

Horizontal transmission of HIV-1 infection in a child: With phylodynamic evidence-case study

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Abstract

Mother-to-child transmission is the predominant mode of transmission of HIV infection in children. Occasionally, horizontal transmission has also been reported. We report a child who was diagnosed HIV positive at the age of 3.5 years born to HIV-negative mother. Based on the available histories, no alternative modes of HIV transmission could be implicated. However, the paternal grandmother of the child was found to be HIV infected. To explore the likelihood that this HIV-infected relative was the most likely source from which this child acquired HIV infection postnatally, Bayesian phylodynamic analysis of the HIV of the child and parental grandmother was performed, which showed evidence of linkage of HIV transmission from an HIV-infected paternal grandmother to a child living with her through unknown route. Studies to identify modes of nonvertical HIV transmission may be useful in devising strategies to avert such nonvertical infections.

Key words: HIV, nonvertical transmission, phylodynamic

INTRODUCTION

The current World Health Organization (WHO) guidelines recommend that combination antiretroviral therapy (cART) should be initiated in all pregnant and breastfeeding women living with HIV infection regardless of their WHO clinical stage, or CD4 count or HIV-1 viral load, and be continued for life.^[1]

Children generally acquire HIV infection through vertical transmission occurring in utero, during labor and delivery, or through breastfeeding after birth. Children below 15 years of age have been reported to account for 12% of the total estimated 86,000 new HIV infections in 2015 in India.^[2] Initiating cART from the second trimester of pregnancy can reduce the vertical transmission rate from 15% to 25% to well below 5%.

There are occasional reports of nonvertical HIV transmission in children through various routes.^[3] Earlier studies have reported administration of contaminated blood products, sexual abuse, surrogate breastfeeding, reuse of unsterile needles, and pre-mastication as the modes of nonvertical HIV transmission in children. However, identification of the source of infection and the route of transmission is not possible in every case.^[4-7] Determination of possible routes of transmission among these children requires comprehensive documentation of these cases and collecting additional evidence to identify and trace possible routes of the infection. It may also involve testing and sequencing of virus among other family members or caregivers who are infected.

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The present study reports a case of nonvertical, nonsexual transmission of HIV to a child whose mother was not HIV infected. In addition, phylodynamic analysis of HIV from the child and his paternal grandmother was performed to provide evidence linking to the source of HIV infection.

STUDY DETAILS

A 3.5-year-old male child born in April 2012 was brought to a private hospital in Mumbai in April 2015. The child had a history of parotitis and a 3-month long history of recurrent fever, cough, and symptoms suggestive of respiratory tract infection in March 2015. The child was found to be infected by HIV. His absolute CD4+ count (CD4%) and plasma viral load were 388 cells/mm³ (13.4%) and 191,000 copies/ml, respectively. This signified severe immunosuppression for his age and suggested that the HIV infection had not been acquired recently. Both the parents were tested and found to be HIV negative. The discordant result of mother and child was baffling, and an explanation was sought for alternate source of infection.

The parents had a nonconsanguineous marriage, and the child was delivered vaginally at term without any complications. He was immunized appropriately for his age. There was no history of sexual abuse, blood transfusion, tattooing, or piercing of body parts of the child. There was no history of surrogate breastfeeding to the child and sharing of a toothbrush or nail clipper. There was no history of premastication according to the family members.

Further history revealed that among the family of four members, his 53-year-old paternal grandmother was a known case of HIV infection and receiving antiretroviral therapy since January 2013. Her existing documented medical records showed an absolute CD4+ count of 123 cells/mm³ (13.9%) and plasma viral load of 11,612 copies/ml at the initiation of cART, which consisted of tenofovir, lamivudine, and efavirenz. Her plasma viral load was undetectable reflecting her excellent adherence in September 2015. The paternal grandmother was the primary caregiver of the child at home as both the parents were working. She helped him in feeding, giving a bath, and other routine activities. The child was treated with cART consisting of zidovudine, lamivudine, and nevirapine from October 2015 and followed periodically.

The investigation of this child was further done at the National AIDS Research Institute, Pune, India, through interviews with the available involved

adults and through a review of the available documented medical records. Written informed consent for HIV testing and other-related tests was obtained from adult family members, while in case of a child, assent was obtained from his parents. HIV testing was performed as recommended by the WHO. Blood specimens from the child and HIV-infected parental grandmother were used for the amplification and sequencing of HIV-1 partial *pol* regions.

The *pol* gene sequence analysis showed 97.18% (94.37% nucleotide identity) amino acid identity between HIV strain from the child and his paternal grandmother. Phylodynamic analysis showed clustering of both the sequences at one node with posterior probability of 1.0, implying that the paternal grandmother was probably the source of HIV-1 infection [Figure 1].

DISCUSSIONS

With the use of potent cART during pregnancy among HIV-infected women, the incidence of mother-to-child transmission has reduced drastically. An undetermined route of transmission has occasionally been reported among HIV-infected children.^[8] In this child, we attempted to identify the probable sources of HIV transmission. Since the mother was HIV negative, the possibility of vertical transmission was ruled out. There is sparse data documenting HIV-positive children having HIV-negative parents from India. A review of 109 pediatric HIV cases from tertiary care center in New Delhi, India, reported unidentified route of HIV transmission in 6.4% children of HIV-negative parents without any history of blood/blood product transfusion to the child.^[5] Another case of an 11-month-old HIV-positive infant with HIV-negative parents was reported from a tertiary care centre in Jaipur, India, with an unidentified route of HIV transmission.^[9] Fourteen cases of unexplained HIV transmissions in children of seronegative parents were also reported from South Africa.^[6] These studies could not identify the source of infection. Rarely, transmission of HIV has been reported in home settings among children residing in the same household, from one child to his sibling, through fomites and through premastication by the caregivers to the children.^[10,11]

The case described suggests that HIV may be transmitted through an unidentified mode of transmission, which was supported by phylodynamic data. The phylodynamic analysis has been widely used to assess the transmission

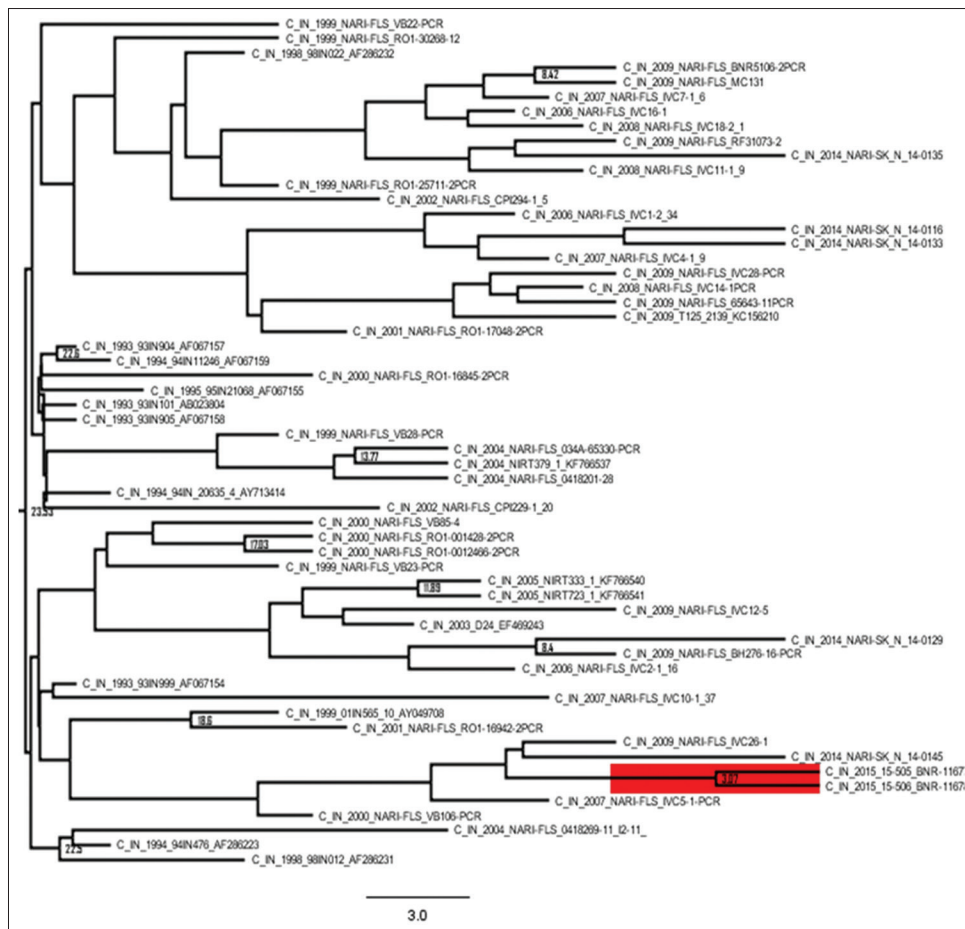


Figure 1: Phylogenetic tree of HIV-1 *pol* genome segments (2135-3338 of HXB2 co-ordinates) derived from the child and parental grandmother. Posterior probability of 1.0 confirms the transmission on linkage about 3.07 years before date of blood collection (September 2015)

linkage of HIV infection.^[12,13] As shown in Figure 1, the partial *pol* sequences from the child converged with a sequence of the parental grandmother with a posterior probability of 1.0. A high posterior probability indicates that the viral sequences from the child and parental grandmother show a high level of similarity and are more closely related to each other over strains circulating in the local area. Thus, the genetic relatedness between the virus from the child and the suspected source was identified, suggesting parental grandmother in this case as the likely source of HIV-1 infection. However, the specific modes of transmission remain unidentified.

The reported risk of household transmission of HIV was 0.2–0.7 infections per 100 years of contact.^[14] HIV Prevention Trials Network 052 study revealed that provision of antiretroviral therapy to index cases in HIV discordant setting reduces the risk of transmission through the sexual route to HIV-negative partner by 93%.^[15] Provision of cART reduces viral load in the blood as well as in other biological fluids. In this case, the child could

have been infected before the caregiver parental grandmother was initiated on cART (i.e., between April 2012 and January 2013).

The present study has limitations since it relies on the recall of events provided by the family members that might account for HIV acquisition and thus are subject to recall bias. The denial of any other known predominant routes of transmission of HIV leads us to infer that the exposure to infected body fluids of the identified HIV-infected caretaker may account for such instance of nonvertical HIV transmission to a child. This is the first case study of its kind from India having phylodynamic study evidence to categorically state that parental grand mother is the source of infection.

CONCLUSION

The case report presented is based on the epidemiological data, and it is very difficult to determine the course of events occurred for transmission of HIV. However, HIV *pol* region from

the child and the HIV-infected grandmother strongly related phylogenetically. This case is presented due to the rarity of its occurrence.

Acknowledgment

The author carried out phylodynamic study at the National AIDS Research Institute (NARI), Pune, India.

Declaration of patient Consent

The author certifies that he has obtained all appropriate patients/ parents consent forms. In the form the patients / parents have given their consent for their images and other clinical information to be reported in the journal. The patients / parents understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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