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Late-Diagnosed Congenital Syphilis in a Toddler: Successful Management with Ceftriaxone

—A Case Report and Literature Review

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Abstract

Background: Congenital syphilis continues to be a re-emerging global health issue despite the availability of effective screening and prevention programs. Penicillin G remains the first-line and only CDC-recommended treatment; however, in resource-limited settings, its unavailability may necessitate alternative therapies. We report a case of congenital syphilis diagnosed beyond infancy, successfully managed with ceftriaxone due to unavailability of penicillin. **Case Presentation:** A 2-year-old female was diagnosed with congenital syphilis following retrospective family-based screening after her father presented with symptoms of secondary syphilis. The father had been unknowingly exposed to syphilis approximately three years prior, before the child's conception. The mother's antenatal syphilis screening during pregnancy was documented as negative. One year after the child's birth, the father developed a palmar rash and genital ulcers. Both parents were found to have reactive treponemal tests, prompting serologic testing of their children. While the two older sons tested negative, the youngest child (our patient) tested positive for both treponemal and non-treponemal antibodies. She was clinically well, with no signs of late congenital syphilis. Maternal RPR titers from pregnancy were not available. Further evaluation excluded neurosyphilis. Due to the **unavailability of benzathine and aqueous penicillin formulations**, the patient was treated with **IV ceftriaxone (100 mg/kg/day for 10 days)**. She showed excellent tolerance and demonstrated a favorable serologic response on follow-up. **Discussion:** This case underscores the diagnostic challenges of congenital syphilis in the absence of maternal symptoms and highlights the importance of postnatal screening in high-risk families. While penicillin remains the gold

standard, ceftriaxone may be a viable alternative in select cases when penicillin is unavailable. A literature review is provided to contextualize treatment options and outcomes. **Conclusion:** In settings where penicillin is inaccessible, ceftriaxone may offer an effective off-label alternative for congenital syphilis, provided that close follow-up and serologic monitoring are ensured.

Keywords

Congenital Syphilis, Ceftriaxone, Treponema Pallidum

1. Introduction

Congenital syphilis is a preventable but re-emerging infection caused by vertical transmission of *Treponema pallidum* from mother to fetus during pregnancy or delivery [1]. Although early screening and treatment have dramatically reduced its incidence in many regions, a global resurgence has been noted in recent years, including among high-income countries [2]. The clinical manifestations of congenital syphilis are diverse, ranging from asymptomatic infection to severe complications such as hepatosplenomegaly, skin lesions, osteitis, anemia, and neurosyphilis [3]. Diagnosis can be delayed, particularly when maternal infection is asymptomatic, inadequately treated, or undiagnosed during pregnancy [4]. Serologic diagnosis relies on a combination of non-treponemal and treponemal-specific tests; however, interpretation in neonates is often complicated by transplacental maternal antibodies, necessitating careful clinical correlation [5]. In high-burden settings or where routine prenatal care is inconsistent, many cases are missed until late infancy or beyond [6]. Aqueous penicillin G remains the gold-standard treatment for congenital syphilis due to its well-established efficacy and central nervous system penetration [7]. Nevertheless, temporary shortages of parenteral penicillin in some healthcare systems have prompted consideration of alternative agents, particularly **ceftriaxone**, which has demonstrated *in vitro* activity against *T. pallidum* and limited clinical support in off-label pediatric use [8].

As previously discussed in the context of the global burden and management of syphilis, delayed diagnosis and treatment of congenital syphilis can lead to serious harm and significantly worsen the patient's prognosis. Moreover, the limited availability of aqueous penicillin due to stock out—unlike other formulations—poses an additional challenge to timely and effective management [1].

So, this report describes a case of congenital syphilis diagnosed in a 2-year-old girl, identified through retrospective family screening, and successfully treated with ceftriaxone due to unavailability of penicillin. A focused literature review is included to explore diagnostic challenges and assess the potential utility of ceftriaxone in such scenarios.

2. Case Presentation

A **2-year-old female** was identified with **congenital syphilis** following retrospec-

tive family screening prompted by her father's delayed diagnosis. Approximately **three years before the patient's birth**, her father was unknowingly exposed to syphilis through unprotected sexual contact. He remained asymptomatic and undiagnosed at the time. Several months later, his wife conceived the current patient. The pregnancy progressed uneventfully, and **maternal syphilis screening during routine antenatal care was reported as negative**. When the child was **1 year old**, the father developed a **palmar rash and genital ulcers**, prompting clinical evaluation. Both parents tested **positive for syphilis** based on **strongly reactive treponemal tests**. Non-treponemal tests (e.g., RPR or VDRL) were not available at the time. The mother remained asymptomatic and both were referred to adult infectious disease specialists. Subsequently, the father arranged for serologic testing of all his children. His two older sons—born before his exposure—tested negative. However, the **2-year-old daughter (index patient)** tested **positive for both treponemal and non-treponemal antibodies**, raising concern for **undiagnosed congenital syphilis**. **Maternal RPR titers during pregnancy were unavailable**, limiting serologic comparison. At the time of evaluation, the child was **clinically well** with **no physical signs of active disease**. Examination revealed no rash, hepatosplenomegaly, lymphadenopathy, or bony abnormalities. **Lumbar puncture was not performed** due to parental refusal. **Ophthalmologic and audiologic assessments were normal**, and **skeletal imaging showed no abnormalities**. Due to the **unavailability of penicillin formulations**, the patient was treated with **intravenous ceftriaxone at 100 mg/kg/day for 10 days**. The treatment was well tolerated. On follow-up, **non-treponemal serology (RPR) became nonreactive**, confirming an appropriate serologic response to therapy. The patient remains clinically well and is under ongoing outpatient follow-up.

3. Literature Review

Congenital syphilis has re-emerged as a global health threat, with increasing incidence even in developed nations due to missed opportunities in prenatal screening and treatment [9]. Inconsistent access to antenatal care, late maternal infection, and failures in follow-up contribute significantly to this resurgence [10]. Clinical manifestations of congenital syphilis are variable and may include hepatosplenomegaly, mucocutaneous lesions, nasal discharge (snuffles), rash, anemia, bone changes, and neurosyphilis [11]. Many infants are asymptomatic at birth and are only diagnosed later through retrospective evaluation or sibling screening, especially in cases where maternal infection went undetected or untreated during pregnancy [12]. Diagnosis in infants requires interpretation of both non-treponemal and treponemal tests in correlation with maternal serologies and clinical features. A fourfold higher RPR or VDRL titer in the infant compared to the mother is suggestive of active infection, although this is not always seen [13]. Imaging studies, such as long bone radiographs, may reveal periostitis or metaphyseal lucencies and can aid in diagnosis [14]. Penicillin G is the treatment of choice for congenital syphilis due to its proven efficacy and CNS penetration. It is the only antibiotic with established outcome

data in both early and late disease [15]. However, in rare situations where penicillin is unavailable due to national shortages or logistical limitations, off-label use of ceftriaxone has been reported [16]. Ceftriaxone, a third-generation cephalosporin, has shown *in vitro* activity against *Treponema pallidum* and has been used with success in both adult and limited pediatric cases of syphilis [17]. In the study by **Shirolkar and Verneker (2024)** conducted in **India**, due to the **unavailability of penicillin**, **ceftriaxone was used for 10 days at a dose of 100 mg/kg/day** in asymptomatic newborns with **positive VDRL titers**, serving as an alternative treatment for congenital syphilis [18]. In the study by Rocha *et al.* (2021), conducted in Fortaleza, Brazil, during a penicillin shortage in 2015, 575 cases of congenital syphilis (CS) were reported, with 469 (81.5%) analyzed. Only 210 (44.8%) received nationally recommended penicillin treatment. Alternative therapies included ceftriaxone (13.8%), cefazolin (3.2%), and combinations of multiple drugs (38.2%) [19]. Although not considered a standard first-line treatment, it may be a viable alternative in selected cases, particularly when accompanied by close serologic follow-up to assess response [20] (**Table 1**).

Table 1. Summary of ceftriaxone use in congenital syphilis cases.

Author(s)	Why ceftriaxone used	Dose of ceftriaxone	Duration
Rocha, A. F. B., *et al.*	Penicillin shortage in Brazil, ceftriaxone used as an alternative treatment for newborns with congenital syphilis.	Not specified; used in 13.8% of cases during the shortage.	Not specified
Shirolkar, M., & Verneker, R.	Penicillin unavailability, ceftriaxone used to treat asymptomatic newborns with positive VDRL titers.	100 mg/kg/day in two divided doses.	10 days

4. Conclusion

This case highlights the diagnostic challenges and clinical variability of congenital syphilis, particularly in settings where maternal infection goes unrecognized and infants remain asymptomatic beyond the neonatal period. The diagnosis in this case was made retrospectively through family screening, reinforcing the importance of comprehensive contact tracing and serologic evaluation of all children when syphilis is detected in a household.

While penicillin remains the cornerstone of treatment, this report demonstrates the potential utility of **ceftriaxone** as an alternative in rare circumstances where **penicillin is unavailable**. The patient responded well to **a 10-day course of intravenous ceftriaxone (100 mg/kg/day)**, with subsequent **serologic clearance** (nonreactive RPR), supporting its clinical effectiveness in this context.

This case further underscores the importance of **routine antenatal screening**, **early maternal diagnosis**, and **follow-up of all exposed infants**. In resource-lim-

ited settings, where diagnostic and therapeutic tools may be constrained, awareness of alternative treatment strategies—when supported by clinical judgment and close follow-up—is essential.

Ongoing surveillance, improved prenatal care, and greater access to first-line therapy are critical to reversing the rise in congenital syphilis and preventing its long-term consequences.

Informed Consent

Written informed consent was obtained from the patient's father for publication of this case report and any accompanying images.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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