**ABSTRACT**

**Background:** Congenital syphilis (CS) is attributable to the transmission of *Treponema pallidum* from the mother to the fetus transplacentally during gestation. The incidence rate of congenital syphilis is 15 per 100,000 newborns by 2020. Mucocutaneous involvement is present in as many as 70% of infants and may be apparent at birth or develop during the first few weeks of life. Cutaneous findings of early CS classically a vesiculobullous or maculopapular rash on the palms and soles may be associated with desquamation. Skeletal manifestations of congenital syphilis occur in 60%-80% of infants, including osteitis (0.7%), metaphysitis (24%), and periostal reaction (34%). It is important to be fully informed regarding the early diagnosis and treatment of congenital syphilis to prevent its devastating complications to death. This case report describes clinical features, treatment, and prognosis of congenital syphilis presented with mucocutaneous lesions and musculoskeletal manifestations.

**Case Representation:** A one-day-old boy preterm infant, 2145 grams, born spontaneously, presented with ruptured bullous lesions and desquamation on the feet and hands. The laboratory revealed thrombocytopenia, elevated C-reactive protein, elevated bilirubin total (10.9 mg/dL) and direct bilirubin (6.21 mg/dL) at 24 days old, indicating an intrahepatic cholestasis caused by syphilis. Serum VDRL 1:128 and TPHA >1:5120. Long bone radiology showed periostitis involving the humerus, ulna, radius dextra and sinistra, femur dextra and sinistra, a feature of congenital syphilis. The patient was treated with procaine penicillin 107,000 international units intravenous every 24 hours for 10 days.

**Conclusion:** The early recognition of mucocutaneous and musculoskeletal involvement as an early manifestation of CS improved with procaine penicillin intravenous for 10 days.

**Keywords:** cholestasis, congenital syphilis, mucocutaneous, musculoskeletal.


**INTRODUCTION**

The rate of reported congenital syphilis in the United States has increased dramatically since 2012. During 2019, a total of 1,870 cases of congenital syphilis were reported, including 94 stillbirths and 34 infant deaths. The 2019 national rate of 48.5 cases per 100,000 live births represents a 41% increase relative. In 2018, the prevalence was about 34.3 cases per 100,000 live births, increasing 477% relative to 2012 (8.4 cases per 100,000 live births). During 2015-2019, the rate of congenital syphilis increased 291.1% (12.4 to 48.5 per 100,000 live births), which mirrors increases in the rate of primary and secondary syphilis among females aged 15-44 years (a 171.9% increase, from 3.2 to 8.7 per 100,000 females).1-3

The World Health Organization (WHO) estimates the prevalence of syphilis in pregnant women to be approximately 1.8 million, and less than 10% are diagnosed so that they do not receive therapy. The prevalence of syphilis in pregnancy in 2016 in Southeast Asia is estimated to be around 0.21% or 78,000 cases of all pregnancies, while the exact prevalence rate in Indonesia has never been reported before. Syphilis cases in pregnancy throughout the world are still quite high, especially in developing countries. There were an estimated 930,000 cases of syphilis in pregnancy in 2012, and in 350,000 cases, there were complications due to syphilis.4,5

Syphilis is an infectious disease caused by *Treponema pallidum*, which belongs to the Spirochaetaceae family. Children usually experience two forms of syphilis: acquired syphilis, which is almost transmitted sexually and congenital syphilis, which is transmitted transplacentally. Syphilis is a progressive disease that may result in death or significant neurologic and musculoskeletal disabilities if treated inadequately.5

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Mucocutaneous and musculoskeletal manifestation as an early symptomatic congenital syphilis: A rare case

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CASE REPORT

According to a Centers for Disease Control (CDC) and Prevention report, untreated syphilis, especially early syphilis, during pregnancy can lead to deafness, neurologic impairment, bone deformities, stillbirth, and neonatal death. Congenital syphilis does not have a primary stage. Early onset disease manifestations are analogous to the secondary stages of acquired syphilis. Late-onset disease is seen in patients older than 2 years and is not considered contagious.1–9

Early congenital syphilis refers to clinical manifestations that appear in the first 2 years of age. Hepatosplenomegaly secondary to either extramedullary hematopoiesis or hepatitis is frequent and may take months to resolve. Thrombocytopenia with petechiae and purpura also occurs frequently. Mucocutaneous lesions are prominent manifestations in 40-60% of affected infants.2

Multiple studies have shown that vertical transmission to the fetus correlates with the stage of maternal syphilis and that the highest transmission rates, up to 60%, are seen in early maternal syphilis. Early congenital syphilis refers to the manifestation of disease within the first 2 years of life. Skeletal changes in early congenital syphilis include osteitis (0.7%), metaphysitis (24%), and periosteal reaction (34%). These changes are typically symmetrical in the involved long bones, keeping with their systemic etiology. Recognition of these imaging findings can help pediatric teams diagnose early congenital syphilis and initiate antimicrobial treatment.5

Congenital syphilis is a multisystemic condition caused by transplacental treponema pallidum infection. The clinical, biochemical, and radiographic findings of congenital syphilis are due to the inflammatory response induced by the spirochete in various organs. Multiple studies have shown that vertical transmission to the fetus correlates with the stage of maternal syphilis and that the highest transmission rates, up to 60%, are seen in early maternal syphilis.3

Diagnosis of congenital syphilis can be difficult because maternal nontreponemal and treponemal immunoglobulin G (IgG) antibodies can be transferred through the placenta to the fetus, complicating the interpretation of reactive serologic tests for syphilis among neonates (infants aged <30 days). Therefore, treatment decisions frequently must be made based on the identification of syphilis in the mother, adequacy of maternal treatment, presence of clinical, laboratory, or radiographic evidence of syphilis in the neonate and comparison of maternal (at delivery) and neonatal nontreponemal serologic titers (RPR or VDRL) by using the same test, preferably conducted by the same laboratory.1

We report a case of skin-ruptured bullous lesions and periostitis musculoskeletal, a feature of congenital syphilis that presents in young infants. This case report aims to describe the clinical and examination aspects of congenital syphilis.

CASE REPORT

A preterm infant, 1 day old, was born to a mother who had untreated syphilis during pregnancy. During subsequent antenatal follow-up visits, serial fetal ultrasound scans demonstrated symmetric intrauterine growth retardation. The fetus was delivered spontaneously vigorously at birth with normal Apgar scores and a weight of 2145 grams.

Immediately after the delivery, the neonate was found to have a bullous on the dorsum manus dextra and dorsum pedis sinistra. After 2-3 hours, the bullae ruptured. Ruptured bullous lesions, scaly and rashes were on his feet and hands on his body. Multiple erythema macula with clear uneven margins and geographic shape 0.1x0.3 cm to 0.5x0.8 cm with a white squama, partially covered with white scales and desquamation and solitary erosion, on dextra wrist, dextra pedis and dextra inguinal. On palmar manus sinistra found desquamation (Figure 1 and 2).

The overall condition of the neonate was seen as yellowish, with no hepatosplenomegaly; physiological reflexes were obtained, and the muscle tone was sufficient. The laboratory tests revealed thrombocytopenia 24 x 10⁹ / μL, anemia 10.1 g/dL, with elevated C-reactive protein 154.60 mg/dL. The patient’s Treponema pallidum particle agglutination (TPPA) test was reactive with reactive VDRL (Venereal Disease Research Laboratory) 1:128 and TPHA (Treponemal pallidum Hemagglutination Assay) >1:5120. Elevated bilirubin total (10.9 mg/dL) and direct bilirubin (6.21 mg/dL) at 24 days old indicate an intrahepatic cholestasis caused by syphilis. Cerebral spinal fluid (CSF) analysis showed results within normal limits; there was no reagent of VDRL and TPHA for CSF analysis.

The mother’s serum of VDRL was reactive (1:256) and TPHA reactive (>1:5120) revealed after the baby’s age of 4 days. The mother did not get any...
CASE REPORT

Proven syphilis was established. The patient was treated with intravenous procaine penicillin (50,000 IU/kg/time) for up to 10 days, hepatoprotector and multivitamins were given to treat cholestasis suspected caused by syphilis, and skin moisturizer for skin lesions given by the dermatology and venereology division.

The neonate’s overall condition remained satisfactory throughout the treatment period. The recommendations were VDRL serological follow-up examination at the age of 1, 2, 3, 6, 12, 24 months until the result is nonreactive, and follow-up examination of the auditory and ENT.

DISCUSSION

Congenital syphilis occurs as a result of maternal transmission of Treponema pallidum in utero. Treponemal and non-treponemal serologic tests mainly diagnose this condition. However, maternal treponemal and non-treponemal IgG antibodies can be transferred through the placenta to the fetus, thus complicating its interpretation. As such, Treponema pallidum hemagglutination assay (TPHA) and non-treponemal rapid plasma reagent (RPR) can show false positive results in uninfected infants of seropositive mothers. In this case, the ruptured bullous skin lesions and periostitis in the long bones radiographic showed that presumed vertical transmission has occurred, mandating immediate treatment.4, 5

The majority of cases of congenital syphilis occur in neonates born to women who fail to undergo clinical examination and adequate treatment for syphilis prior to or during pregnancy. In 30% to 40% of the cases, untreated intrauterine syphilis infections cause abortion, stillbirth, exitus lethalis immediately after birth, or preterm delivery. Two-thirds of neonates with congenital syphilis have no symptoms after birth. Without treatment, clinical symptoms usually emerge at the age of 5 to 12 weeks.6

Specific clinical signs of congenital lues include fever, maculopapular rash (frequently on palms and soles), petechiae, lip swelling, radial tears (healing with scarring, Parrot’s signs), blisters, giant condylomas, mucosal ulcers, snuffles (rhinitis syphilitica), pseudoparalysis...
(due to osteochondritis or periostitis in the area of the epiphyses of forearm or other bones), interstitial hepatitis, lymphadenopathy, treatment-resistant enteritis, laryngitis, hemolytic anemia, and glomerulonephritis. Symptoms of meningitis usually emerge between the ages of 3 and 6 months, and other types of CNS (Central Nervous System) damage (hydrocephalus or convulsions) are possible.\textsuperscript{7}

Specific signs of late congenital lues include the true stigmas: “saddle nose,” Parrot radial lines (rhagades), Hutchinson’s triad (interstitial keratitis inflammation of the cornea), Hutchinson’s teeth, and deafness, Clutton’s joints, a high palatal vault, bossing of the frontal bone, a short maxilla, a protruding mandible, thickening of the sternoclavicular joint, and other signs (paroxysmal cold hemoglobinuria, neurological impairment, or gummas in parenchymal organs).\textsuperscript{7}

A neonatologist needs to know the tactics of the examination and treatment of a neonate born to a mother with syphilis. The detection of Treponema pallidum best confirms the diagnosis of congenital lues via the application of dark field microscopy, direct immunofluorescence, or polymerase chain reaction. However, serological tests (with the mother’s and the child’s blood) are most commonly used to detect treponemal TPHA and RPR antibodies, and IgM immunoblot for \textit{Treponema pallidum} is used as well.\textsuperscript{10}

If the mother is still TPHA-positive during pregnancy, the child will always be positive because of IgG passively crossing the placenta barrier; the test will become negative after 7 or 8 months of life. VDRL and RPR indicate an acute infection, and their titers drop when effective therapy is applied.\textsuperscript{10} A complete blood count in the presence of congenital lues shows anemia, leucopenia or leucocytosis, and thrombocytopenia. An X-ray examination of the long bones is advisable to detect possible bone damage.\textsuperscript{11}

The treatment of congenital syphilis should be immediately initiated in neonates whose lues-infected mothers had not been adequately treated, as well as in neonates in whom congenital syphilis was diagnosed via laboratory testing. The most effective treatment for congenital syphilis is benzylpenicillin 150 000 IU/kg/day for 10 to 14 days. If neurosyphilis is diagnosed, a higher dose of penicillin for a longer treatment period should be undertaken (150,000-200,000 IU/kg for 14-21 days). Prevention, that is, early antenatal serological screening and effective treatment of pregnant women, is especially important.\textsuperscript{11}

Skeletal manifestations of congenital syphilis occur in 60%-80% of infants with clinical signs of congenital syphilis and in 20% of infants who appear clinically normal. Long bone radiographs are useful in demonstrating skeletal manifestation of early congenital syphilis. Neonatal radiographs showing a periosteal reaction, diffuse or localized osteitis, and metaphysitis fulfill the criteria for presumed congenital syphilis. In this case, lucency at metaphysis and diaphysis dextra proximal dextra humerus and dextra proximal ulna is a feature of periostitis in congenital syphilis. On radiographs, lucency and destruction on metaphysis dextra et sinistra humerus, a feature of Wimberger’s sign manifested a feature of syphils congenital.\textsuperscript{3}

Prompt treatment of congenital syphilis is important in order to avoid later complications that usually manifest after 2 years of life. The most specific sign of late congenital syphilis is Hutchinson’s triad, which consists of Hutchinson’s teeth, eighth cranial nerve deafness, and interstitial keratitis. These complications result from persistent inflammation or scars caused by \textit{treponema pallidum} infection in various organs.\textsuperscript{3}

Repeat RPR testing assesses the treatment response in infants who have completed the standard antibiotic regime. Retreatment or repeat CSF study is indicated if there is an absence of fourfold titer reduction over 12-18 months or if titers increase. In this case, the patient was advised to evaluate serum VDRL at ages 1, 2, 3, 6, 12, 24 months or until the result is nonreactive.\textsuperscript{3}

Congenital neurolyes is characterized by cytosis with predominant lymphocytes and elevated CSF protein levels. The venereal disease reference laboratory test (VDRL) with CSF is conducted to detect antibodies. In this case, cerebral spinal fluid (CSF) analysis showed results in normal limit; there was no reagent of VDRL and TPHA for CSF analysis. Neonates with congenital syphilis had symptoms at birth or within the first 4 weeks of life. The risk of symptoms was higher, with mothers receiving no treatment at all. In this case, the infant had a symptom right after delivery, and the mother did not receive any treatment.\textsuperscript{12,13}
CONCLUSION

The early recognition of mucocutaneous and musculoskeletal involvement as an early manifestation of CS improved with procaine penicillin intravenous for 10 days.

DISCLOSURE

Funding

None.

Ethical Consideration

The patient’s parents signed the informed consent and agreed that the medical data would be published as a case report in medical scientific journals.

Conflict of Interests

The author reports no conflicts of interest in this work.

Author contribution

All authors contributed equally.

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