

Management of Syphilis with Ceftriaxone and Azithromycin in a Pregnant Woman with Penicillin Allergy and Persistently Raised Rapid Plasma Reagin [RPR]: A Case Report

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Abstract

The case report indicates that the use of ceftriaxone and azithromycin should be considered for the prevention of congenital syphilis (CS) when the mother is allergic to penicillin, and when desensitisation or de-labelling to penicillin is declined. Persistently raised RPR does not correlate with poor outcomes in a treated patient.

Keywords: Syphilis; Pregnancy; Ceftriaxone; Penicillin; RPR

Introduction

Since 2014, the overall rise in infectious syphilis cases has included an increase in heterosexual cases, which had previously remained relatively low and stable. In 2019, diagnoses in women increased by 135% to 597 and doubled in men to 1016 [1] in England, in comparison to 2010.

Treponema pallidum readily crosses the placenta, and vertical (mother-to-child) transmission can occur at any stage of pregnancy. The risk of transmission varies with the syphilis stage and is greatest in early disease [2,3]. Accordingly, transmission was associated with rapid plasma reagin (RPR) titres $\geq 1:8$ (risk ratio 18.1, $p < 0.001$) in one cohort study [4].

There is a risk of fetal infection which can cause miscarriage, stillbirth, or neonatal death after delivery in of cases in untreated cases of syphilis [5]. The signs of early congenital syphilis (CS) evident in the first 2 years are inflammation of long bones with or without fractures, rash, hepatosplenomegaly, copious nasal discharge, and central nervous system abnormalities. Late syphilis after 2 years has symptoms of intellectual disability, physical deformities, and Hutchinson's triad (teeth deformity, interstitial keratitis, eighth-nerve deafness). The effective treatment of the mother during the first three months of pregnancy can prevent CS [6].

The only acceptable treatment to prevent CS is penicillin therapy. We report a case where ceftriaxone and azithromycin were used as an alternative therapy to prevent congenital syphilis as the mother was allergic to penicillin and declined penicillin desensitisation; with persistently raised RPR.

Case History

This is a case of syphilis in pregnancy with penicillin allergy where the patient declined desensitisation. A 40-year-old woman was referred to the Genito-urinary clinic by the obstetrics service for the treatment of syphilis in pregnancy with a penicillin allergy. She was 16 weeks of the pregnancy of her fifth pregnancy and was positive for syphilis with an RPR titre of 1:32. She declined any history of syphilis. She tested negative for syphilis in her last pregnancy 5 years earlier. She admitted to having a painless oral ulcer for 2 months, 4 months before this diagnosis. She was diagnosed with early latent syphilis. She reported an allergic rash to penicillin as a child - the details were unclear, but it was believed to be an itchy rash with hives.

Based on this information, she was advised referral to an immunologist for desensitisation or de-labelling of penicillin allergy which she declined. She was treated at 16 weeks of gestation with a 14-day course of intravenous ceftriaxone 2g every 24 hours in the inpatient and outpatient settings. She was retreated with a 10-day course of Azithromycin 1 gm daily at week 28 of her pregnancy as her RPR remained unchanged at 1:32.

Initial syphilis RPR titre was 1:32 at week 16; the RPR titre remained 1:32 by the end of gestational week 32, indicating unsuccessful maternal treatment. The baby was delivered by a caesarean section at week 37 weeks of her pregnancy. The baby was treated with benzylpenicillin 25 mg/kg 12hrly intra-venous for 7 days, then 8 hourly on days 8, 9, and 10 (total of 10 days) as per BASHH guidelines.

At 3 months postpartum - her RPR was 1:8 and she was retreated with a 2-week course of Doxycycline 100 mg twice daily. The RPR remained at 1:8 at 6 months. There was no evidence of reinfection as the partner was treated for syphilis at another unit and denied further sexual contact.

The patient consented at all stages of her treatment, including the publication of this case report.

Discussion

Outpatient oral penicillin challenge procedures can carry out the de-labelling of low-risk reactions. Specialist immunology input for skin testing or desensitisation procedures would only be required if patients with a potential history of a possible immediate type 1 hypersensitivity reaction [7].

Pregnant women with penicillin allergy be advised for desensitization and treated with penicillin-based therapy. During the second and third trimesters of pregnancy avoid treatment with tetracycline and doxycycline. Erythromycin and azithromycin should not be used as it is ineffective in curing maternal infection. There is not sufficient data to consider ceftriaxone or other cephalosporins for the treatment of maternal infection and prevention of congenital syphilis.

The treatment with ceftriaxone was chosen for the patient and was based on the BASHH guidelines [8]. The decision was made after discussion with the patient and multidisciplinary meetings between infectious diseases, obstetrics, and paediatrics to prevent CS.

The penicillin-based therapy is the only treatment with proven efficacy for the treatment of syphilis in pregnancy. Alternative ceftriaxone may be considered for the treatment of early syphilis in pregnancy [9,10] as it also crosses the placenta and is safe for the fetus [11].

The ISOSS data suggest that the majority of women who were treated received benzathine penicillin (343 of 359, 95.8%), in line with British Association of Sexual Health and HIV (BASHH) syphilis guidance [12].

The congenital syphilis is diagnosed in infants by positive RPR testing from blood, physical examination findings and X-rays.

High baseline syphilis RPR can be a factor for congenital syphilis, neonatal death, stillbirth, and premature birth, especially in patients with RPR titers of $\geq 1:8$ [13]. Despite persistently raised RPR at 1:32, our patient delivered a normal baby and therefore ceftriaxone can be used in persistently raised RPR.

Conclusion

For pregnant syphilis patients with a penicillin allergy ceftriaxone can be used as an effective therapy to prevent congenital syphilis. Persistently raised RPR does not affect the outcome in treated patients with ceftriaxone.

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