

Case Report

Congenital syphilis: a rare presentation of a forgotten infection

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Abstract

Congenital syphilis (CS), a common but forgotten disease has a broad spectrum of clinical presentation. Vertical transmission of this spirochaetal infection from the pregnant mother to the foetus can result in varied manifestations ranging from asymptomatic infection to life-threatening conditions in the form of stillbirth and neonatal death. The haematological and visceral manifestations of this disease can closely mimic various conditions including haemolytic anaemia and malignancies. Congenital syphilis should be considered as a differential in any infant presenting with hepatosplenomegaly and haematological abnormalities even if the antenatal screen was negative. We report a 6-month-old infant with congenital syphilis presenting with organomegaly, bicytopenia and monocytosis. A strong index of suspicion and early diagnosis is the key to the good outcome as treatment is simple and cost-effective.

Keywords: Congenital syphilis; monocytosis; anemia; thrombocytopenia.

J Infect Dev Ctries 2023; 17(1):135-138. doi:10.3855/jidc.15498

(Received 20 June 2021 – Accepted 25 January 2022)

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Introduction

Congenital syphilis (CS) occurs due to the transplacental transfer of *Treponema pallidum* from the infected mother to the fetus. According to recent estimates, it is the second leading cause of preventable stillbirths globally [1]. Mother-to-child transmission of this disease can result in serious consequences like stillbirth, neonatal death, prematurity, low birth weight and other congenital deformities [2]. Congenital syphilis can present with numerous and complex manifestations which may mimic several other conditions. Diagnosis can be difficult because more than two-thirds of affected infants are asymptomatic at birth, and signs in symptomatic infants may be nonspecific or subtle which contributes to delay in treatment [3]. We report a case of congenital syphilis with an unusual hematological presentation and without skin or skeletal abnormalities.

Case report

A four-month-old female infant, second born to a non-consanguineously married couple was brought with a history of progressive pallor and abdominal distension of one week duration. There was no history of previous pregnancy losses in the mother. The antenatal period during the current pregnancy was uneventful. The mother had antenatal checks at the local health care center and the child was an outborn

baby. However, there was no documentation regarding Venereal Disease Research Laboratory (VDRL) test or details of any treatment received for a sexually transmitted disease by either or both the parents. The baby was born at term with a weight of 2.7 kg. The postnatal period was unremarkable and the baby was exclusively breastfed and gained weight satisfactorily with normal developmental milestones. There was no history of recurrent fever, skin rash, jaundice or bleeding manifestations. The baby was alert and active with no excessive irritability. There was no history of persistent nasal discharge. Examination findings revealed a well appearing alert baby with normal growth parameters and a normal head circumference. Severe pallor was noticed involving the palms and soles. There was no jaundice, skin rash, petechiae/purpura or significant lymphadenopathy. There was no visible skeletal abnormality. Systemic examination revealed moderate and firm hepatosplenomegaly. There were no murmurs audible and there were no neurological deficits.

Investigations revealed severe anemia with leucocytosis and monocytosis and moderate thrombocytopenia. Peripheral smear showed normocytic hypochromic anemia with elliptocytosis, tear drop cells and polychromasia with some nucleated red blood cells. Differential diagnosis considered were congenital hemolytic anemia and congenital infections

like toxoplasmosis or cytomegalovirus, tropical infections like malaria, storage disorders and haematolymphoid malignancy. The smear was negative for malarial parasites. Serology for congenital infections including toxoplasmosis and cytomegalovirus infections was negative. However, the VDRL test was positive with a titre of 1:64. Since bone marrow examination is an invasive procedure, it was deferred. Serology was positive for syphilis. The plan was to proceed with bone marrow aspiration and biopsy to look for features suggestive of a storage disorder as well as to rule out the remote possibility of malignancy if there was no improvement in the child's clinical condition or the hematological parameters. Parents' samples for the VDRL test were sent and both were positive. *Treponema pallidum* Hemagglutination Assay (TPHA) performed on the patient and parents' serum samples was positive. In order to rule out central nervous system involvement, the cerebrospinal fluid (CSF) examination was done and it was normal and CSF VDRL was negative. The Skeletal survey did not show any evidence of perichondritis. Ophthalmic examination including fundoscopy was normal and there was no evidence of chorioretinitis or cherry red spot. A hearing assessment was done and it was normal. Both parents were examined and did not have any signs of active infection. In view of positive VDRL and TPHA reports in both the patient and the parents, the child was diagnosed with congenital syphilis and treated with benzyl penicillin for 14 days. The child also received a packed cell transfusion during hospital stay for initial stabilization. The parents were treated accordingly with benzathine penicillin. After 1 week of treatment, the counts improved, the absolute monocyte count returned to normal and at the end of treatment there was a considerable reduction in the organomegaly. Four weeks following discharge, the patient was reviewed in the outpatient clinic and the investigations were repeated. The progressive normalization of blood counts after treatment initiation is depicted in Table 1. The blood counts revealed mild anemia with complete normalization of white cell count, absolute monocyte count and platelet count. Repeat VDRL titres were less than 1:4 which confirmed

adequate response to treatment. The child was followed up clinically every 3 months for the first year. At present, she is 18 months of age, clinically well with no neurodevelopmental sequelae.

Discussion

CS usually occurs due to the transplacental transmission of *Treponema pallidum* during pregnancy and in rare circumstances, during birth by direct contact with the infected skin lesions of the mother [4]. Untreated syphilis during pregnancy has a transmission rate close to 100% and causes fetal or perinatal death in 40 % of affected infants [5]. Recognition of this condition is often challenging as clinical features are non-specific and variable. Most infants are asymptomatic at birth and may present only after several weeks to months of life [6]. Congenital syphilis can be classified into early and late varieties based on the age of presentation being before and after 2 years respectively.

Clinical presentation can vary from mucocutaneous involvement in the form of vesiculobullous/maculopapular rash on palms and soles to neurological, hematological or skeletal system abnormalities [4]. There may be other symptoms in the form of fever, growth failure, non-immune hydrops, jaundice and respiratory involvement in the form of snuffles or syphilitic rhinitis and pneumonitis. Skeletal involvement is evident radiographically in almost all symptomatic and in 25 percent of asymptomatic infants. The lesions are symmetrical and mainly involve long bones. Periostitis of long bone metaphysis can result in pseudo-paralysis. Late congenital syphilis can lead to permanent deformities, including Hutchinson's triad of interstitial keratitis, Hutchinson's teeth, and sensorineural deafness. In a study conducted in Brazil by Eleonor G Lago *et al.* on 398 infants born with CS, only 10 percent of the infants were symptomatic in the first month of life [7]. Hepatosplenomegaly, pallor, cholestasis and neurological symptoms were the most common clinical features observed. Other rarer findings included fever, pneumonitis, petechiae, hydrops, rhinitis, pulmonary hemorrhage and nephrotic syndrome. In the above study, among the 120 infants

Table 1. Laboratory parameters at presentation and follow up.

Laboratory parameter	At presentation	One week after penicillin	Four weeks post treatment
Hemoglobin (Hb)	6.4 g/dL	9.6 g/dL	9.5 g/dL
Leucocytes	32000 cells /mL	20,940 cells /mL	6400 cells /mL
Neutrophils	19%	43%	18%
Monocytes	41%	3%	2%
Lymphocytes	40%	54%	80%
Platelet count	60000 cells /mL	105000 cells /mL	230000 cells/mL

who could be followed up, 16 infants (13.3%) had sequelae in the form of psychomotor delay, microcephaly, anemia, hearing loss and visual defects.

Hematological manifestations in CS are varied and non-specific, often mimicking a neoplastic or inflammatory process. These include anemia, leukopenia or leucocytosis and thrombocytopenia. Among these, anemia is the most frequent hematological abnormality and may be multifactorial due to hemolysis, suppression of erythropoiesis, hypersplenism and concomitant nutritional deficiency [8]. In our patient there was microcytic hypochromic anemia with low reticulocyte count, probably due to ineffective erythropoiesis. Thrombocytopenia was seen in 30% of the patients affected with CS which is probably due to decreased platelet survival by immune complex mechanisms, hypersplenism or maturation arrest in thrombopoiesis [6]. Bleeding can occur according to the severity of thrombocytopenia. In our case thrombocytopenia was not associated with any bleeding and responded to treatment.

Absolute lymphocytosis or monocytosis and leukemoid reactions which are lymphocytic or myelocytic have also been described in CS. A monocytic leukemoid reaction is defined as more than 30% monocytes with a total white cell count exceeding 30,000 cells/mm³. A plausible explanation for the presence of monocytosis in CS is that monocytes are actively involved in the cellular response to *Treponema pallidum*. In a retrospective analysis by Karayalcin *et al.* on 10 infants diagnosed with CS, 8 infants had an absolute monocyte count well above the normal range and had a much higher mean absolute monocyte count (2,250 cells/mm³; SD = 664) than normal newborns [9]. Our patient had leucocytosis with monocytic predominance and an absolute monocyte count of 13,200 cells/mL at presentation which normalized after treatment.

Bone marrow findings in CS show nonspecific findings which include erythroid hypo or hyperplasia, granulocytic hyperplasia and severe monocytosis with a variable megakaryocytic response. Bone marrow biopsies may show irregular or discontinuous trabeculae with marked fibrosis at the osseous cartilaginous junction which is termed as syphilitic granulation tissue [6].

Tests for syphilis are classified into treponemal and non-treponemal tests. VDRL is a non-treponemal test and used as a screening tool for syphilis. Following complete treatment, the VDRL test may turn negative. Treponemal tests like TPHA and fluorescent treponemal antibody absorption tests (FTA-Abs) are

diagnostic and continue to remain positive even after treatment. A confirmed case of CS is an infant in whom *Treponema pallidum* is identified by dark field microscopy, fluorescent antibody, or other specific stains in specimens from lesions, placenta, umbilical cord or autopsy material. Our child was a presumptive case of congenital syphilis who had a reactive treponemal test for syphilis with evidence of congenital syphilis on physical examination [10]. In our patient, the hematological abnormalities and marked monocytosis raised the suspicion of CS although there was no skin, skeletal or neurological involvement. Subsequently, the positive VDRL and TPHA tests in the patient and the parents corroborated the diagnosis.

Treatment for a confirmed or probable cases of CS includes aqueous crystalline penicillin G or aqueous procaine penicillin for a duration of 10 to 14 days. The non-treponemal tests should become non-reactive by 1 year of age if treated appropriately. Those infants with persistently positive titres should be considered for a repeat course of treatment [10].

In conclusion, with increasing reports of the resurgence of forgotten diseases, it is important to differentiate infants with congenital syphilis from other infantile conditions like congenital leukemia or acute hemolytic anemia. Diagnosis and management of CS is based on maternal history, clinical findings and non-treponemal and treponemal tests [10]. It is important to keep congenital syphilis as an entity in the differential diagnosis of an infant who presents with hematological cytopenia as treatment is relatively easy and inexpensive and obviates the need for extensive investigations.

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Conflict of interests: No conflict of interests is declared.