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Retreatment in Congenital Syphilis Following Serologic Titer Elevation

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ESTUDO DE CASO

ABSTRACT

Congenital syphilis results from transplacental transmission of *Treponema pallidum* in pregnant women with active infection and remains a significant public health concern. Although it is a potentially curable condition, it requires systematic clinical and serological follow-up, including serial monitoring of non-treponemal tests such as the Venereal Disease Research Laboratory (VDRL) test to assess therapeutic response. We report the case of an infant with confirmed congenital syphilis who, despite receiving guideline-recommended treatment, exhibited a subsequent rise in non-treponemal titers during outpatient follow-up. This case raises important considerations regarding the interpretation of post-treatment serologic dynamics and the potential determinants of titer elevation, including therapeutic failure, reinfection, or atypical serologic response, thereby underscoring the need for rigorous longitudinal surveillance in exposed children.

Keywords: Congenital syphilis; Retreatment; Follow-up.

INTRODUCTION

Syphilis is a systemic infection caused by *Treponema pallidum*, transmitted through sexual contact or transplacentally. Early diagnosis is feasible based on characteristic clinical manifestations and the wide availability of serologic testing[1]. Although preventable and curable, syphilis remains a significant public health concern. World Health Organization estimates reported 661,000 cases of congenital syphilis (CS) worldwide in 2016, while in Brazil, 49,013 cases of syphilis in pregnant women and 24,666 cases of CS were notified in 2017, highlighting the substantial disease burden, particularly in settings with limited healthcare access[2].

Congenital syphilis primarily results from transplacental transmission of the pathogen in untreated or inadequately treated pregnant women[3]. Maternal management consists of benzathine penicillin G according to clinical stage, initiated at least 30 days before delivery, with follow-up using non-treponemal tests to assess therapeutic response[4].

Fetal outcomes range from miscarriage and stillbirth to early or late manifestations in symptomatic or initially asymptomatic newborns[5]. All exposed neonates should undergo clinical and laboratory evaluation and, when indicated, receive penicillin G (crystalline, procaine, or benzathine), followed by outpatient follow-up with serial VDRL titers[6].

Given the epidemiological magnitude and the potential for morbidity and mortality, we report the case of an infant who demonstrated a post-discharge increase in non-treponemal titers requiring retreatment, underscoring the critical importance of longitudinal serologic surveillance.

CASE REPORT

On 07/08/2025, I.S., a female neonate, was born via vaginal delivery at 38 weeks of gestation, weighing 2,537 g, with Apgar scores of 5 and 9 at the 1st and 5th minutes, respectively. She required admission to the neonatal intensive care unit (NICU) and was managed with noninvasive ventilation.

Prenatal care included seven visits at a primary health care unit, without reported complications. Second-trimester serologic screening was negative for toxoplasmosis, HIV, syphilis, and HBsAg. At admission for delivery, the mother was febrile and had a positive rapid test for syphilis, without cutaneous or genital lesions.

At NICU admission, the newborn presented with disseminated petechiae, rash on the lower limbs, abdominal distension with hepatosplenomegaly, anemia (Hb 8.2 g/dL), thrombocytopenia (13,000/mm^3), and metabolic acidosis. Empirical antibiotic therapy with ampicillin and gentamicin was initiated, along with platelet and packed red blood cell transfusions.

On 08/08/2025, maternal VDRL was 1:128 and neonatal VDRL was 1:16, confirming congenital syphilis; intravenous crystalline penicillin G was initiated. The patient persisted with thrombocytopenia, anemia, and direct hyperbilirubinemia, requiring fresh frozen plasma, packed red blood cell transfusions, parenteral nutrition, and mechanical ventilation. On 09/08, abdominal ultrasound demonstrated hepatosplenomegaly and ascites, and transfontanellar ultrasound suggested grade I germinal matrix hemorrhage. On 10/08, an additional packed red blood cell transfusion was administered and enteral feeding was initiated. On 11/08, successful extubation was performed and gentamicin was discontinued after negative blood cultures. On 14/08, lumbar puncture revealed cerebrospinal fluid with reactive VDRL (1:16), pleocytosis, hypoglycorrhachia, and elevated protein levels.

The newborn was discharged on 16/08 after completing 10 days of intravenous crystalline penicillin G, weighing 2,525 g, receiving breastfeeding supplemented with formula, and with resolving jaundice. Outpatient follow-up was scheduled in one month with serial VDRL testing. The mother was discharged from rooming-in care 48 hours postpartum and was instructed to complete weekly benzathine penicillin treatment.

On 21/08/2025, the infant's VDRL titer increased to 1:64. At a subsequent visit on 28/08/2025, the titer remained 1:64, with persistent zone 5 jaundice and hepatomegaly; the mother reported not having completed postpartum treatment as recommended. I.S. was readmitted on 04/09/2025 for retreatment of syphilis, presenting with anemia (Hb 9.8 g/dL; Ht 29.7%) and periostitis on long-bone radiographs. She completed a 10-day course of treatment without complications and was again referred for outpatient follow-up.

After the second treatment course, she showed a progressive decline in VDRL titers and has remained clinically stable to date

DISCUSSION

During the first hospitalization, I.S. presented with prematurity, hepatosplenomegaly, anemia, thrombocytopenia, and rash, in addition to cerebrospinal fluid (CSF) VDRL 1:16 and findings consistent with neurosyphilis. During the second hospitalization, a two-dilution increase in serum VDRL titers and radiographic evidence of periostitis indicated active disease. In both instances, the case met the definition of congenital syphilis according to Informative Note No. 2-SEI/2017 – DIAHV/SVS/MS, characterized by clinical manifestations, cerebrospinal fluid or radiologic abnormalities associated with a reactive non-treponemal test or rising titers during follow-up.

Penicillin G remains the treatment of choice for congenital syphilis and should be initiated immediately after diagnosis[7]. Consolidated evidence demonstrates its effectiveness in reducing neonatal mortality and neurological sequelae, attributed to its sustained bactericidal activity[8]. However, the literature still lacks robust comparative

studies evaluating alternative therapeutic options in cases of suspected treatment failure.

Clinical and serological follow-up with serial VDRL testing (at 1, 3, 6, 12, and 18 months) is essential to assess therapeutic response[9]. A progressive decline in titers, with seroreversion by six months in adequately treated cases, is expected[10]. Titer elevation, as observed in this report, suggests active disease and may result from therapeutic failure or reinfection.

International reports describe rising titers associated with inadequate regimens or incomplete treatment, with subsequent decline after retreatment with penicillin[11]. Unlike those cases, this patient received a complete and timely regimen, raising the question of possible therapeutic failure, although available evidence strongly supports the high efficacy of penicillin[12].

Reinfection must also be considered, given that the mother did not complete postpartum treatment and continued breastfeeding. Although transmission of *Treponema pallidum* through breast milk is poorly documented, studies have detected the pathogen in untreated lactating women, with negativization after initiation of penicillin therapy[13].

In conclusion, longitudinal follow-up of children with congenital syphilis is essential, with VDRL monitoring serving as a central tool for assessing cure. Despite the observed titer elevation, penicillin G remains the standard therapy, with efficacy widely supported in the literature.

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