

Varied Clinical Presentations of Congenital Syphilis in Infants: A Case Series of 7 Cases

KS SANJAY¹, USHA BANGALORE KANTHARAJANNA², RATAKONDA SRUTHI³, CHANDANA KALAVALA⁴

ABSTRACT

Congenital Syphilis (CS), also known as mother-to-child transmission of syphilis is caused by *Treponema pallidum*. Infected pregnant women can transmit the infection vertically to the foetus. Diagnosis of CS can be difficult because more than two-thirds of affected infants remain asymptomatic at birth, and signs may be non-specific or subtle. In this case series, seven cases of CS with varied presentations are described. In cases 1, 2, 6, mothers were screened after the baby was tested positive for Venereal Disease Research Laboratory (VDRL) test. In two cases (Case-4,6), the mothers received inadequate treatment for syphilis antenatally. In the present case series, Case-6 presented with renal manifestations early in the course of the disease, Case-2 had skin manifestations like vesicular lesions and peeling of skin and Case-7 had symptoms suggestive of meningitis. Because of its varied presentations, high index of suspicion is the key to diagnosis and treatment of CS and prognosis. Screening of pregnant women and treating them is the most effective way in preventing CS and its related morbidity and mortality.

Keywords: Meningitis, Renal manifestations, Venereal disease research laboratory, Vesicular lesions

INTRODUCTION

Congenital Syphilis (CS) continues to affect infants worldwide. As per the World Health Organisation (WHO) report 2016, prevalence of maternal syphilis is 0.69% and about 473 per one million live births are positive for CS with a total estimate of 661,000 cases globally. Out of these 3,55,000 cases had adverse birth outcomes [1,2]. The foetus acquires infection from mother either trans-placentally or during intra-partum through direct contact with the lesion [3]. As the stage of pregnancy advances the risk of infection increases; also higher transmission rates are seen in secondary and early latent syphilis stage in pregnant women [4]. During pregnancy, syphilis in mother can lead to preterm births, spontaneous abortion, stillbirth, perinatal death, and non-immune hydrops. Syphilis can infect newborns leading to two characteristic syndromes of clinical disease, i.e., early (symptoms arising before two years of age) and late CS (symptoms appearing after two years of age) [4]. Penicillin is an effective antimicrobial agent for prevention and treatment of foetal infection and CS [5]. It is the second leading cause of preventable still birth worldwide [6]. As cases of CS are rising, there is a dire need for identifying and treating these cases early in the course of the disease.

Case 1:

A 30-day-old male baby was presented to the Paediatric Outpatient Department (OPD) with the complaint of a mass on the right-side of the abdomen, which was noticed by the mother on day 15 of life. The baby was evaluated at a private hospital and later referred to the authors for further management. The baby was born to non consanguineous married couple by normal vaginal delivery. The mother did not have antenatal health checkups. Both the parents were asymptomatic and apparently healthy. There was a history of sibling death at two months of age due to jaundice.

On examination, vitals were stable and the baby had pallor. On palpation on right-side of the abdomen, Hepatosplenomegaly (HSM) was found and other systemic examinations were normal. Hearing and ophthalmological evaluation was also normal. Complete

Blood Count (CBC) showed haemoglobin of 9.5 g/dL and platelets of 66,000 /mcL. The baby was found positive for Herpes-2 in Toxoplasmosis, Rubella, Cytomegalovirus, Herpesvirus Simplex Virus (TORCH) profile. Screening for Human Immunodeficiency Virus (HIV) of parents was negative. Venereal Disease Research Laboratory (VDRL) test was positive for the baby with 1:256 titre and for mother also with titre 1:16. Treponema Pallidum Haemagglutination Assay (TPHA) of the baby was found to be positive with 1:1280 titre. Radiology of long bones, Cerebrospinal Fluid (CSF) analysis, Liver Function Tests (LFT) were normal. The baby was diagnosed as a case of CS and was treated with crystalline penicillin 50000 IU six-hourly for 10 days and was followed up till one year of age and there was no recurrence of the disease and was normal for his age.

Case 2:

A 90-day-old female baby was presented to the Paediatric OPD with complaints of fluid filled skin lesions and peeling of palms and soles since two months of age. The baby was first born to non consanguineous parents at eight months of gestation by vaginal delivery with birth weight of 2.5 kg and cried with tactile stimulation. There was a history of genital lesions in parents for which the father and mother had taken penicillin injections and no records were available as to the duration and type of drug received as lesions healed two years back. Antenatally, serology of the mother was not done.

On examination, the child had bullous rash with peeling of skin over the extremities and rhinitis [Table/Fig-1a,b]. Systemic examination revealed HSM and blood investigations like CBC revealed haemoglobin 8.4 g/dL. Hearing assessment with otoacoustic emission was normal and ophthalmological assessment was normal. Peripheral smear, LFT, X-rays of long bones, CSF analysis and renal function tests (RFT) were normal. Considering CS as a possibility, VDRL test was done and the baby tested positive (1:128) and mother (1:64). The mother and baby were also TPHA positive (1:2560) titre and father had 1:2 titre. Both of them were screened for other Sexually Transmitted Diseases (STD) and found to be

negative. The baby was treated with crystalline penicillin injection 50000 IU six-hourly for 10 days. As the lesions resolved in 3 weeks, the baby was discharged. The baby is still on follow-up and there is no recurrence of lesions.



[Table/Fig-1]: a) Scaly rashes with desquamation involving palms b) Target macules with erythema and desquamation involving soles.

Case 3:

A 30 day old asymptomatic female baby was referred for evaluation of syphilis as the mother was diagnosed with syphilis in last trimester of pregnancy. The mother was treated with three doses of benzyl penicillin.

The baby was screened with VDRL test which was positive (1:64), TPHA positive (1:640), CSF negative. However, CBC, CSF analysis and radiology of long bones were normal. Both the parents were screened for other STDs and the father was found to be positive for HIV and VDRL. Hearing and ophthalmological assessment was done, which were normal. The baby was treated with crystalline penicillin 50000 IU six-hourly for 10 days and was discharged. The baby is still on follow-up and doing well.

Case 4:

A 90 day old female baby was admitted with the complaint of increasing pallor and abdominal distension, which was noticed by the mother at two and half months of age during vaccination. Family history revealed intrauterine death at six months of gestation in first pregnancy. Antenatal screening for syphilis in the mother was found to be positive; subsequently the father tested positive. The parents gave history of treatment for syphilis, however, the records of treatment received were not available. Hence, VDRL test of the baby was done, which was found to be positive.

CSF analysis revealed normal values for protein and cells and was negative for VDRL test. Blood investigations revealed elevated WBCs (22,000 per microlitre) and decreased haemoglobin level (7.2 g/dL). Peripheral smear showed microspherocytes and leucoerythroblastosis. LFT and RFT were normal. In view of HSM, anaemia and microspherocytes in peripheral smear, Osmotic Fragility Test (OFT) was done, which was within normal limits. Further Eosin-5-Maleimide (EMA) binding test was done to rule out hereditary spherocytosis, which was normal. Haemoglobin electrophoresis was normal. TORCH profile was negative and radiology of long bones was normal. Hearing assessment and fundus examination were normal.

Anaemia was corrected by giving Packed Red Blood Cell (PRBC) transfusion of 10 mL/kg twice. The baby was treated with crystalline penicillin 50000 IU six-hourly for 10 days. The parents were screened for other STDs and the father was found to be positive for HIV. Once the general condition improved, the baby was discharged from the hospital. The baby was stable on follow-up after a month with repeat haemoglobin of 10.3 g/dL.

Case 5:

A 40 day old male baby was admitted with complaints of a lump noticed in the abdomen by the mother and pallor from 20 days of life. The neonatal period was uncomplicated and uneventful. The mother's VDRL test was done in the first trimester and was found to be negative.

The baby was evaluated for anaemia with leucocytosis (38,000/ mL) and HSM. On right-side abdomen palpation, liver span was 7.5 cm and there was moderate splenomegaly [Table/Fig-2]. As peripheral smear showed atypical lymphocytes suggestive of Juvenile Myelomonocytic Leukaemia (JMML) with thrombocytopenia, bone marrow aspiration was done, which showed atypical monocytes and monocytoid precursors. Haematologist opinion was taken and leukaemia was ruled out. Work-up for anaemia with HSM and leucocytosis was done, including screening for TORCH infections. Results showed a positive TPHA with 1:80 titre. His Cytomegalovirus (CMV) IgM was positive, but urine Polymerase Chain Reaction (PCR) for CMV was negative with elevated TPHA titres. CSF analysis was done and was negative for VDRL. Hearing assessment was normal. Fundus examination and radiology of long bones were normal. The baby received PRBC transfusion of 10 mL/kg twice for anaemia (haemoglobin 5.5 g/dL) and crystalline penicillin for a period of 10 days. The parents were evaluated for STDs, including HIV and herpes, at the general hospital and found to be normal except for a positive VDRL test. They received injection of crystalline penicillin 1.5 lac IU, BD for 10 days. The baby was followed-up in OPD for CBC, which was normal. Neurodevelopmental outcome was normal till one year of age.

Case 6:

A four-month-old male baby admitted with complaints of passing red coloured urine since one week, fast breathing and pallor noticed four days before admission. There was history of genital ulcers in the mother, however, the mother was not screened antenatally for syphilis. The mother's palms showed hyperpigmented patches at the time of admission of the baby [Table/Fig-3].



[Table/Fig-2]: Abdominal distension due to hepatosplenomegaly. **[Table/Fig-3]:** Rashes in mother involving palms. (Images from left to right)

On examination, the baby had intercostal retractions, skin lesions [Table/Fig-4], haematuria, hypertension (BP 100/54 mmHg, >95th centile) and HSM. Investigations revealed anaemia with haemoglobin of 5 g/dL and thrombocytopenia (90,000 cells/mL). Further work-up for anaemia was done in which peripheral smear showed autoagglutination. Direct Coombs test was done to rule out autoimmune causes of anaemia and was found to be negative. Chest X-ray was performed as there were features suggestive of Lower Respiratory Tract Infection (LRTI), which was confirmed to be pneumonia. Urine examination revealed nephrotic range proteinuria (urine albumin 4+) and presence of plenty of RBCs in urine. Fundus

examination was found to be normal, ruling out cataracts. Hearing assessment was normal. X-ray of long bones and LFT were normal. As there was a history of genital ulcers in the mother, VDRL test was done in the baby to rule out CS, which turned out be positive (1:16 titre). For confirmation TPHA was done, which was positive (1:1280). CSF VDRL test was negative.

Based on the clinical features and investigations, the baby was diagnosed as a case of CS with nephrotic-nephritic syndrome. Supportive therapy, PRBC transfusion 10 mL/kg given once and antihypertensives were given as treatment along with injection of crystalline penicillin 50000 IU six-hourly for 10 days for treating syphilis.

Screening of the parents for syphilis was done, which tested positive. The parents were counselled for screening of other STDs. They were treated with benzyl penicillin. The baby improved with the above treatment and on follow-up, urine tests were normal and blood pressure was within normal limits. Also, the baby was gaining weight adequately for his age.

Case 7:

A single term 40-week-old male baby with birth weight of 3.2 kg born by vaginal delivery to a non consanguineous married couple at a primary health centre brought to Emergency Room (ER) at around 18 hours of life with complaints of not crying immediately after birth, associated with poor physical activity. Antenatal history was significant as mother was VDRL reactive on routine screening and received Inj. benzathine penicillin 2.4 million IU single dose intramuscularly. Further doses of treatment was not received by the mother as she was lost to follow-up.

On examination, the baby had respiratory distress associated with bluish discoloration of the limbs and was actively convulsing when presented to the ER. Oxygen support was given, antiepileptic drugs (phenobarbitone, sodium valproate) were loaded and the baby was shifted to the Neonatal Intensive Care Unit (NICU). Physical examination showed that the baby had weak cry with pooling of saliva, suggestive of pseudobulbar palsy and increased tone in all the limbs. Abdominal examination revealed hepatomegaly (liver span of 6.5 cm). Investigations revealed increased leucocytes (27,800 cells/mcL) with neutrophilic predominance (N 83, L 10) and thrombocytopenia (102,000/ mcL). Septic markers were elevated (Procalcitonin 17.6 ng/mL). Mild hepatic dysfunction was present. CSF analysis showed elevated counts (TC-35, N83, L27) and culture was negative. As the mother was serologically positive, VDRL test was done on the baby. It revealed VDRL test positivity. For confirmation TPHA was done, which showed positivity with titres of 1:640 in the mother and 1:1280 in the baby. CSF for VDRL was negative. Magnetic Resonance Imaging (MRI) showed severe encephalomalacic changes with significant thinning of the cortex in bilateral cerebral hemispheres and thinned out corpus callosum and



[Table/Fig-6]: X-ray of long bones suggestive of diaphyseal periostitis.

basal ganglia [Table/Fig-5]. X-ray of long bones showed symmetrical rarefaction in the humerus involving diaphysis and also in ulna and radius, suggestive of periostitis [Table/Fig-6].

Suspecting as a case of CS with probable syphilitic meningitis, the baby was treated with Inj. aqueous crystalline penicillin 50000 IU/kg/dose given BD for seven days then TID for 10 days. The parents were also treated with benzathine penicillin 2.4 million IU I.M., one dose weekly for three weeks. The baby has delay in motor milestones on follow-up.

Characteristic features of all the cases are tabulated in [Table/Fig-7].

DISCUSSION

Congenital syphilis has varied clinical presentations of which majority of the infected neonates are asymptomatic (70%). There are high chances of delay or missing the diagnosis. This leads to infected infants presenting later in life with late clinical manifestations [Table/Fig-8] [7]. Newborns suspected to have syphilis should be evaluated with CBC, quantitative VDRL testing, X-rays of long bones, CSF examination, LFT and hearing assessment. Screening for other STDs should be done. In all the cases reported above, the authors have followed this for the diagnosis of CS in infants [3,8].

In the present case series, the authors have presented various cases with different presentations. In one case, the baby presented with vesicular eruptions and skin peeling as the presenting complaint, which is similar to a case report by Kim HY et al., [9]. In another case report, VDRL was negative in the mother during first and second trimesters. When screened postnatally, as features of CS were present in the baby, the test turned out to be positive in both mother and baby, which is similar to the present case [10]. In a case report by Mannelli L et al., a three-month-old child presented to the ER with features of CS. X-rays of long bones showed periostitis, which was similar to the present case but in the present case, the baby presented early [11]. Though first trimester screening was negative in the above case reports, it was found that third trimester testing helped make a diagnosis in the baby. Also, in two cases, the mother was tested after the baby had symptoms. In the present study, in three cases, antenatal screening was missed, which is similar to other case reports [12].

The risk of transmission of infection from mother to foetus is related to the stage of infection and gestational age. Primary and secondary syphilis carries 60-100% risk of transmission. Early and late latent phase carries 40% and <8% risk, respectively [13-15]. According to the Centers for Disease Control and Prevention (CDC) and WHO, in communities that have high risk of CS in addition to the first trimester



[Table/Fig-4]: Erythematous targetoid maculopapular rashes. **[Table/Fig-5]:** MRI of the brain showing severe encephalomalacic changes with significant thinning of cortex in bilateral cerebral hemispheres and thinned out corpus callosum and basal ganglia. (Images from left to right)

Variables	Case-1	Case-2	Case-3	Case-4	Case-5	Case-6	Case-7
Maternal symptoms	Nil	Nil	Nil	Nil	Nil	Genital ulcers present	Nil
Antenatal screening for syphilis	Not done	Not done	Positive	Positive	Done -negative in 1 st trimester	Not done	Positive
Treatment received	Postnatally treated with penicillin	Postnatally treated with penicillin	Antenatally treated with penicillin	Antenatally treated with penicillin	Postnatally treated with penicillin	Postnatally treated with penicillin	Antenatally treated with penicillin
Child age at presentation	30 days	90 days	30 days	90 days	40 days	120 days	1 day
Symptoms	Pallor, HSM	Skin lesions	Asymptomatic	Pallor, HSM	Pallor, HSM	Red coloured urine, hurried breathing, hypertension	Birth asphyxia, convulsions, meningitis
Investigations	Anaemia, thrombocytopenia, VDRL, TPHA positive	VDRL, TPHA positive	VDRL, TPHA positive	VDRL, TPHA positive	VDRL, TPHA positive	Urine-nephrotic range proteinuria, plenty of RBCs, anaemia, X-ray chest-pneumonia	Anaemia, thrombocytopenia, CSF- raised TC
Specific abnormality						Nephrotic-nephritic syndrome	Meningitis
Outcome	Improved	improved	Improved	Improved	Improved	Improved	Delayed milestones

[Table/Fig-7]: Characteristic features of cases.

HSM: Hepatosplenomegaly; VDRL: Venereal disease research laboratory test; TPHA: *Treponema pallidum* haemagglutination assay

Early Congenital Syphilis (CS)	Late Congenital Syphilis (CS)
Asymptomatic (m/c)	Perioral fissures (rhagades)
Skin rash, snuffles	Saddle nose deformity
CNS infection, neurosyphilis	Frontal bossing
Jaundice, HSM, generalised lymphadenopathy, failure to thrive, hepatitis	Hutchinson's triad (peg-shaped, notched, widely spaced permanent upper central incisors; interstitial keratitis; and the eighth cranial nerve deafness)
Coombs-negative haemolytic anaemia, thrombocytopenia	Multicusped first molars (mulberry molars), perforation of the hard palate
Skeletal abnormalities - 1) Lucencies (demineralisation) 2) Erosions (osseous destruction) of the proximal medial tibial metaphysis (Wimberger sign) 3) Metaphyseal serrated appearance at the epiphyseal margin of long bones (Wegener's sign) 4) Diaphyseal periostitis, irregular areas of increased density and rarefaction ("moth-eaten" appearance) 5) Multiple sites of osteochondritis or periostitis (painful) (pseudoparalysis of Parrot)	Painless effusion of knees (Clutton's joints), scaphoid scapula, anterior bowing of shins (saber shins)
Pneumonia	Mental retardation

[Table/Fig-8]: Clinical manifestations in early and late Congenital Syphilis (CS).

serologic testing, further evaluation during early third trimester and at delivery should be done [8,16,17]. Various studies showed that if penicillin is administered early in the pregnancy there is reduction in adverse infant and pregnancy outcomes. Further testing in early third trimester and at delivery helps to detect CS cases and to start treatment early [18-20]. Currently in India, screening during pregnancy in third trimester and at the time of delivery involves only women who are at high risk for syphilis, those who live in areas of high prevalence, those who had adverse outcomes in previous pregnancies and those not tested in first trimester, in order to detect reinfection in syphilis positive women whose partners were not treated [21].

Though our Sustainable Development Goals (SDG) are working towards detection and treatment of maternal syphilis, elimination of CS is still a dream. Increase in Point of Care (PoC) centres, testing of pregnant women in third trimester can help India get WHO validation for elimination of mother-to-child transmission of HIV and syphilis [8,22,23].

CONCLUSION(S)

Congenital syphilis presenting in this era is rare and with the increasing number of cases, re-emergence should be prevented by educating health care workers regarding early diagnosis, educating sexual partners, reporting, screening, contact tracing, and treatment.

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PARTICULARS OF CONTRIBUTORS:

1. Professor and Director, Department of Paediatrics, IGICH, Bangalore, Karnataka, India.
2. Associate Professor, Department of Paediatrics, SABVMCRI, Bangalore, Karnataka, India.
3. Assistant Professor, Department of Paediatrics, MSRMCRI, Bangalore, Karnataka, India.
4. Senior Resident, Department of Paediatrics, IGICH, Bangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Usha Bangalore Kantharajanna,
No. 22, 4th Main, 10th Cross End, Arekempnahalli Layout, Wilson Garden,
Bengaluru-560027, Karnataka, India.
E-mail: ushasumuk@gmail.com

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