

DOI: 10.4274/tpa.145

Perinatal HIV and prophylaxis: three case reports

Aslinur Özkaya Parlakay, Ateş Kara, Ali Bülent Cengiz, Melda Çelik, Mehmet Ceyhan

Hacettepe University Medical Faculty, Department of Pediatrics, Division of Pediatric Infectious Diseases, Sıhhiye, Ankara, Turkey

Summary

After the onset of epidemics in 1981, acquired immunodeficiency virus (HIV) has approximately infected 60 million people and caused the death of 25 million people. In 2008, nearly 430 000 [240 000-610 000] children were born as infected with HIV and so the number of HIV infected children under 15 years of age was increased to 2.1 million [1.2 -2.9 million] (Figure 1). Perinatal transmission is responsible of AIDS in 90% of children and nearly all new AIDS cases in children are caused by perinatal transmission. In this case report, clinical pictures of 3 babies born to HIV positive mothers are mentioned with the recent updates of literature concerning HIV. (*Turk Arch Ped* 2012; 47: 59-62)

Key words: AIDS, prophylaxis, HIV

Introduction

Acquired immunodeficiency virus (HIV) is a significant health problem which is responsible of infection in 33.4 million people worldwide. Although mostly found in men aged 15-39 years, young patients constitute 40% of all adult (older than 15 years of age) patients (1). Sub Sahara Africa is the region where 67% of all HIV cases occur and 91% of pediatric cases are found (1). In this region, 14 million children have been left orphan because of HIV epidemics (1).

Turkey is among the countries where HIV/AIDS has a low incidence. The first case from our country was reported in 1985 and the total number of cases reported until December 2009 reached 3898 (2) (Figure 1). In the last 3 years the number of cases increased (300 cases yearly). According to 2008 AIDS data transmission from the mother to the baby constitutes 2,4-2,6% of all transmission forms (2). While there were 4 pregnant women who received antiretroviral therapy in 2006, four cases were reported in 2007 and prophylactic treatment was given to the babies born until serology results became negative (3). Between October the 1st 1985 and December the 31st 2009, HIV transmission from the mother was found in a total of 64 infants 31 of whom were female (2). In our hospital, 3 infants born to HIV positive mothers are being followed up. In this article, follow-up and prophylactic treatment of children of HIV

positive mothers were attempted to be summarized by supporting with case reports.

Case 1

It was learned that HIV was found to be positive at the 22nd gestational week in the mother of the baby who was born by cesarean section at the age of 38 weeks and 3 days with a birth weight of 2760 g as the first living child from the third pregnancy of a HIV(+) mother of 23 years of age and Zidovudin (2x300 mg), Lamivudin (2x150 mg) and Ritonavir (2x3 capsule) treatment was started in the mother. Virus load which was 6 600 copies before treatment became 13 600 copies after one month of treatment and 539 copies after 3 months of treatment. Prophylactic treatment with zidovudine was administered to the mother during delivery (2 mg/kg before delivery, 1 mg/kg during delivery). The infant was given zidovudine for prophylaxis (8 hours after delivery by intravenous route for the first two days and 4x1.5 mg/kg/dose by oral route for 6 weeks). For pneumocystis carinii trimethoprim- sulphamethoxazole was started at the age of 6 weeks and continued for 2 weeks. At birth, HIV antibody was positive in the cord blood and HIV virus load was found to be negative. At the age of 2 months, anti HIV antibody was positive (18,7) and HIV virus load was found to be negative. Other tests revealed that immunoglobulins were

Address for Correspondence: Aslinur Özkaya Parlakay MD, Hacettepe University Medical Faculty, Department of Pediatrics, Division of Pediatric Infectious Diseases, Sıhhiye, Ankara, Turkey
Phone: +90 312 305 11 66 E-mail: aslinur@hacettepe.edu.tr **Received:** 03.26.2010 **Accepted:** 08.24.2010

Turkish Archives of Pediatrics, published by Galenos Publishing

normal, numerical increase was present in the distribution of CD4/CD8 4,9, CD4 and decrease was present in the distribution of CD8. HIV virus load was negative at the 6th and 9th months in the infant who was followed up with acquired immune deficiency virus load. It was observed that HIV antibody became negative at the 9th month.

Case 2

The mother of a female baby born by cesarean section at the age of 35 weeks and 6 days with a birth weight of 2250 g as the

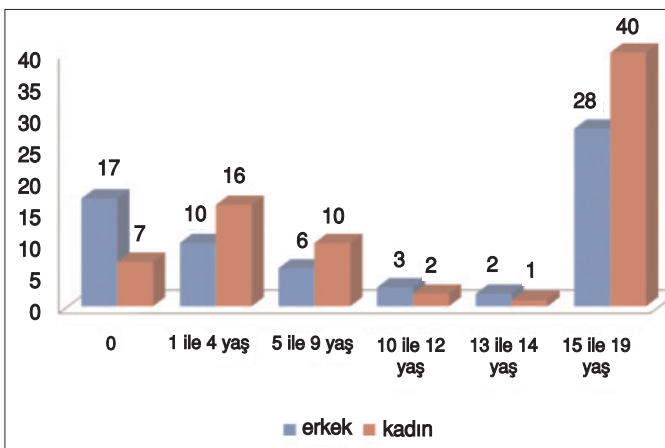


Figure 1. The distribution of HIV(+) pediatric patients in Turkey by age and gender (October the 1st, 1985-December the 31st, 2009)

second living child (she has a 15 years old HIV(-) sibling) of a 32-year old HIV (+) mother was infected by HIV one year ago. The virus load decreased from 2 880 copies/ml at the 23rd gestational week to 83 copies at the 27th gestational week with zidovudine treatment administered throughout the whole pregnancy and became negative at the 29th gestational week. For prophylaxis zidovudine 2 mg/kg/dose four times a day and lamivudine 2 mg/kg dose 2 times a day were started in the baby. Anti HIV antibody tested after birth and HIV virus load were found to be negative in the baby. The baby was followed up with virus load on the 15th day and at the first, third and sixth months. It was found that HIV antibody became negative at the 6th month.

Case 3

It was learned that the mother of a female baby born by cesarean section at the age of 37 weeks and 6 days with a birth weight of 2 770 g as the third living child from the 3rd pregnancy of a 34 year-old mother did not receive antiretroviral treatment during pregnancy, did not present for follow-up in the last two years, although it was known that she was HIV(+) for 13 years, received retroviral treatment throughout her pregnancy of the other 2 siblings and the siblings also received prophylactic treatment. Zidovudine treatment was given to the patient for 6 weeks at a dose of 2 mg/kg/dose 4 times a day. At birth, HIV virus load was negative in the cord blood and HIV antibody was positive. The patient was followed up at the first and third month and HIV antibody was found to become negative at the third month.

Table 1. Scheme of approach in infants exposed to HIV (15)

	At birth	14 days	4 weeks	6 weeks	8 weeks	4 months	12-18 months
History and physical examination ^a	X		X				
Evaluation in terms of other infections	X						
ARV prophylaxis ^b							
Prohibition of breastmilk	X						
Complete blood count	X		X ^c		X ^c		
HIV-1 DNA or RNA ^d	e	X ^f	X		g	X	
PCP prophylaxis ^h				X			
HIV antibody ⁱ							X

^a Maternal history should be interrogated in detail.

^b ARV (antiretroviral) prophylaxis should be started in the first 12 hours after birth, zidovudin should be continued for 6 weeks

^c Should be measured at the age of 4 weeks. If found low at the fourth week, it should be repeated at the 8th week

^d Viral tests of all infants exposed to HIV should be checked at the 14-21st days. If the results are negative, it should be repeated at the age of 1-2 and 4-6 months. If it is found positive, the test should be repeated immediately

^e HIV-1 DNA PCR or RNA shows in utero infection on the first days of life. If it is found negative the test should be repeated

^f If HIV-1 RNA or DNA was not checked at birth, it would be more appropriate to wait for 2 weeks, since the sensitivity will be increased. Negative results obtained at the 14th day and at the age of 4 weeks suggest uninfected infant with a high possibility and negative results obtained at the age of one and four months suggest uninfected infant absolutely

^g If HIV-1 RNA or DNA results are negative at the age of 2 and 4 weeks, no test is required at the age of 8 weeks. A negative result at the age of 8 weeks suggests possibly uninfected infant

^h PCP prophylaxis should be started in infants exposed to HIV at the age of 4-6 weeks (If HIV-1 RNA or DNA results are negative at the age of 2 and 4 weeks, PCP prophylaxis is not needed). If the infant is HIV positive the prophylaxis should be continued until one year of age

ⁱ At the 12-18th month, HIV DNA is expected to become negative in HIV(-) patients

Discussion

Studies have shown that the delivery mode is effective in preventing HIV transmission from the mother to the baby in perinatal HIV transmission. It was reported that HIV transmission decreased by 50% in deliveries performed by cesarean section at appropriate conditions and cesarean section prevented HIV transmission by 80% with administration of antiretroviral treatment to the mother during and after delivery (4). In our cases, cesarean section at appropriate conditions were preferred.

It was found that HIV viral load of the mother had no effect on transmission, but administration of antiretroviral treatment with high activity to the mother decreased transmission markedly (5). In our first case, viral load of the mother decreased after treatment. In our second case, the viral load of the mother became negative, but the viral load status of our last case is not known, since she was not followed up.

It was shown that the rate of transmission by breastmilk which is a significant way of viral transmission from HIV(+) positive mother to the baby was approximately 16.2% and transmission by breastmilk occurred in the early period of life. It was reported that formula use instead of breastmilk prevented transmission by 44% and this was efficient to increase survival of babies of HIV(+) mothers to a certain degree (6).

To decrease perinatal HIV transmission use of zidovudine was recommended by the Ministry of Health of the United States in 1994 (7). With the accomplishment of these recommendations HIV transmission and pediatric AIDS cases registered since 1992 was found to be decreased by 75% (8). In prevention of HIV transmission from the mother to the baby, the time of starting zidovudine use was shown to have an effect on preventing transmission (9). It was reported that the rate of transmission was 6.1% when prophylactic treatment was started before delivery, 10% when prophylactic treatment was started during delivery, 9.3 when prophylactic treatment was started in the first 48 hours after delivery, 18.4% when prophylactic treatment was started after the third day and 26.6% when prophylactic treatment was not started (9). In 2 of our cases, prophylactic zidovudine treatment was started before delivery, but no treatment was given to the other pregnant woman, since she was not followed up.

Because of difficulties in fighting with acquired immune deficiency virus infection the necessary interventions in newborns infected with HIV should be performed by experts in the subject. Detailed history related to psychosocial factors (economic insufficiency, substance addiction, depression etc.) should be taken from the mother. If the history taken is not sufficient, the necessary serological tests should be performed.

Positive immunoglobulin G crossing the placenta found by ELISA (enzyme-linked immunosorbent assay) and Western Blot analysis in infants younger than 18 months suggests infection in the mother, but does not give information about the

infection in the baby. Positive HIV antibody after 18 months shows HIV infection in the infant (10). In rare cases of hypogammaglobulinemia, the test may be false negative (11).

Since HIV antibody test may not be sufficient in newborns, HIV DNA polymerase chain reaction (PCR) or viral culture may be required. Polymerase chain reaction or viral culture should be repeated at birth and when the infant is one or two months old, but cord blood should not be used for the test. If the test result is positive, the test should be repeated. If the test results are negative and the subject has no complaints, PCR or viral culture should be repeated, when the infant is 3-4 months old (if a finding develops, the test should be repeated immediately). In cases where polymerase chain reaction or viral culture can not be performed, p24 antigen can be tested, but the sensitivity of this test is lower. In infants who have negative PCR or viral culture results at the age of four months, the possibility of not being infected is more than 95% (12).

However, these patients are recommended to be followed up for 12 months and more in terms of showing that HIV antibody has been eliminated. For an infant exposed to acquired immune deficiency virus to be considered as not being infected by HIV, virologic test results should be negative, immunological test results should be normal and two or more negative HIV antibody results should have been obtained after the age of 12 months. American Pediatric HIV Center recommends measurement of anti-HIV antibody at the age of 24 months even if two or more negative anti-HIV antibody test results are present (13).

Pneumocystis carini pneumoniae (PCP) is frequently found in HIV-infected children at the age of 3-6 months. For polymerase chain reaction prophylactic treatment is recommended to be started at the age of 4-6 months in all infants born to HIV-infected mothers independent of CD4 count. Treatment can be discontinued in patients with 2 negative viral culture or negative PRC test results. In patients infected with acquired immune deficiency virus or whose HIV infection status is not clear, PCP prophylactic treatment should be continued until one year of age. After one year of age the inhibition status of the immunity should be evaluated according to CD4 count and the treatment should be continued or discontinued.

To prevent other opportunistic infections the families of HIV-infected patients should be elucidated about the ways of preventing Cryptosporidium, Giardia, Toxoplasmosis and Bartonellosis (including not consuming uncooked meat, giving attention to the hygiene of drinking water, limiting contact with animals). Starting treatments for prevention of Mycobacterium avium-intracellulare complex, Cryptococcus, Histoplasma, Coccidioides or Cytomegalovirus should be planned according to the status of the patient. Infants in whom antiretroviral treatment is started during the newborn period should be followed up closely in terms of toxicities. Complete blood count should be performed at birth and when the infant is 4 and 6 weeks old in terms of mild, transient

anemia which is a complication of 6-week zidovudine treatment in particular. On 6-year follow-up, short-term zidovudine treatment was reported to be safe in women and infants (14), but longer follow-up is required for long-term results. According to the data potential rare toxicity of prophylactic treatment seems to be ignorable, when the fatal dimension of HIV infection is considered, but subjects who have received in utero antiretroviral treatment or prophylactic treatment are still recommended to be followed up closely.

References

1. UNAIDS 2009 AIDS epidemic update. http://data.unaids.org/pub/FactSheet/2009/20091124_FS_global_en.pdf.
2. Sağlık Bakanlığı HIV/AIDS verileri 2010. <http://pozitifyasam.org/assets/files/Aralik2010verileri.htm>
3. UNGRASS indicators country report. http://data.unaids.org/pub/Report/2008/turkey_2008_country_progress_report_en.pdf
4. Lindsay MK, Grant J, Peterson HB, Willis S, Nelson P, Klein L. The impact of knowledge of human immunodeficiency virus serostatus on contraceptive choice and repeat pregnancy. *Obstet Gynecol* 1995; 85: 675-9.
5. Cooper ER, Charurat M, Mofenson L, et al. Women and infants' transmission study. Group combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr* 2002; 29: 484-94.
6. Nduati R, Mbori-Ngacha D, John G, et al. Breastfeeding in women with HIV. *JAMA* 2000;284: 956-7.
7. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med* 1994; 331: 1173-80.
8. Mofenson LM. Technical report: perinatal human immunodeficiency virus testing and prevention of transmission. *Committee on Pediatric Aids. Pediatrics* 2000; 106: E88.
9. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med* 1998;339: 1409-14.
10. El-Sadr W, Oleske JM, Agins BD. Managing early HIV infection. Agency for health care policy and research. *Clin Pract Guidel Quick Ref Guide Clin* 1994;7: 1-37.
11. Borkowsky W, Krasinski K, Paul D, Moore T, Bebenroth D, Chandwani S. Human-immunodeficiency-virus infections in infants negative for anti-HIV by enzyme-linked immunoassay. *Lancet* 1987;1: 1168-71.
12. Hanson IC, Shearer WT. Diagnosis of HIV infection. *Semin Pediatr Infect Dis* 1994; 5: 266-71.
13. Working group on antiretroviral therapy: National pediatric HIV resource center. Antiretroviral therapy and medical management of the human immunodeficiency virus-infected child. *Pediatr Infect Dis J* 1993;12: 513-22.
14. Hanson IC, Antonelli TA, Sperling RS, et al. Lack of tumors in infants with perinatal HIV-1 exposure and fetal/neonatal exposure to zidovudine. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999; 20: 463-7.
15. Havens PL, Mofenson LM, American Academy of Pediatrics Committee on Pediatric AIDS. Evaluation and management of the infant exposed to HIV-1 in the United States. *Pediatrics* 2009;123: 175-87.