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Amoxicillin as an Option in Congenital Syphilis Management: A Case Report

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Abstract

BACKGROUND: Congenital syphilis (CS) is the second leading cause of preventable stillbirth globally. This case report shows that CS baby can be managed by amoxicillin with good results.

CASE PRESENTATION: A term female baby was born through section cesarean on suspicion of syphilis of a 29-year-old mother, G4P3A0, 39 weeks gestation with normal APGAR score, and birth weight was 2330 g, birth length was 46 cm, and head circumference 32 cm. There are no abnormalities on physical examination. The baby is active and clinically sound. In history taking, the mother was diagnosed with syphilis in the first trimester of pregnancy but did not want to be treated. After birth, maternal serology showed that *Treponema pallidum* is reactive. Maternal VDRL was reactive at 1:1, while TPHA was reactive at 1:2560. Baby laboratory results showed Hb 18.4 g/dL, leukocytes 33,480/μL, platelets 278,000/μL, and hematocrit 54.7%. A peripheral blood smear showed neutrophilia with hypersegmentation and monocytosis due to suspected chronic inflammation. Baby VDRL was reactive at 1:16, while TPHA was reactive at 1:1280. The diagnosis was congenital syphilis with low birth weight and small for gestational age. After one month of treatment with oral amoxicillin, baby VDRL was reactive at 1:2, while TPHA was reactive at 1:320. At 1½ months, the baby's hemoglobin is 10.1 g/dL. X-rays for chest, abdomen, and skeletal were within normal limits. The baby was given oral amoxicillin 50 mg/kg/day for a total of 3 months. When the baby was 4 months old, her growth and development were good with the VDRL reactive 1:1 and the TPHA reactive 1:160.

CONCLUSION: In the unavailability of benzathine penicillin, amoxicillin may be considered an option in CS management.

Introduction

Congenital syphilis (CS) is caused by the transmission of the spirochete *Treponema pallidum* from the mother straight into the fetus's bloodstream, causing spirochetemia, which spreads to most organs, including bones, kidneys, spleen, liver, and heart. This leads to widespread inflammation throughout these organ systems resulting in a multitude of clinical presentations ranging from asymptomatic, premature birth, low birth weight, small for gestational age, and a wide array of clinical signs and symptoms to stillbirth [1], [2], [3], [4]. *Treponema pallidum* is a motile spirochete, a helically coiled, corkscrew-shaped bacterium that is 6–15 micrometers long and 0.1–0.2 micrometers wide [5]. Mother-to-child transmission of syphilis will occur when pregnant women with syphilis are not detected or not treated early in pregnancy, causing 50–80% CS baby [4]. Both primary and secondary syphilis confer a highest risk of transmission (60–100%). The estimated rates of vertical transmission for early latent and late latent are 40% to 83% and 10%, respectively [6]. The Centers for Disease Control and Prevention (CDC) reported that in the United States in 2017, the incidence of CS was 23.8 cases per 100,000 births [1]. Congenital syphilis is the second leading cause of preventable stillbirth globally [7].

Treatment with penicillin in pregnant women with syphilis is 98% effective at preventing CS [8]. Furthermore, its consequences can be minimized with early diagnosis and prompt treatment of syphilis mothers, especially in the first trimester. This case report shows that in the unavailability of benzathine penicillin, amoxicillin may be considered an option in CS management.

Case Presentation

A term female baby was born through section cesarean operation on suspicion of syphilis of a 29-year-old mother, G4P3A0, 39 weeks gestation with normal APGAR score, and birth weight was 2330 g, birth length was 46 cm, and head circumference 32 cm.

There are no abnormalities on physical examination. The baby is active and clinically good. In history taking, the mother was diagnosed with syphilis in the first trimester of pregnancy but did not want to be treated. The mother's education was low, and the family income was low too. After birth, maternal serological showed anti-HIV rapid test: Non-reactive, HBsAg: Non-reactive, and IgG and IgM anti-SARS-Cov-2: Non-reactive. *Treponema pallidum* test is reactive. Maternal VDRL was reactive at 1:1, while TPHA was reactive at 1:2560.

The baby laboratory results showed Hb 18.4 g/dL, leukocytes 33,480/μL, platelets 278,000/μL, and hematocrit 54.7%. Differential count showed basophils 0, eosinophils 0, neutrophil band 4, neutrophil segment 63, lymphocytes 22, and monocytes 11. A peripheral blood smear showed neutrophilia with hypersegmentation and monocytosis due to suspected chronic inflammation. *Treponema pallidum* baby test was reactive. Then, a quantitative serologic examination was performed. Baby VDRL was reactive at 1:16, while TPHA was reactive at 1:1280. The working diagnosis was congenital syphilis with low birth weight and small for gestational age.

After one month of treatment with oral amoxicillin 50 mg/kg/day, baby VDRL was reactive at 1:2, while TPHA was reactive at 1:320. The baby is clinically good. At 1½ months, the baby's Hb level was 10.1 g/dL, MCV 91.6 fL, MCH 31.6 pg, reticulocyte 1.85% (N: 0.5–1.5%), and Ret-He 32.1 pg. Erythrocyte sedimentation rate (ESR) at 1h was 16 mm and at 2h was 34 mm. Direct bilirubin was 0.53 mg/dL (N: <0.25 mg/dL), indirect bilirubin was 1.02 mg/dL (N: <0.75 mg/dL). AST and ALT are within normal limits. X-rays for chest, abdomen, and skeletal are within normal limits. At this time, the diagnosis is CS with anemia of chronic disease. The baby was still given amoxicillin.

After 3 months of treatment, oral amoxicillin is discontinued due to the baby being clinically good. When the baby was 4 months old, her growth and development were good with the VDRL reactive 1:1 and the TPHA reactive 1:160.

Discussion

In the first trimester of pregnancy, the mother was diagnosed with syphilis but did not want to be treated. Mother was embarrassed and rejected suffering from syphilis, so she did not want to do prenatal care anymore to health workers at the community health center. Hence, the mother did not receive treatment for her syphilis. This is suit to a review of CS cases reported by the CDC in 2014 that showed that 30% received inadequate treatment and 43% received no treatment for syphilis during their pregnancy among mothers of infants with CS who had prenatal visits [8]. As in this case, the low mother's education and poverty play an essential role [8], [9].

The diagnosis of CS, in this case, was established based on the results of the reactive *Treponema pallidum* test in the mother before delivery and after birth, the VDRL reactive 1:1, and TPHA reactive 1:2560. Moreover, the baby's VDRL was 1:16, 16 times from mother's VDRL. Satyaputra *et al*. stated that CS is proven if a baby's VDRL ≥4x mother's VDRL [6]. A peripheral blood smear showed neutrophilia with hypersegmentation and monocytosis due to suspected chronic inflammation. Moreover, clinically, the CS is supported by the baby's low birth weight and small for gestational age. In one study, CS babies are usually associated with preterm birth, low birth weight, and small for gestational age [10]. On the other hand, most neonates born with CS are asymptomatic at birth [11]. The clinical manifestation, laboratory findings, and radiographic findings of CS are shown in Table 1 [3], [12], [13], [14].

Table 1: The clinical manifestation, laboratory findings, and radiographic findings of congenital syphilis

Congenital syphilis	Signs and symptoms
Early congenital syphilis (<2 years of age)	Physical examination findings
	Stillborn
	Preterm
	Non-immune hydrops fetalis
	Intrauterine growth restriction/small for gestational age
	Hepatomegaly with or without jaundice
	Splenomegaly
	Skin rash
	Adenopathy (characteristical palpable epitrochlear nodes)
	Rhinitis (snuffles)
	Mucus patch
	Condylomata lata
	Pseudoparalysis of parrot
	Eye: Chorioretinitis, cataract
	Central nervous system: Asymptomatic invasion, cranial
	Nerve palsies, seizures
	Laboratory findings
	Anemia
	Thrombocytopenia
	Hypoglycemia
	Cerebrospinal fluid pleocytosis, elevated protein content
	Liver transaminitis and direct hyperbilirubinemia
	Radiographic findings
	Bone abnormalities: Periostitis, osteochondritis
	Pneumonia alba
	Other
	Nephrotic syndrome, pancreatitis, myocarditis, fever, gastrointestinal malabsorption, hypopituitarism, DI
Late congenital syphilis (>2 years of age)	Ophthalmologic
	Interstitial keratitis, uveitis, blindness
	Central nervous system
	Hydrocephalus, seizures, intellectual disability, optic nerve atrophy, deafness, paralysis
	Skeletal
	Anterior bowing of shin (saber shins), frontal bossing, sternoclavicular thickening (Higoumenakis sign), symmetric painless knee swelling (Clutton joints)
	Dental
	Small, widely spaced, notched central incisors (Hutchinson teeth), mulberry molars
	Dermatologic
	Saddle nose, perforation of hard palate, perioral scarring (Rhagades)

It is generally accepted that parenterally administered penicillin is the treatment of choice for syphilis. Procaine penicillin G, 50,000 units/kg/day intramuscularly (IM) for 10–14 days, was the drug of choice for the treatment of CS as early as possible, especially in the 1st week of life. However, if the baby CS is asymptomatic, the recommended drug was benzathine penicillin G 50,000 units/kg per dose IM in

a single dose [12]. Three months regimen of penicillin will increase clinical and serological improvement [15]. In this case, benzathine penicillin was unavailable. Many countries experience the unavailability of this drug, so CS elimination is challenging even if the drug is cheap. A study stated that the amoxicillin regimen is an alternative to single-dose parenteral penicillin in managing syphilitic patients with suspected CNS involvement. Amoxicillin was chosen because of high serum levels resulting from complete gastrointestinal absorption and the subsequent high levels in CSF [16]. Another study stated that clinical manifestations usually appear in untreated infants by 3 months [11] Click or tap here to enter text.. Therefore, considering various aspects (effectiveness and safety of the drug, the price, and the availability of the drug), the baby was given oral amoxicillin 50 mg/kg/day for 3 months. In this case, after up to 4 months of monitoring, the clinical condition and growth of the baby were excellent. On the other hand, the baby did not show any amoxicillin side effects.

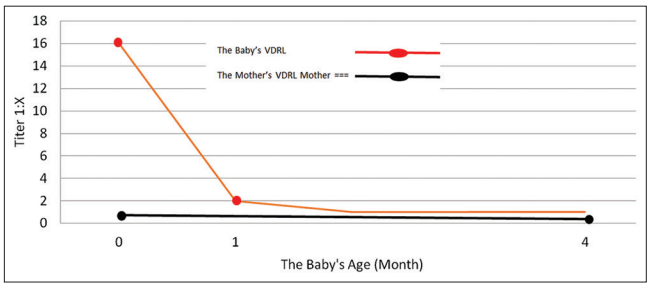

Figure 1: The follow-up of the baby's VDRL and the mother's VDRL

In this case, anemia of chronic disease due to CS, characterized by MCV, MCH, and Ret-He, was within normal limits, increased ESR and VDRL were still reactive 1:2. Hence, the baby was still given amoxicillin for total 3 months. Monitoring for the next 4 months showed that the baby's growth and development were excellent. On the other hand, the baby VDRL and TPHA were progressively lower (Figures 1 and 2). The VDRL serology of CS infants often remains reactive for months later, rarely until seronegative. Therefore, what is important is the clinical assessment of the baby [6]. In 5 years of monitoring, CS babies have good results if they receive optimal treatment from the 1st week of birth [10].

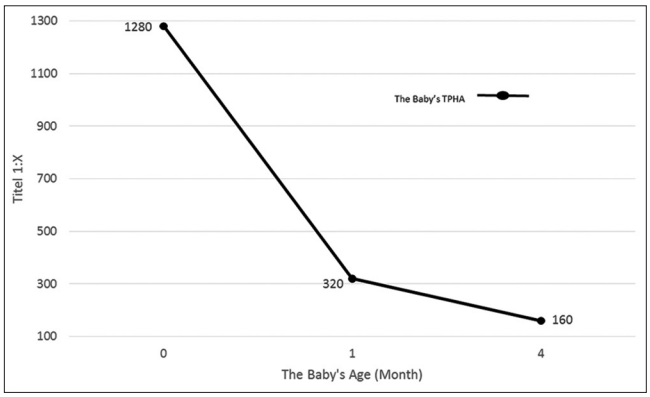

Figure 2: The follow-up of the baby's TPHA

Congenital syphilis is easily averted. Furthermore, complications can be minimized with early diagnosis and prompt treatment of syphilis in pregnant mothers, especially in the first trimester [13]. Benzathine penicillin 2.4 million unit IM is the drug of choice for prevention [9]. Clinically, there was no significant difference between benzathine penicillin and procaine benzylpenicillin administration in preventing congenital syphilis [15]. In another hand, oral amoxicillin was potentially effective for preventing CS cases among pregnant women with early syphilis [17].

A 2018 CDC report stated that the main problem with failure of prevention programs was 30.7% due to inadequate maternal treatment despite the timely diagnosis of syphilis during pregnancy and 28.3%, not timely prenatal care [3]. Universal syphilis screening in the first and third trimester of pregnancy should be done within an existing prenatal care program as an effective way to trim syphilis-associated adverse outcomes [18], [19], [20]. To lessen the spread of syphilis, health professionals have to educate on safe sexual practices [21]. It is time to upscale the endeavor to cease the escalation of this relatively preventable congenital disease and its associated morbidities and mortalities.

Conclusion

Congenital syphilis can be prevented with early diagnosis and prompt treatment of syphilis in pregnant mothers, especially in the first trimester. To lessen the spread of syphilis, health professionals have to educate on safe sexual practices. In the unavailability of benzathine penicillin, amoxicillin may be considered an option in CS management.

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