HIV Transmission Through Breastfeeding: Still Possible in Developed Countries

We describe here the case of a 13-month-old boy who acquired HIV infection postnatally through breastfeeding in a developed country in 2012. His mother had regular pregnancy follow-up and was found to be seronegative for HIV on 2 consecutive screening tests (during pregnancy and just after delivery). However, 1 year later, diagnosis of HIV infection arose in both of them after a pediatric emergency department visit for bronchitis when unexplained hepatosplenomegaly and inflammatory syndrome were noted. The negative maternal viral load found just after delivery confirmed that the mother’s seroconversion occurred postnatally, which allowed for active HIV transmission during lactation and lack of the efficient preventive measures that have implemented in Belgium for years. We discuss this uncommon but still existing mode of HIV transmission in industrialized countries and highlight the importance of implementing new targeted health education interventions in addition to constant clinicians’ awareness.
Mother-to-child transmission (MTCT) of HIV remains a major public health problem, particularly in low-resource settings such as sub-Saharan Africa and South Asia.1 Worldwide, new pediatric HIV infections are almost all due to MTCT, occurring during pregnancy, during labor and delivery, or through breastfeeding.2,3 In the developing world, where extended breastfeeding until age ∼2 years is the predominant practice, the rate of MTCT is estimated to be 5% to 10% during pregnancy, 10% to 15% during labor, and 15% to 20% during prolonged breastfeeding when strategies to reduce HIV transmission are not adopted.2,3 Consequently, breastfeeding may be responsible for one-third to one-half of total HIV infections in some developing nations. In industrialized countries, in contrast, HIV-infected mothers are discouraged from breastfeeding their infants because safe alternatives to human milk are available in an environment where infectious diseases are not the main cause of infant mortality.4–7 In this situation, the estimated risk of MTCT, before preventive interventions were available, reached 5% to 10% during pregnancy, 10% to 15% during labor, and 0% during breastfeeding.2,3

The risk of MTCT HIV infection also needs to be considered among women who acquire primary HIV infection during lactation, however.8–14 It is well documented that these mothers who seroconvert during breastfeeding are at high risk of postnatal HIV transmission.8,9 This mode of transmission is however believed to be currently virtually absent in industrialized countries. Indeed, to the best of our knowledge, no description of postnatal infection from mothers who acquired HIV infection during lactation has been reported from North America, Europe, or Australia over the past 20 years.

We describe here the case of a 13-month-old boy who postnatally acquired HIV infection through breastfeeding in Belgium in 2012 and whose mother was found to be seronegative for HIV infection on 2 consecutive screening tests during pregnancy and just after delivery. We discuss this uncommon but still existing mode of HIV transmission in industrialized countries to highlight how constant vigilance of clinicians is crucial despite implemented standardized procedures.

CASE REPORT

Figure 1 details the mother’s and child’s clinical features. This boy was born at term by vaginal delivery and weighted 3620 g. During pregnancy, his mother’s serological screening tests were negative for Toxoplasma gondii, hepatitis C virus, and syphilis but revealed immunity for rubella and cytomegalovirus as well as the presence of circulating hepatitis B antigen. The mother had no group B Streptococcus vaginal carriage at 35 weeks, and the gestation period was uncomplicated. Physical examination of the infant was reported to be fully normal at birth and before maternity discharge (day 2). He received his first dose of hepatitis B vaccine plus specific immune globulins in the delivery room.

His 41-year-old mother and 43-year-old father, both from the Democratic Republic of Congo, were healthy, as were his 3 siblings.

FIGURE 1
Flowchart of mother and child’s clinical features. EBF, exclusive breastfeeding; Hepatsplen, hepatosplenomegaly.
The infant was exclusively breastfed for 3 months (as strictly defined elsewhere), followed by nonexclusive breastfeeding until he was 6 months of age.

No medical problems occurred until the child was 10 months old, when he required a short hospitalization for middle lobe pneumonia and neutropenia (95 polymorphonuclear cells/mm³). Complete and rapid recovery was observed after intravenous cefepime treatment, followed by oral cefuroxime axetil.

At 13 months of age, his neuro-developmental and nutritional status were excellent (weight and height both on 85th percentile of the World Health Organization curves). However, he was examined in the emergency department for a febrile bronchitis episode when a substantial hepatosplenomegaly raised clinicians’ concern. Concomitant laboratory investigations revealed elevated erythrocytes sedimentation rate (120 mm/h), increased immunoglobulin G level (29.98 g/L; normal range for age 2.73–16.6 g/L), and decreased CD4+ lymphocytes count (426/mm³; normal range: 1000–4600/mm³). Even though maternal HIV status was negative after delivery, the results of child’s HIV-1 serological testing were positive by both a fourth-generation enzyme-linked immunosorbent assay (ELISA; Architect HIV Ag/Ab Combo; Abbott Diagnostics, Abbott Park, IL) and Immunoblot (Innogenetics, Gent, Belgium) and were confirmed by the fourth generation antibody assay (Lia HIV I/II Score; Innogenetics, Gent, Belgium) and were confirmed on a second blood sample. His HIV viral load at diagnosis achieved 201,000 copies/mL (5.30 log copies/mL).

His mother had been tested for HIV antibodies at 4 months of pregnancy and 2 days after delivery; both results were retrospectively double-checked and confirmed to be negative. Moreover, the maternal blood sample taken on day 2 postdelivery revealed a negative HIV viral load (<200 copies/mL). When the suspicion of HIV infection arose 13 months later in her infant, she was sampled again and found to be HIV positive (ELISA and Immunoblot tests). At that time, her HIV viral load was 33,000 copies/mL. The likely source of infection was her husband who had traveled for several weeks in Central Africa after his son’s birth and was also found to be HIV positive.

**DISCUSSION**

We provide here a rare description of a breastfeeding-related HIV transmission occurring in the 21st century in a developed country where comprehensive screening procedures are already carried out. This situation is of concern and raises important questions about the additional preventive and educational measures that should be implemented.

In 1985, Ziegler and colleagues in Australia described the first case of HIV transmission through breastfeeding. This infant was infected after being breastfed by his previously healthy mother, who received a postpartum transfusion of HIV-contaminated blood. This finding was confirmed by other case reports and case series from different countries. In general, these case reports described acquisition of HIV infection by infants of breastfeeding mothers, with the mothers being HIV seronegative until acquisition of infection after delivery, usually through contaminated blood transfusions, heterosexual exposure, or intravenous drug use. Descriptions of children infected through wet-nursing or through pooled human milk have also been reported.

Soon after the recognition of transmission of HIV through breastfeeding, it became clear that mothers who acquired HIV infection during lactation were at high risk of transmitting HIV to their infants. A systematic review of published studies available in 1992 estimated the risk of transmission to be 29% (95% confidence interval [CI]: 16–42). On the basis of a case series of 10 Australian breastfeeding women, the estimated risk of breastfeeding transmission among women with acquisition of HIV-1 infection after delivery was 27% (95% CI: 6–61). More recently, Liang et al investigated HIV transmission via breastfeeding in 104 mothers who postnatally acquired the infection through blood transfusion in Hubei and Hebei, in China. Thirty-eight (35.8%; 95% CI: 26.7–44.9) of 106 children were infected. High plasma and breast milk viral load associated with primary HIV infection are the most likely reasons to explain this increased risk of transmission. MTCT was also assessed in a prospective cohort study in urban Zimbabwe of 14,110 women and infants. Breastfeeding-associated transmission was high among mothers who seroconverted postnatally (34.6 infants per 100 child years [95% CI: 26.6–44.9]). Among those women, around two-thirds of breastfeeding-associated transmission occurred while they were still in the “window period” of an antibody assay and hence tested HIV negative using only ELISA methods. In this study, an estimated 18.6% to 20.4% of all breastfeeding-associated transmission in Zimbabwe occurred among mothers who seroconverted postnatally.

Although postnatal transmission can occur when mothers acquire HIV infection during lactation, transmission is most common from women known to be infected before or at delivery. In the early 1990s, the additional risk of transmission from breast milk among women with established HIV infection at the time of delivery was estimated to be ~15% when breastfeeding was prolonged. The results of a randomized clinical trial in Nairobi, Kenya, where infants of HIV-infected mothers were allocated to either breastfeeding or formula feeding in the absence of antiretroviral treatment, showed a cumulative probability of HIV of 36.7% in the breastfeeding arm and 20.5% in the...
Transmission of HIV through breastfeeding may happen at any time during lactation. The early postnatal period (before 6–8 weeks of breastfeeding) appears to be a particularly high-risk time for HIV transmission, but it remains difficult to distinguish intrapartum from breastfeeding passing during this time period. On the other hand, late postnatal transmission through breastfeeding has been reliably estimated. The Breastfeeding and HIV International Transmission Group carried out a meta-analysis of 9 randomized controlled trials conducted in high-prevalence, resource-limited settings. Late postnatal transmission was defined as a negative HIV test at or after 4 weeks of age, followed by a positive result. The study included 225 children with late postnatal transmission. The cumulative probability of late postnatal transmission at 18 months was 9.3% (95% CI: 3.8–14.8%). The global risk of late postnatal transmission was 8.9 per 100 child-years of breastfeeding (95% CI: 7.8–10.2) and was significantly higher with lower maternal CD4+ counts. The longer the duration of breastfeeding, the higher the cumulative risk of postnatal transmission of HIV. In summary, worldwide, most postnatal pediatric HIV infections result from prenatally infected lactating women; however, the risk of MTCT is the highest if the maternal infection occurs after delivery.

On another hand, among all HIV-infected children, survival in the group that was postnatally infected has been repeatedly shown much higher than in children with infection acquired around delivery. The immaturity of the immune system of the newborn might explain its inability to control viral replication during the first weeks after birth. It has been convincingly demonstrated that young HIV-infected infants receiving early antiretroviral therapy have reduced infant mortality and HIV progression compared with those receiving deferred treatment. It is unknown, however, if deferred therapy may have a negative impact on the natural history of children infected postnatally from mothers acquiring primary infection during lactation, as in the case we report.

There are other factors associated with transmission of HIV through breastfeeding apart from the duration of breastfeeding, seroconversion during lactation, and clinical and virological status of the mother. They include mothers’ breast health (mastitis, abscesses, or cracked nipples) and pattern of infant feeding. Indeed, exclusive breastfeeding is associated with a lower risk of postnatal transmission of HIV compared with breastfeeding with formula, other fluids, or solids. It has been hypothesized that the higher risk of transmission with mixed feeding could result from damage to the intestinal mucosa after early introduction of non-breast milk foods. Alternatively, intestinal immune activation resulting from early priming with foreign antigens or enteric pathogens may be involved. The mother in the case we describe here denied any breast problems during lactation, and no stomatitis or oral candidiasis were reported in the child before HIV infection was diagnosed.

In recent years, the rate of MTCT of HIV and the transmission by blood products have been reduced dramatically in developed countries. For example, during the past decade, <200 children have been infected perinatally each year in the United States, and only 188 were diagnosed in the European Union and European Economic Area in 2011. Now that this goal has been reached, it may be time to address the issue of the rare but devastating cases of postnatal transmission through breastfeeding in industrialized countries. Because the majority of breastfeeding HIV transmissions from women seronegative at delivery seems to happen before the mothers become seropositive, the detection by serological testing during lactation is difficult to organize and appears to be of extremely low interest, even when using the most sensitive assays and especially if no suspicion of risky behavior is identified. Moreover, clinical presentation is unreliable to guide HIV screening in adult primary HIV infection. We believe that targeted health educational interventions are crucial to ensure efficient prevention of this seldom mode of transmission. These interventions should focus on parents from high-HIV-incidence countries and also on health care professionals counseling pregnant women who might be unaware of the possible risk associated with breastfeeding. Counseling should address condom use and also include education on the high risk of HIV postnatal transmission after heterosexual exposure during breastfeeding.

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