

Case Report



The Case Report of Newborn Prenatally infected by Human Immunodeficiency Virus in Republic of Korea

Kyoung Eun Lee , Won Young Lee , Eui Kyung Choi , Jeong Hee Shin ,
Byung Min Choi , Yun-Kyung Kim

Department of Pediatrics, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, the Republic of Korea

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Correspondence to

Yun-Kyung Kim

Department of Pediatrics, Korea University Ansan Hospital, Korea University College of Medicine, 123 Jeokgeum-ro, Danwon-gu, Ansan 15355, the Republic of Korea.
E-mail: byelhana@hanmail.net

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ORCID iDs

Kyoung Eun Lee

<https://orcid.org/0000-0002-4235-5120>

Won Young Lee

<https://orcid.org/0000-0001-7736-4652>

Eui Kyung Choi

<https://orcid.org/0000-0003-2192-2648>

Jeong Hee Shin

<https://orcid.org/0000-0003-3718-968X>

Byung Min Choi

<https://orcid.org/0000-0003-0931-2353>

Yun-Kyung Kim

<https://orcid.org/0000-0003-4396-8671>

Conflicts of Interest

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

ABSTRACT

Trans-placental neonatal human immunodeficiency virus (HIV) infection is common in Africa; however, it is not yet reported in the Republic of Korea. With the increasing incidence of HIV infection, especially in the reproductive age group, the risk of the vertical transmission of HIV is also increasing. We report the first case of HIV infection acquired in-utero in a newborn in Korea. The baby is growing well with normal development.

Keywords: Prenatal transmission; Infection; HIV

INTRODUCTION

Human immunodeficiency virus (HIV), a *Lentivirus* (a subgroup of *Retrovirus*), causes infection and over time leads to acquired immunodeficiency syndrome (AIDS), a condition in humans wherein progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Recently, the number of newly diagnosed HIV infections has been increasing in the Republic of Korea, especially in individuals in the reproductive age, including adolescents. Women of reproductive age with HIV is at risk of the mother-to-child transmission, which leads to increased newly pediatric HIV infection. Most of pediatric infections is acquired through mother-to-child transmission during pregnancy, delivery, or breast-feeding. Trans-placental neonatal HIV infection is common in Africa, but it has not been reported in the Republic of Korea. Antiretroviral prophylaxis is effective in preventing most of mother-to-child transmission. However, we encountered a case of a HIV-infected newborn via mother-to-child transmission despite of prophylaxis on vertical transmission. This is the first case report of HIV infection through mother-to-child transmission in utero in Republic of Korea, which was thought to be a safe area for HIV infection relatively. We would like to share our experience in the management and treatment of pediatric HIV infections caused by failure to prevent vertical infection and raise awareness about the spread of HIV and to help Korean public health care.

CASE

A 32-year-old Uzbekistan woman working for a Korea company was newly diagnosed with HIV infection by prenatal lab check at gestational age 9 weeks and 4 days, and was referred to the department of infectious disease at the Korea University Ansan Hospital. She had taken

Author Contributions

Conceptualization: Kim YK; Data curation: Kim YK, Lee KE, Choi EK, Shin JH, Choi BM; Formal analysis: Lee KE, Choi EK, Shin JH; Investigation: Kim YK, Lee KE; Methodology: Kim YK; Project administration: Kim YK; Resources: Kim YK; Software: Lee KE; Supervision: Choi BM, Shin JH, Kim YK; Validation: Kim YK; Visualization: Kim YK; Writing - original draft: Lee KE; Writing - review & editing: Choi BM, Lee KE, Choi EK, Shin JH, Kim YK.

combined antiretroviral combination treatment (ARCT) with Tenofovir, Emtricitabine, and Raltegravir from intrauterine pregnancy 12 weeks. Her initial lymphocyte count was normal. However, her HIV ribonucleic acid (RNA) copy number in the blood increased to 33,400 copies/mL and 805/ μ L CD4⁺ cell count, due to poor compliance with treatment at 37 weeks. For prophylaxis of vertical transmission, she was administered with zidovudine (ZDV), loading dose (2 mg/kg/over 1 hour), followed by a continuous intravenous (IV) infusion of 1 mg/kg/h until delivery. Her drug resistance tests of HIV did not show any resistance. A term boy was delivered via scheduled caesarean section with a birth weight of 2,700 g (25th percentile) at gestational age of 37 weeks 3 days. The general condition at birth was good with an Apgar score of 9/10. His blood collected for laboratory tests at the time of birth, including HIV RNA reverse transcription polymerase chain reaction (RT-PCR). The results of the baby's first complete blood count, toxoplasma, others, rubella, cytomegalovirus, herpes (TORCH), and liver function test were all normal. ZDV (4 mg/kg orally twice daily) was prescribed for prophylaxis and breast milk feeding was prohibited. He gained weight appropriately. When he was 3 weeks old, the HIV RNA RT-PCR in the blood at birth was reported as positive, with 45 copies/mL, showing a high possibility of HIV infection via mother-to-child transmission in utero. The following HIV RNA RT-PCR at 4 weeks old was also showed positive, with 392 copies/mL. Since then, we increased up to 12 mg/kg orally twice daily with ZDV. However, his mother did not revisit us and respond to our contact until the baby was 2 months old. And during that time, she irregularly administered ZDV to the baby owing to postpartum depression. And ARCT with nucleoside reverse transcriptase inhibitor (NRTI)+protease inhibitor (PI) combination (ZDV+3TC[®] [lamivudine]+Kaletra[®] [lopinavir/ritonavir]) was started at 2 months old considering drugs availability in the Republic of Korea and mother's drugs history. His mother was educated again to ensure better adherence. At the beginning of ARCT, his lymphocyte subset was as follows: lymphocyte subset WBC count of 8,020/ μ L, absolute CD4 count of 3,487/ μ L, CD4/CD8 ratio of 2.3, and the HIV RNA copy number was 70,900 copies/mL. Two months after starting the treatment (4 months old), the HIV RNA copy number was decreased to 5,920/mL. However, during the first 4 months of treatment, he was not administered an appropriate dose of Kaletra[®] and 3TC[®]. The baby threw up just after swallowing Kaletra[®] due to its bitter taste, and the caregiver did not give additional doses. Furthermore, the caregiver administered only a half the dose of 3TC[®] for the first 2 months of treatment due to misunderstanding. The HIV RNA copy number elevated again to 73,000 copies/mL at 6 months and 108,000 copies/mL at 9 months (**Fig. 1**). We checked HIV drug resistance

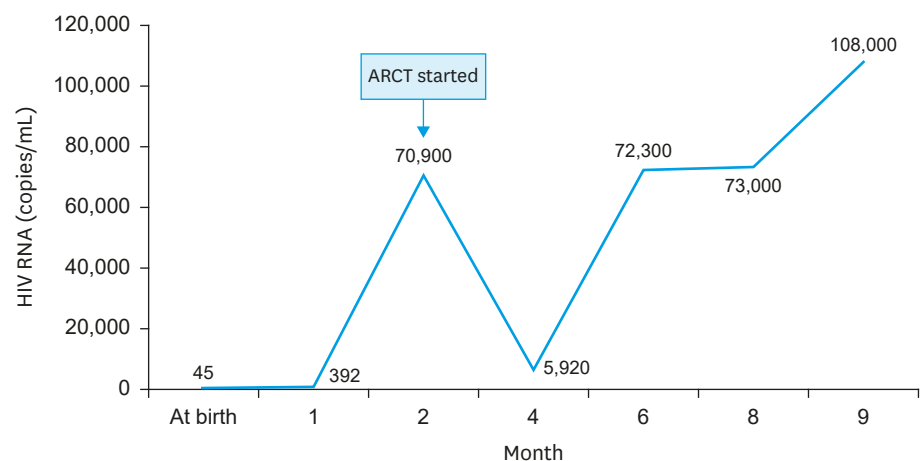


Fig. 1. The graph of the baby's HIV viral load (HIV RNA RT-PCR). Abbreviations: HIV, human immunodeficiency virus; RNA, ribonucleic acid; RT-PCR, reverse transcription polymerase chain reaction; ARCT, antiretroviral combination treatment.

mutation and found high level resistance to on 3TC[®]. The baby has been asymptomatic with 90 percentile weight, and no clinical adverse effect of ARCT. While planning for ARCT regimen modification, the baby's family moved to another country and he was lost to follow-up.

The study protocol was approved by the institutional review board of the participating facility (IRB No. 2018AS0182). Written informed consent was exempted on the basis of simple review of medical record.

DISCUSSION

We report the first case of newborn HIV infection acquired in utero via mother-to-child transmission in the Republic of Korea. Our goal of antiretroviral treatment is to promote the healthy living of children with HIV, including preventing and reducing HIV-related morbidity and mortality through maximally and continuously suppressing viral replication and preserving immune function. The baby is growing well without any medical problems.

The majority of pediatric HIV infections occurs via mother-to-child transmission at three distinct time points: in utero, intrapartum, or through breast milk. According to a one study in Zimbabwe, transmission rates in women not receiving ARCT are approximately 5–10% in utero, 10–20% intrapartum, and 5–15% through breast milk. This study defined in utero infection (IU) of HIV as infants who tested PCR-positive at birth and intrapartum infection (IP) as infants who tested PCR-negative at baseline but PCR-positive at 6 weeks.¹⁾

Perinatal infected infants are particularly at risk of death between 2 and 6 months. The earlier the children were infected, the shorter was their survival after the infection. Among them, IU infants had the lowest survival probability.¹⁾ However, this baby developed quite well and normal without any other infection, although he was diagnosed with neonatal HIV infection in utero with a high viral load.

Several studies have attempted to reduce the risk of vertical transmission. In 1994, the AIDS Clinical Trials Group 076 trial showed that the combined prenatal, intrapartum and postnatal use of ZDV reduced the rate of mother-to-child transmission of HIV.²⁾ This trial used the combination of elective cesarean section with ZDV prophylaxis to eliminate vertical transmission. The risk of mother-to-child transmission can be reduced to $\leq 2\%$ in this trial.^{1,5)} Also, we reported 10 years (2003–2013) of experiences with 9 babies from 8 HIV positive mothers in our hospital.⁶⁾ The viral load of 7 mothers remained below 1,000 copies/mL before delivery (undetectable up to 390 copies/mL) by ART. However, one mother has a viral load of 2,320 copies/mL HIV RNA at delivery. Four out of 9 newborns received IV ZDV during delivery, and the remaining 5 did not. Besides 2 babies who were lost to follow-up, 7 were concluded as HIV negative.⁶⁾ Among the various theories about how antiretroviral therapy decrease perinatal transmission, the most important is that if the drugs are administered during pregnancy, they decrease the viral load in the mother's blood and vaginal discharge, which decrease transmission to the newborn.^{6,10)} In our case, the mother's high viral load during pregnancy might be the major risk factor of mother-to-child transmission despite of chemoprophylaxis.

The maternal human immunodeficiency viral load should be kept as low as possible. If maternal human immunodeficiency viral loads are uncontrolled, a medical provider should consider the possibility of mother-to-child transmission during pregnancy.

Supporting the baby's care-giver is important both medically and socially.¹¹⁾ Furthermore, the presence of HIV infection, and especially AIDS, has been reported to have a profound psychological impact. Depression is commonly reported among persons with AIDS, and adjustment disorder with depressive mood is the most common diagnosis for HIV-infected persons with psychiatric disorders.¹²⁾ Considering that the mother's psychological problem can interfere with treatment and adherence of both her and the baby, they should be carefully monitored by a multidisciplinary team since the beginning of treatment. This will lead to successful treatment and comprehensive patient care.

In this case, there was a period when the HIV RNA copies of the baby uncontrolled, which might be caused by poor drug compliance. The mother in postpartum depression did not regularly give antiretroviral medicine to the baby. The baby spitted out and vomited the drug. The reasons of poor drug compliance were maternal depression and extremely bitter taste of the Kaletra[®] syrup. Therefore, we changed the formula from syrup to powder, educated caregivers on how to make the baby swallow the drug, and checked the remaining medicine twice a week by phone to ensure the baby took the medicine properly.

At 9 months after starting the treatment, the patient's viral load was not suppressed but increased up to 108,000 copies/mL. We suspected antiretroviral resistance. In general, children tend to maintain longer treatment duration, challenges with adherence, and have limited treatment option.¹³⁾ In South Africa, they reported $\leq 86\%$ of 1 mutation in 2-years-old children (median age) who were born from mothers treated with ART for the prevention of mother-to-child transmission.¹⁴⁾ Based on these facts, the possibility of ART resistance was very high in our case, because of inadequate treatment due to poor adherence and limited time to get an active treatment. The use of a single agent (ZDV) for the first 2 months since birth, increases the possibility of drug resistance. Consequently, he had a high-level resistance for NRTI.

We suggest two lessons learned from our case. First, if maternal HIV RNA is not controlled during pregnancy, close observation should be done in cooperation among obstetricians and pediatricians in advance. Second, after the diagnosis of pediatric HIV diagnosed, the patient along with his/her parents should get help from the multidisciplinary team, which consist of obstetrics, pediatrics, infection clinic, nutrition clinic, growth clinic, and pharmaceutical departments, as well as psychiatric medical, and social team. As the mother's physical and mental health affects children's health, prenatal and postpartum care are important to treat pediatric HIV infection.

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요약

신생아의 태반을 통한 사람면역결핍바이러스 감염은 아프리카에서 흔하지만, 대한민국에서는 아직 보고된 적이 없다. 대한민국에서 사람면역결핍바이러스 감염자의 수는 증가하는 추세이며, 특히 생식연령에서의 사람면역결핍바이러스 감염자의 수가 증가하고 있다. 이는 사람면역결핍바이러스 수직 감염의 위험성을 높인다. 저자들은 아직 국내에 보고되지 않은 자궁 내 전파를 통한 신생아의 사람면역결핍바이러스 감염을 경험하였기에 보고하는 바이다. 자궁 내 전파를 통한 사람면역결핍바이러스 감염의 예후는 좋지 않으나 본 증례의 남아는 생후 9개월 경까지 정상 성장과 발달을 보였으며 특별한 의학적 문제가 없었다.