Congenital syphilis in a neonate born to an adequately treated mother

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Abstract

The burden of syphilis has increased significantly in the United States, mirrored by a spike in rates of congenital syphilis. Treatment inadequacies exist and may be due to complexity of disease staging. This report describes a case of congenital syphilis in a neonate whose mother appeared to have been adequately treated; it also provides support for the necessity of accurate staging of disease at the time of treatment.

A 39-year-old gravida 8 para 7 presented to the office for an initial prenatal visit in her third trimester. She had a history of secondary syphilis treated with a single-dose penicillin regimen 18 months prior to her initial prenatal visit. At that time, her initial RPR titer was 256. She did not follow up with the health department for serial titers but was noted to have a greater than four-fold decline (RPR titer of 32) at her initial prenatal visit with our clinic. Based on this and her asymptomatic status, adequate treatment was presumed.

Despite adequate treatment, the patient subsequently delivered an infant with congenital syphilis. Her staging was unclear – reinfection by new partner versus late latent syphilis versus serofast state. Standard of care treatment calls for a single-dose of penicillin, but a three-dose regime has been shown to decrease the rate of treatment failure. In a woman of reproductive age in danger of being lost to follow-up, the risk of perinatal mortality may outweigh any concerns regarding antibiotic resistance and justify a more aggressive treatment regime.

Introduction

The burden of syphilis has increased significantly in the United States. The rate of reported primary and secondary syphilis cases increased by 10.5% from 2016 to 2017 [1]. The national rate of congenital syphilis has mirrored this trend, increasing by 43.8% over the same time period to reach 23.3 cases per 100,000 live births [1].

Congenital syphilis is preventable, but complications in screening and treatment likely contributed to the recent rise in cases. Lack of maternal screening in women with insufficient prenatal care is one major culprit, as well as deficiencies in late trimester or time of delivery rescreening in high-risk women. There has also been a noted lack of appropriate follow-up and treatment of syphilis in pregnancy [2]. Even after treatment, there remains a significantly higher risk of adverse pregnancy outcomes compared to uninfected pregnancies [3].

The complexity of disease staging may be contributing to these treatment inadequacies. Distinguishing between latent infection, insufficient treatment of prior early infection, and the serofast state is nearly impossible. In fact, no testing algorithms exist to differentiate between previously treated and untreated syphilis in the setting of discordant treponemal and non-treponemal results [3].

This report describes a case of congenital syphilis in a neonate whose mother met criteria for adequate treatment; it also provides support for the necessity of accurate staging of disease at the time of treatment.

Methods

A comprehensive online PubMed literature review of syphilis epidemiology, clinical presentation, diagnosis, staging and treatment, as well as congenital syphilis was performed. Approval for this report was obtained by the Saint Francis Hospital Ethics and Internal Review Board. The Saint Francis electronic medical record was accessed on a protected server to collect only patient information which proved pertinent to this report. The de-identified data collected is presented in the following text.

Results

The patient was a 39-year-old G8 P7007. She presented to establish care at 39-weeks gestational age, dated by last menstrual period, having received no prior prenatal care. Her past medical history revealed a prior diagnosis of secondary syphilis treated eighteen months prior. Review of state health department records confirmed the diagnosis and treatment of the infection. Records indicate the patient's initial RPR titer was 1:256 with confirmatory positive FTA. She received the CDC recommended treatment regimen consisting of a single dose, 2.4 MU, Penicillin G Benzathine. She was certain of the source partner of her infection and had not had any further contact with him following her diagnosis and treatment.

Eight months after treatment, she became pregnant by a new partner. The father of the baby for this gestation told the patient he had tested positive for syphilis in years past, but had been treated. No confirmatory documentation was available regarding the father's infection history. A posttreatment RPR titer was not evaluated until the patient presented for the initial prenatal visit. Her first posttreatment titer showed a value of 1:32, a greater than four-fold decline. Physical exam during the visit was negative for all signs of any stage of syphilis. In the absence of symptoms, and with appropriate titer decline, she met criteria for adequate treatment. All other serological testing, including HIV, was negative.

She underwent medical induction of labor at 41-weeks 1-day gestational age due to non-severe preeclampsia. Bedside ultrasound on admission showed a fetus measuring 37-weeks with severe polyhydramnios (amniotic fluid index of 48 cm). She was GBS positive and received the standard prophylactic intrapartum dosing of 5 MU Penicillin G potassium loading with 2.5 MU every four hours until delivery thereafter. Physical exam on admission and at the time of amniotomy showed no rash or other findings consistent with primary or secondary syphilis. She ultimately underwent primary cesarean delivery for category III fetal heart tones. Upon delivery the infant was pulseless and apneic requiring chest compressions and intubation. APGARS of 1, 3, 6 were recorded; arterial blood gas showed pH 7.08, CO2 57.9, PO2 102, HCO3 17.03, BE -13.

Upon delivery a markedly enlarged, hydropic and circumvallate placenta was noted, all features consistent with untreated or inadequately treated syphilis. The placenta was sent for full pathologic examination and cultures were ordered immediately postpartum; unfortunately, it was mistakenly placed in formalin precluding further histochemical staining.

The infant remained intubated in the NICU with signs of congenital syphilis including desquamating rash, thrombocytopenia, hepatosplenomegaly, severely elevated LFTS and bilirubin. Neonatal RPR titer was found to be 1:16 and lumbar puncture for VDRL was negative.

The infectious disease team was consulted for recommendations regarding further maternal treatment as the true stage of syphilis was unclear. Lumbar puncture showed maternal CSF VDRL was negative. It was suggested that the patient may have been re-exposed to syphilis, or treatment was inadequate as the RPR titer did not reach zero. Treatment for latent syphilis with three doses of penicillin 2.4 MU was recommended.

Discussion

American College of Obstetrics and Gynecology recommends routine syphilis screening beginning at the initial prenatal visit and re-screening of high-risk women early in the third trimester and at time of delivery [4]. Although reverse algorithm testing has been described, testing traditionally consists of a nontreponemal test first, and if positive, followed by a confirmatory a treponemal test, [5].

Staging of disease can be complex but is divided broadly into two categories: early and late disease. Early syphilis includes primary (localized infection; chancre), secondary (systemic illness with disseminated rash), and early latent syphilis (asymptomatic infection present for less

than 12 months) [6]. Late syphilis refers to untreated earlier stages which can progress to an asymptomatic late latent disease (present for more than 12 months), and neurosyphilis [7].

The CDC recommends administration of a single-dose, 2.4 MU, of Penicillin G Benzathine for early syphilis, and a three-dose course, 2.4 MU given every week for three weeks, for treatment of late disease. [8]. A four-fold decline or greater in non-treponemal titers constitutes successful treatment [8]. Follow-up non-treponemal titers usually fall to zero, but approximately 15% of patients maintain a serofast state, in which a four-fold decline in titer is observed but never reaches zero [13]. A persistent low-level non-treponemal titer creates a situation that further complicates staging of disease.

Vertical transmission can occur via transplacental transfer of spirochetes at any point during pregnancy or during labor if the baby comes into contact with an infectious lesion. Overall fetal risk and likelihood of fetal abnormalities increases with infection later in gestation [11]. The immature fetal immune system may partially account for the less pronounced fetal response in early gestation [3]. Untreated primary or secondary syphilis is more detrimental to the fetus than latent disease [10, 11]. The risk of congenital infection in term infants is approximately 50% for primary and secondary syphilis, and 40% for early latent untreated syphilis [2]. A correlation between the risk of congenital syphilis and severity of maternal spirochetemia has been suggested [12]. While patients with late latent syphilis are not infectious to sexual partners, there is a risk of vertical transmission to a fetus of an infected mother for up to four years after acquisition [8, 2].

Determining between treatment failure versus reinfection is difficult, if not impossible [9]. This is problematic because timing of fetal infection is significant. While a single dose regimen has proved effective in mothers, the risk for fetal treatment failure still exists, especially in patients with longer duration of disease and higher initial treponemal load [9].

This case was unique because despite documented adequate treatment, the patient delivered a congenitally infected infant. The complexities regarding her disease staging likely contributed to this poor outcome. The risk of infection to infants born to mothers in the serofast state, or to those with latent syphilis remains incompletely understood. This begs the question of whether a single dose of penicillin is appropriate in a woman of reproductive age with significant risk factors. However, the presumption of adequate treatment was potentially confounded by a initially high treponemal load, medical non-compliance (lack of follow-up titers after initial treatment, late initiation and limited prenatal care) and possible re-exposure.

A reasonable and simple solution would be to treat all women, with any stage of syphilis, with a three-dose regimen. One study suggests, compared to a single dose, three doses of penicillin may reduce the risk of perinatal mortality by more than half [14]. While further research is needed, in high-risk reproductive-age and pregnant women, the risk of perinatal mortality may outweigh any concerns regarding antibiotic resistance justifying a more aggressive treatment regime.

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