

## Case Report



# A Case of Successful Treatment of Congenital Syphilis in an Extremely Preterm Baby With Severe Respiratory Distress

Yoon Kyung Cho , Yeon Kyung Lee , Sun Young Ko

Department of Pediatrics, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Uijeongbu, the Republic of Korea



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### Correspondence to

Sun Young Ko

Department of Pediatrics, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 271 Cheonbo-ro, Uijeongbu 11765, the Republic of Korea.  
Email: kosymdneo@gmail.com

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### ORCID iDs

Yoon Kyung Cho   
<https://orcid.org/0000-0003-1377-4446>  
Yeon Kyung Lee   
<https://orcid.org/0000-0001-8618-109X>  
Sun Young Ko   
<https://orcid.org/0000-0002-1607-0754>

### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## ABSTRACT

We report a case of successful treatment of congenital syphilis in an extremely preterm baby. A 1,395 g female infant was born by emergency Caesarean section due to preterm labor and breech presentation at gestational age at 29 weeks and 3 days with an Apgar score of 2 and 4 at 1 minute and 5 minutes, respectively. The mother of the newborn, an illegal immigrant who did not receive any antenatal care, was diagnosed as active syphilis infection by reactive rapid plasma regain (RPR) (titer 1:128) just before the delivery. Upon birth, the newborn presented with various clinical manifestations, including severe respiratory distress syndrome, persistent pulmonary hypertension of the newborn, disseminated intravascular coagulopathy, desquamation and scaling of the whole body, and osteolytic changes of long bone ends. Results of laboratory tests showed signs of early congenital syphilis, including positive syphilis reagent test (12.7 R.U.), reactive with RPR titer of 1:64, and positive for immunoglobulin (Ig) M and IgG fluorescent treponemal antibody absorption test. However, after completion of penicillin G treatment for two weeks, laboratory results dramatically improved, showing a negative syphilis reagent test (0.5 R.U.) and non-reactive in RPR. In conclusion, the incidence of congenital syphilis is prone to be resurgent in South Korea, neonatologists should be fully aware of the clinical features of congenital syphilis because early diagnosis and prompt treatment are essential in order to reduce the social and economic burden due to congenital syphilis.

**Keywords:** Syphilis; Congenital; Infant; Premature

## INTRODUCTION

When a pregnant woman infected with *Treponema pallidum* is left untreated, it can result in various adverse outcomes including early fetal loss, stillbirth, congenital syphilis, prematurity, low birth weight, and neonatal death.<sup>1)</sup> Especially congenital syphilis (syphilis transmitted through the placenta from mother to fetus) is accompanied by a wide range of clinical manifestations that can lead to high economic and social costs.<sup>2)</sup>

To prevent the spread of congenital syphilis, mass screening of all pregnant women and treatment of syphilis at its early stage are implemented in many developed countries.<sup>3)</sup> However, the incidence of syphilis has recently increased in developing and developed countries.<sup>4)</sup> The incidence of congenital syphilis has also increased in South Korea.<sup>5)</sup>

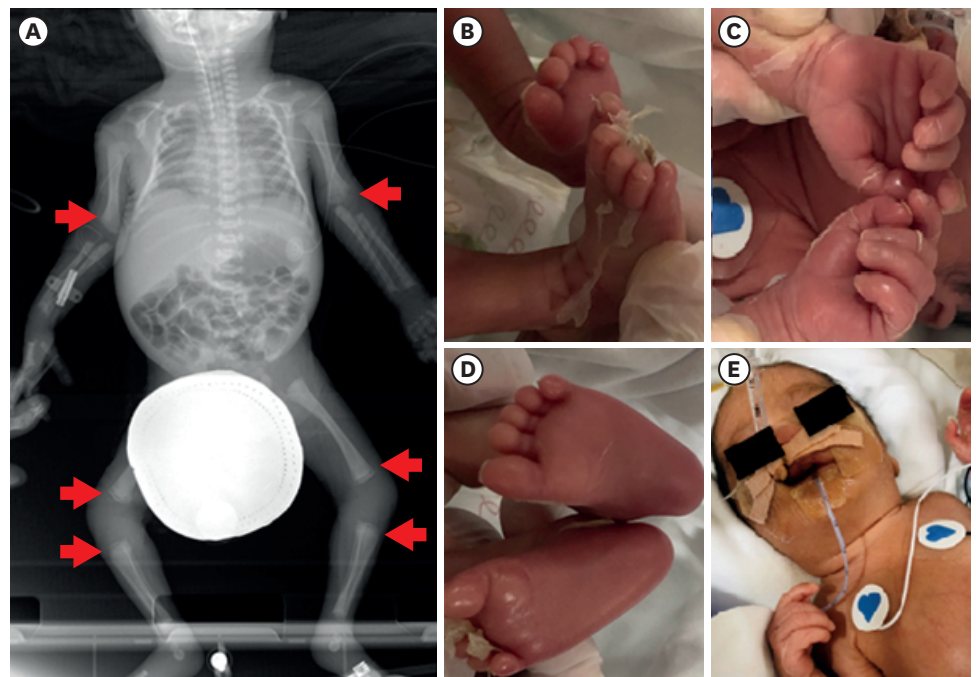
We report a case of congenital syphilis in an extremely premature infant from an illegal immigrant showing severe respiratory failure and a wide range of clinical manifestations.

## CASE

The mother of a newborn, an illegal immigrant from Thailand, did not receive any antenatal care. When she visited the antenatal care clinic for the first time just one week before delivery, she was diagnosed with an active syphilis infection. Due to preterm labor, she was transferred to our hospital. An emergency Caesarean section was performed to deliver a 1,395 g female infant due to breech presentation at a gestational age of 29 weeks and 3 days. The infant had Apgar scores of 2 and 4 at 1 minute and 5 minutes, respectively.

Upon birth, the newborn presented with whole body skin lesions and severe respiratory failure. Since she showed no respiratory effort and her heart rate was <100/min, she was intubated immediately in the delivery room. She was also given a dose of surfactant because severe hypoxia did not improve. She was stabilized after applying high-frequency oscillatory ventilation (HFOV) and 20 ppm of nitric oxide (NO) inhalation.

There were desquamation and scaling of the whole body, especially on both hands and feet (**Fig. 1B, C, and D**). *Pemphigus syphiliticus*, a characteristic fluid-filled bullous eruption, was observed with the peeling of the skin. X-rays of the long bone ends of all limbs showed osteolytic changes (**Fig. 1A**). She also showed jaundice and hepatosplenomegaly. But she did not have ocular lesions such as chorioretinitis.



**Fig. 1.** (A) X-ray of the patient on the 8th hospital day. Red arrows indicate osteolytic changes on the long bone ends. (B-D) Desquamation and peeling of the patient's hands and feet. (E) Jaundice in the face and body of the patient.

Initial laboratory results of the newborn showed 7.6 g/dL of hemoglobin,  $101 \times 10^3/\mu\text{L}$  of platelets, 30.9/2.07 mg/dL of blood urea nitrogen/creatinine (BUN/Cr), and 10.61 mg/dL (normal <0.5 mg/dL) of C-reactive protein. Coagulation profile and liver function test (prothrombin time of 23.1s, activated partial thromboplastin time of 52.5 seconds, the international normalized ratio of 2.00, aspartate transaminase (AST)/alanine aminotransferase (ALT) of 211/19 U/L, and total bilirubin/direct bilirubin of 6.82/4.15 mg/dL) suggested signs of hepatitis, jaundice (**Fig. 1E**), disseminated intravascular coagulation (DIC), and anemia. For the treatment of anemia and DIC, a transfusion of packed red blood cell (PRC), fresh frozen plasma (FFP), and platelet concentrate (PC) was done.

We began treatment immediately with an intramuscular injection of 50,000 IU/kg of benzathine penicillin and an intravenous injection of ampicillin and cefotaxime before the arrival of penicillin G from the Korea Orphan & Essential Drug center. The test results for congenital syphilis had a syphilis reagin value of 12.7 R.U. (normal <1.0), reactive rapid plasma regain (RPR) titer of 1:64, and positive for both fluorescent treponemal antibody absorption (FTA-ABS) immunoglobulin (Ig) M and IgG. In comparison, the mother's syphilis tests on admission in our hospital showed a syphilis reagin value of 1.3 R.U., reactive RPR titer of 1:128, and positive for FTA-ABS IgG.

On the 3rd day after birth, the respiration of the newborn improved. Thus, the ventilator mode was changed from HFOV to assist control mandatory ventilation mode and the concentration of NO was reduced. In addition to laboratory tests, cerebrospinal fluid (CSF) study and screening tests for other congenital infections were also done. The results of the CSF study were within normal ranges.

On the 6th day after birth, laboratory results improved to the hemoglobin of 11.2 g/dL, BUN/Cr of 15.5/1.41 mg/dL, and AST/ALT of 44/7 U/L. On the 7th day, penicillin G arrived from Korea Orphan & Essential Drug Center. We were able to start penicillin G treatment. Penicillin G was administered at 50,000 IU/kg/dose every 8 hours for 14 days. After the completion of penicillin G treatment, the syphilis reagin test showed 2.0 R.U. On the 8th day after birth, we tried to extubate the ventilator from the newborn. However, she was re-intubated due to bleeding from the endotracheal tube, although the echocardiogram was normal. On the 13th day after birth, the second attempt to extubate her from the invasive mechanical ventilator was successful. The newborn was moved to a noninvasive positive-pressure ventilation and later to a high-flow nasal cannula on the 16th day. On the 70th day, the results of all laboratory tests were further improved: syphilis reagin value, 0.5 R.U.; TPHA, reactive; FTA-ABS IgM, negative; and RPR test, non-reactive. Before discharge, we checked her brain with magnetic resonance imaging and the result was normal. Finally, the newborn was discharged without complications after recovering from congenital syphilis, respiratory distress syndrome, and prematurity. Unfortunately, follow-up could not be done at our clinic because she went back to her mother's country.

Informed consent for publication was obtained from the parents of the patient. This work was approved by Catholic Medical Center Institutional Review Boards (no. UC22ZISI0057).

## DISCUSSION

Congenital syphilis shows a wide range of clinical manifestations leading to high economic and social costs. From mothers with syphilis, the 25–75% of newborns gets congenital syphilis and without the treatment, the mortality rate is 1–3%.<sup>6)</sup> According to another study, it has shown that about 70% of infected women would have an adverse pregnancy outcome without screening or early treatment.<sup>7)</sup> It has been shown in developed countries that mass screening and early treatment are efficient and cost-effective for controlling congenital syphilis.<sup>8)</sup> Consequently, the incidence of congenital syphilis was used to be generally very low in developed countries.<sup>9)</sup> However, syphilis incidence is on the rise worldwide.<sup>10)</sup> For example, there was a high prevalence of syphilis in Italy among immigrant women, mostly from Eastern Europe, who do not always receive adequate prenatal care.<sup>11)</sup> The increase in the incidence of congenital syphilis in Italy was correlated with a high incidence of syphilis among immigrant women.

For the last 10 years in South Korea, the incidence of congenital syphilis has increased, which may be related to the increasing number of international marriages.<sup>5)</sup> These immigrants do not receive adequate health care including prenatal care possibly due to low socioeconomic status according to another study.<sup>12)</sup>

As in our case, of which the patient was born at gestational age of 29 weeks and 3 days, preterm neonates exhibit more severe clinical manifestations of congenital syphilis than term neonates in previous studies.<sup>13)</sup> Our patient suffered from severe respiratory distress, and refractory hypoxia unresponsive to conventional treatment. She required HFOV, administration of surfactant, and even inhalation of NO gas. There were physical abnormalities such as hepatosplenomegaly and desquamation and scaling of the whole body with osteolytic changes of long bone ends of all limbs. In laboratory findings, there were DIC, hepatitis, and acute renal failure which required multiple transfusions of PRC, FFP, and PC. We did not use ceftriaxone in our case because she had jaundice and renal failure. We used benzathine penicillin and cefotaxime before the arrival of penicillin instead.

Due to the shortage of penicillin antibiotics in South Korea, it took some time to receive the medication from Korea Orphan & Essential Drug Center. As syphilis increases, we need to build a faster and more effective way to get penicillin antibiotics immediately after diagnosis. After the arrival and start of treatment, the newborn recovered from congenital syphilis very quickly. She was discharged without further complications of congenital syphilis.

Incidence of congenital syphilis is prone to be resurgent in South Korea, similar to the increasing trend worldwide. Neonatologists should be aware of the clinical features of congenital syphilis because early diagnosis and prompt treatment are essential to reduce the social and economic burden caused by congenital syphilis.

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## REFERENCES

1. Kollmann TR, Dobson SR. Syphilis. In: Wilson CB, Nizet V, Maldonado YA, Remington JS, Klein JO, editors. Remington and Klein's infectious diseases of the fetus and newborn infant. 8th ed., Philadelphia: Saunders, 2016:512-43.
2. World Health Organization (WHO). Investment case for eliminating mother-to-child transmission of syphilis: promoting better maternal and child health and stronger health systems [Internet]. Geneva: WHO; 2012 [cited 2012 Sep 24]. Available from: <https://www.who.int/publications/i/item/9789241504348>.
3. Blandford JM, Gift TL. The cost-effectiveness of single-dose azithromycin for treatment of incubating syphilis. *Sex Transm Dis* 2003;30:502-8.  
[PUBMED](#) | [CROSSREF](#)
4. Nelson R. Congenital syphilis increases in the USA. *Lancet Microbe* 2022;3:e171.  
[PUBMED](#) | [CROSSREF](#)
5. Kang SH, Lee JH, Choi SH, Lee J, Yoon HS, Cha SH, et al. Recent change in congenital syphilis in Korea: retrospective 10 year study. *Pediatr Int* 2015;57:1112-5.  
[PUBMED](#) | [CROSSREF](#)
6. Phiske MM. Current trends in congenital syphilis. *Indian J Sex Transm Dis AIDS* 2014;35:12-20.  
[PUBMED](#) | [CROSSREF](#)
7. Hawkes S, Matin N, Broutet N, Low N. Effectiveness of interventions to improve screening for syphilis in pregnancy: a systematic review and meta-analysis. *Lancet Infect Dis* 2011;11:684-91.  
[PUBMED](#) | [CROSSREF](#)
8. Hong FC, Liu JB, Feng TJ, Liu XL, Pan P, Zhou H, et al. Congenital syphilis: an economic evaluation of a prevention program in China. *Sex Transm Dis* 2010;37:26-31.  
[PUBMED](#) | [CROSSREF](#)
9. Walker DG, Walker GJ. Forgotten but not gone: the continuing scourge of congenital syphilis. *Lancet Infect Dis* 2002;2:432-6.  
[PUBMED](#) | [CROSSREF](#)
10. Centers for Disease Control and Prevention (CDC). Congenital syphilis - United States, 2003-2008. *MMWR Morb Mortal Wkly Rep* 2010;59:413-7.  
[PUBMED](#)
11. Tridapalli E, Capretti MG, Sambri V, Marangoni A, Moroni A, D'Antuono A, et al. Prenatal syphilis infection is a possible cause of preterm delivery among immigrant women from eastern Europe. *Sex Transm Infect* 2007;83:102-5.  
[PUBMED](#) | [CROSSREF](#)
12. Park HO, Lim JW, Jin HS, Shim JW, Kim MH, Kim CS, et al. Comparative study of newborns of Asian immigrant and Korean women. *Korean J Pediatr* 2009;52:1119-26.  
[CROSSREF](#)
13. Zhou Q, Wang L, Chen C, Cao Y, Yan W, Zhou W. A case series of 130 neonates with congenital syphilis: preterm neonates had more clinical evidences of infection than term neonates. *Neonatology* 2012;102:152-6.  
[PUBMED](#) | [CROSSREF](#)

### 요약

본 증례는 극소미숙아에서 선천매독을 성공적으로 치료한 것에 대한 내용이다. 재태주수 29주 3일, 1,395 g의 여아가 응급 제왕절개 분만으로 태어났으며, 당시 1분 아프가 점수는 2점, 5분 아프가 점수는 4점이었었다. 산모는 산전진찰을 전혀 받지 않았던 불법 체류자로, 분만 직전에 매독으로 진단받았다. 환아는 심각한 호흡곤란 증후군, 신생아 폐 고혈압 지속증, 파종성 혈관 내 응고증, 피부의 낙설, 긴 뼈 끝 부위에 골용해성 변화 등을 보였었다. 2주간 Penicillin G 치료를 받았으며, 퇴원 시에는 다른 합병증 없이 건강한 상태로 퇴원할 수 있었다. 최근 한국뿐만 아니라 전 세계적으로 선천 매독의 발생률이 늘어나고 있다. 신생아 진료의들은 선천 매독의 임상 양상을 충분히 알고 미리 대처하여 장기적 합병증 및 사회적, 경제적 부담을 줄일 수 있도록 해야 할 것이다.