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CONGENITAL SYPHILIS. NEW QUESTIONS ABOUT A NEGLECTED BUT RE-EMERGING CONDITION

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In this issue of Case Reports, Cifuentes-Cifuentes *et al.* (1) describe a case of congenital syphilis (CS) in a newborn resulting from the first pregnancy of a woman who, despite having been diagnosed with syphilis through serological tests four years earlier, had not received treatment.

At 21 weeks pregnant, the mother attended a prenatal check-up where she was ordered a VDRL test that showed a 1:4 dilution, as well as a treponemal test that was positive. Therefore, she was diagnosed with gestational syphilis (GS) and was prescribed a weekly dose of 2 400 000 IU of benzathine penicillin for 3 weeks.

At the time of delivery, both the mother and the newborn underwent a VDRL test, and although the mother had a 1:1 dilution, which was interpreted as a satisfactory response to treatment, the result in the newborn was a 1:4 dilution. Since the infant also had elevated liver enzyme levels and his urinalysis showed signs of renal failure, he was considered to be a case of CS. Treatment was started with 150 000 IU of intravenous crystalline penicillin every 12 hours for 10 days, which resulted in improvement of the signs of renal failure and liver disease, as well as a negative VDRL test result at 3 months.

This case presents relevant and novel information about the management of CS since Cifuentes-Cifuentes *et al.* (1) concluded that the recommended treatment for GS was insufficient to prevent CS. Consequently, they indicated that clinical and serological follow-up is required to confirm whether maternal treatment was effective in the fetus.

Given the relevance of this publication, I would like to make some reflections that could explain the failure to treat CS when treating GS.

POSSIBLE MATERNAL RE-INFECTION WITHIN 30 DAYS PRIOR TO DELIVERY

According to the case report, the pregnancy occurred in a woman with late latent syphilis, who became pregnant as a result of a consensual relationship that lasted 3 months; however, it is unclear whether or not the patient had sexual intercourse with this or another partner after the administration of the therapeutic regimen given to her at week 22 of gestation based on the stage of her infection. Thus, reinfection in the mother (primary syphilis) cannot be ruled out as a cause of CS, especially if it was acquired within 30 days after delivery and had little effect on the maternal serological test (2,3). Data about a new sexual contact may not be presented because the patient was not asked for it, or she did not respond or answered incorrectly. In other words, this case report neither confirms nor denies this possibility.

It is important to keep in mind that, as described in Cifuentes-Cifuentes *et al.* (1), international guidelines do not consider the administration of benzathine penicillin to the mother as effective for the treatment of GS if it is administered 30 days before delivery, which is consistent with what has been reported in the literature (2,3).

UNDERTREATMENT OF CS

According to Workowski *et al.* (2), a single dose of 2 400 000 IU of benzathine penicillin is effective in curing 97% of CS cases if administered more than 30 days before delivery and if there is no reinfection. Therefore, the case of Cifuentes-Cifuentes *et al.* (1) could be among the 3% of patients who do not respond to treatment or could be a case of decreased response of fetal *Treponema pallidum* to benzathine penicillin administered to the mother. However, this cannot be validated because the evidence supporting the effectiveness of GS treatment in terms of fetal or neonatal outcome is considered to be of low certainty since the majority of the information is derived from observational studies (4).

In this regard, in the case published by Cifuentes-Cifuentes *et al.* (1), more than explaining reinfection, the mechanism that would explain the success of treatment in the mother but the failure of treatment in the fetus remains unclear.

Another interesting aspect of the case presented by Cifuentes-Cifuentes *et al.* (1) is that infection in the newborn was confirmed by a polymerase chain reaction (PCR) test to detect *T. pallidum*, which is one of the most sensitive and specific diagnostic tests to identify this bacterium (2). This is relevant because the diagnosis of syphilis is still based on treponemal and non-treponemal tests, as diagnosis and treatment in a single time have been prioritized for both pregnant women and high-risk populations (5); however, these tests do not perform well in primary syphilis, where microscopy techniques of genital or oral ulcer samples are preferred (2). It is worth mentioning that a very interesting application of PCR tests is that they detect strains resistant to macrolides (2) or tetracyclines (3).

In summary, this case report raises several problems that should be addressed by researchers and public health agencies regarding syphilis infection in Colombia:

For researches, different questions arise, such as: what is the effectiveness, in terms of fetal outcomes, of crystalline penicillin compared with benzathine penicillin in the treatment of CS when detected within 30 days prior to delivery?; what is the resistance profile of *T. pallidum* to macrolides and tetracyclines in Colombia?; and what is the effectiveness of therapeutic alternatives for syphilis in case of penicillin resistance or shortage of this drug?

In turn, health authorities should consider whether it would be important to know the magnitude of the syphilis problem in the general population of the country, given that surveillance reports published by the Ministry of Health and Social Protection of Colombia indicate that the prevalence rate of gestational syphilis is 1.3 cases per 100 live newborns (2). This would allow determining if there is an undeclared epidemic of population-based syphilis, what measures are being taken to control syphilis outbreaks in the general population, and what surveillance methods are being implemented for dealing with antibiotic-resistant *T. pallidum*.

The situation of GS and CS in Colombia may be a warning sign of the syphilis situation in the general population; therefore, it must be viewed as a public health issue, as the disease cannot be eradicated if the foci of infection are not controlled. In this sense, the researchers must work to ensure that the entities responsible for its prevention, treatment, follow-up and control, both individual and collective, provide the necessary resources to seek solutions that enable an interdisciplinary approach to care for patients with syphilis and to generate strategies to prevent and eradicate this infection.

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