is the consequence of skin contact with healthy skin or mucous membranes, through sexual contact. The risk of transmission is about 30%.

Vertical Transmission

The transplacental passage during maternal spirochetemia takes place from 14-16 weeks of amenorrhea (SA), the fetal infection is immediately disseminated, like secondary syphilis.

The risk of transmission is 60-100% for primary or secondary syphilis, 40% for early latent syphilis (<1 year) and 8% for late latent syphilis (>1 year) The risk of transmission increases with progression of the pregnancy. [5.6]

Postnatal transmission is exceptional. No case of transmission through milk has been reported.

The infection is not immunizing and recontamination is possible after complete treatment.

Clinical

Maternal Syphilis

Syphilis is a slow-growing, chronic disease. It consists of a succession of short symptomatic phases and prolonged asymptomatic phases. After contact with the bacteria, the incubation period is 10-90 days (3 weeks on average), this is the most contagious period.

- The primary infection is characterized by an ulcer or chancre, usually painless. It can persist for 3 to 8 weeks and is accompanied by satellite lymphadenopathy.
- Secondary infection is the phase of dissemination of the infection by several mucocutaneous eruptions (syphilitic roseola, palmoplantar papular syphilides, mucous patches, angina, angular cheilitis, alopecia), sometimes associated with fever, asthenia, arthralgia and adenopathies.
- Latent infection detected by serological tests, has no clinical manifestations
- o Early latent syphilis < 1 year after infection
- Late latent syphilis > 1 year after infection of unknown duration
- Tertiary infection is characterized by cardiovascular involvement (aortitis), neurological involvement (dementia, tabes, meningeal involvement 10%) and skin involvement (gums 10%)
- Neurosyphilis can occur at any stage of syphilis.
- Early symptomatic neurosyphilis in 5% of cases in the form of lymphocytic meningitis, damage to the cranial pairs, cerebral vascular syphilis and ophthalmological forms (uveitis)
- Late neurosyphilis (tabes, general paralysis), may be asymptomatic.

In the Fetus and Newborn [1,14,15]

Congenital syphilis is complicated by fetal death in utero in 40% of cases, prematurity in

25%. Neonatal infection classified as early, onset of signs in the first 2 years of life, (1/3 of cases) and late, onset of signs after the age of 2 years, (2/3 of cases).

Early congenital syphilis (<2 years)

It is manifested by hepatomegaly, splenomegaly, jaundice, nephrotic syndrome, rhinorrhea, palmoplantar bullous skin lesions, central neurological involvement, meningitis.

Late congenital syphilis (>2 years)

It is manifested by a frontal deformity (bumps), facial deformities (short jawbones, saddle nose), palatal deformity and rhagades (periorificial skin clefts), dental lesions (Hutchinson's tooth), interstitial keratitis

This neonatal infection is rapidly fatal in 20% of cases. It is complicated by serious sequelae in adulthood in 20% of cases. Any fetal loss after 20 weeks of amenorrhea must be explored by syphilitic serology. [1.14]

The antenatal sonographic warning signs are detailed in Table 1. [15]

Call signs
Fetal death in utero
Intrauterine growth retardation
Bony striae
Hydrops fetalis
Placental thickening
Ascites
Hepato-splenomegaly,
Intestinal hyperechogenicity
Hydrocephalus, cerebral calcifications

Table 1: Sonographic signs suggestive of congenital syphilis

Clinical signs Percentage
Early congenital syphilis (first sign before age 2)
Osteochondritis or arthritis 61%
Hepatomegaly 51-100%
Splenomegaly 49%
Petechiae 41%
Other skin lesions (contagious)
Flat or nodular lesions of the trunk
Palmoplantar bullous lesions 35%
Meningitis with central neurological involvement, including pseudoparalysis of a limb 15-25%
Lymph nodes 32%
Jaundice 30%
Anemia and other cytopenias often appearing between 2 and 8 weeks of life 30%
Rhinorrhea 23%
Nephrotic syndrome 20%
Late congenital syphilis (first sign after age 2)
Frontal deformation (bumps)
and facial deformities (short jaws, saddle nose) 30-87%
Palatal deformity and rhagades (periorificial skin clefts) 76%
Dental lesions (Hutchinson tooth) 55%
Interstitial keratitis 20-50%
Scarring bone lesions 30-46%
Nasal deformation 10-30%

Table 2: Clinical presentation of congenital syphilis

Adapted from [6]

Among the signs of early congenital syphilis, the presence of rhinorrhea, contagious very rich in treponemes, has a strong orientation value; it occurs 1-2 weeks before the eruption. Cutaneous signs predominate on the extremities and are highly contagious.

Late congenital syphilis lesions are essentially "scarring" lesions which are the consequence of early lesions: deforming bone, dental, neurological and cutaneous damage. Among them we distinguish the triad of Hutchinson: teeth of Hutchinson + interstitial keratitis + deafness by attack of the auditory nerve.

Maternal Care: Screening

Screening should be performed during the prenatal examination of the first trimester of pregnancy, repeated at 28 weeks if the patient is at risk (multiple partners, recent or current STI). It must also be carried out before leaving the maternity ward for any unmonitored pregnancy. [7]

It is based on a treponemal TT test (TPPA/Elisa) and a non-treponemal TNT test (VDRL/RPR). [8]

Direct Diagnosis

Any suspected case of congenital syphilis must be assessed by the CNR IST Bacterial Syphilis expertise which performs genomic detection of TPP by (nested PCR) on the samples of placenta, cord blood, cord, amniotic fluid, nasal, oral, gastric secretions, CSF and skin lesions. [9, 15]

Indirect “serological” diagnosis

The specific treponemal test or TT detecting IgG and IgM by the automated ELISA / EIA tests (replacement of the TPHA), supplemented by a quantitative non-treponemal test or TNT (VDRL / RPR) on the same serum if it is positive. [8]. the interpretation of the serological results is presented in Table 3

TT
EIA/CLIA (IgG/IgM) DTT
(RPR/VDRL) Additional examination Interpretation
Negative
Negative
Not performed No treponematosis
If syphilis suspected, check on a second serum in 2 to 4 weeks.
Positive
Negative
IgG immunoblot
Positive or doubtful A. Syphilitic treponematosis
1.Very recent syphilis before TNT seroconversion
2. Old untreated syphilis (late latent)
3.Syphilis treated (serological scar)
B. Possible non-venereal treponematosis (yaws, bejel, pinta)

Positive
Negative
IgG immunoblot
Negative False positive probable TT
Causes: spirochetes, borreliosis, leptospirosis.
If syphilis in the incubation phase or primary syphilis suspected, remote control on a second serum.
Positive
Positive
IgG immunoblot
Positive or doubtful Probable syphilitic treponematosis
1. primary, secondary or early latent (high titers)
2. Late latent (low titers)
3.Tertiary (low titers)
4.Processed with TNT persistence
Negative
Positive
Negative False positive of TNT
Causes: collagenoses, pregnancy, injection drugs, viral infections.
If syphilis

Table 3: Interpretation of serological results

Adapted From [7]

TT: treponemal test; TNT

Non-treponemal test: The diagnosis of syphilis requires performing a complete assessment of other possibly associated infections (HIV serology, HBV, Chlamydia/gonococcal PCR on a vaginal sample), and screening and treatment of the partner(s) of the last 3 months .

Maternal Treatment

Treatment in the first trimester reduces the risk of perinatal mortality by more than 90%. The challenge is therefore to detect and treat before 16 weeks [10,11]. The treatment and follow-up methods are detailed in Table 4.

Stage Molecule Tracking
Primary syphilis
Secondary syphilis
Latent syphilis < 1 year Benzathine Penicillin
Two administrations of 2.4 million units 1 week apart Control serology at 1, 3, 6, and 12 months with TNT (titer divided by 4 every 3 months)
Latent syphilis > 1 year
or not datable
Tertiary syphilis Benzathine Penicillin

Table 4: Modalities for the treatment of syphilis and follow-up in pregnant women, according to the stage of infection

Three administrations of 2.4 million units with a 1-week interval between each administration Control serology at 6, 12 and 24 months with TNT (titer divided by 4 every 6 months)

Neurosyphilis Penicillin G IV 3-6 Million Units/4H (20 Million U/d) 14 days Control serology at 6, 12 and 24 months by TNT

In case of maternal allergy to penicillin, the recommended treatment remains penicillin, and prior desensitization must be performed. No study has evaluated the efficacy of ceftriaxone in syphilis in pregnant women, and this treatment cannot be recommended in case of allergy. [12,14]

Neonatal evaluation of a child whose mother has been diagnosed with syphilis [13]

The elements to be collected at birth to assess the child's risk are as follows:

- Age of maternal infection, maternal term at the time of treatment
- Clinical signs of congenital syphilis (hepatomegaly, rash, pseudo paralysis of one extremity, rhinitis, hydrops).

Syphilis PCR is to be performed on a placental cotyledon, any nasal secretions or skin lesions, if present, and on 1ml of cord blood in a dry tube, systematically at birth. It is recalled that any suspected case of congenital syphilis must be assessed by the National Reference Center for Syphilis.

A non-treponemal test should be performed on the child's blood sample (1ml) (note that cord blood is not suitable) with a specific IgM assay and a maternal serum sample (2ml) should be taken at the birth.

Depending on these elements, different situations can be individualized, leading to different management strategies detailed in Table 5.

Clinical situation Management
Confirmed/very likely (CDC scenario 1 and 2) or probable (CDC scenario 3) case
Confirmed Case:
Clinical signs are present: hepatomegaly, splenomegaly, jaundice, nephrotic syndrome, rhinorrhea, palmoplantar bullous skin lesions, central neurological involvement, meningitis.
Positive PCR on a NN sample: cord blood, placenta, nasal and oral secretions, CSF and skin lesions

Table 5: Management of a child born to a mother with positive syphilitic serology. [13]

Very likely case:

Maternal treatment not done, or badly done AND

1. DTT serum NN ≥ 4 x maternal serum or

2. Positive NN serum TNT and suggestive clinical signs

3. IgM Elisa NN positive

Likely case:

Maternal treatment not done, badly done, not documented, or < 4 weeks before delivery, absence of maternal serological decrease

Adapted From [13]. NN newborn; + positive

Cerebral involvement is found in 50% of probable or confirmed cases of congenital syphilis, justifying the systematic performance of LP in this context. The criteria for neonatal neurosyphilis are:

- CSF hypercellularity. Neonatal neurosyphilis criteria > 25/mm3,
- Proteinorachia > 1.5g/L (>1.7g/L c/o premature),
- Positive PCR in CSF.

The diagnosis of congenital syphilis is sometimes made after birth, by the pediatrician, in children born to mothers who are not monitored or not screened. The clinical signs are those of the late forms listed above. Biologically, the persistence of positive TT and TNT serology at 12 months confirms the infection.

Paraclinical assessment includes maternal syphilitic serology, CSF analysis (cellularity, VDRL and PCR), NFS, liver assessment and long bone X-ray. The rest of the assessment is guided by the clinical context: ophthalmological consultation, transfontanellar ultrasound, auditory evoked potentials.

The treatment is based on penicillin G IV 150,000 U/kg/day (in 6 doses every 4 hours) for 10 days (14 days if neurosyphilis). Serological monitoring is identical to that of children diagnosed at birth.

Declaration of Interests

The authors declare that they have no conflicts of interest in relation to this article

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