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Clinical Notes

Failure to prevent human T-cell leukemia virus type 1 mother-to-child transmission in Japan

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Key words discordant couple, human T-cell leukemia virus type 1, mother-to-child transmission, sexual transmission.

Human T-cell leukemia virus type 1 (HTLV-1) is the pathogen of adult T-cell leukemia–lymphoma. HTLV-1 is endemic in southern Japan, the Caribbean, Latin America, and western Africa.

In Japan, the nationwide mother-to-child transmission prevention program for HTLV-1 was introduced in 2011.[1] In the program, screening of pregnant women for HTLV-1 infection was implemented, and positive results confirmed on western blot. Confirmed pregnant women with HTLV-1 are recommended to use three feeding methods: formula feeding, short-term breast-feeding, and feeding with thawed frozen milk to prevent mother-to-child transmission. After the children reach 3 years of age, it is recommended that the children are screened for antibodies against HTLV-1.

The HTLV-1-negative pregnant women in the program, however, are considered not likely to transmit HTLV-1 to their child, and therefore their feeding methods are not limited.

In this report, however, we present a case of HTLV-1 mother-to-child transmission, despite the mother being HTLV-1 negative on screening in the nationwide mother-to-child transmission prevention program for HTLV-1 in Japan. Informed consent was obtained from the parents of the patient for publication of this case report.

Case report

This case involved a 4-year-old girl who was the second-born child. She was healthy without any developmental delays. She had not received blood transfusion.

She lived with her parents and two healthy siblings. Her father was an HTLV-1 carrier, but her mother was not a diagnosed HTLV-1 carrier, given that both HTLV-1 screening tests during her first and second pregnancies were negative. The mother breast-fed both children.

Three years after the birth of the second child, however, the mother was diagnosed as an HTLV-1 carrier on passive particle agglutination and western blot during her third pregnancy. The mother had not received a blood transfusion. She became anxious about her children's infection status and had her children tested. The first-born child was HTLV-1 antibody negative, but the second child had confirmed HTLV-1 antibodies on western blot.

Discussion

We regard this case as mother-to-child transmission after the mother was infected with HTLV-1 by sexual transmission from her husband because transmission via blood transfusion or sexual transmission to the child were improbable. It is unclear, however, whether the mother was infected before or after HTLV-1 screening test, and it remains unclear whether we could have prevented this infection.

Human T-cell leukemia virus type 1 cannot be detected during the window period (i.e. the time taken for seroconversion). If the mother was infected before the HTLV-1 screening test, it is possible that the screening was done during the window period. The HTLV-1 window period is not clear. It is possible that the HTLV-1 window period is >1 year after exposure because children born to seropositive mothers can acquire HTLV-1 antibodies by 3 years of age.[2] If the HTLV-1 window period is longer than pregnancy, the HTLV-1 screening test is not useful for HTLV-1 discordant couples.

Maternal high HTLV-1 provirus load in peripheral blood mononuclear cells is a predictor of mother-to-child transmission.[3] If the HTLV-1 proviral load is high during the acute stage of infection, such as during HIV infection, the chances of transmission to the child might increase. The chronologic changes in HTLV-1 proviral load after sexual transmission, however, are unknown. In contrast, maternal antibodies can inhibit HTLV-1 infection.[4] It is possible, however, that a low

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level of maternal antibodies against HTLV-1 might not be able to prevent infection, especially if there is not enough time to produce them. While there is limited evidence supporting these hypotheses, pregnancies occurring immediately before and after HTLV-1 sexual infection may be at high risk of mother-to-child transmission.

Finally, if the nationwide mother-to-child transmission prevention program for HTLV-1 continues to be carried out, increasing numbers of men will know if they are HTLV-1 carriers. Sexual transmission mainly occurs from men to women.[5] Due, however, to the dearth of material on HTLV-1-discordant couples, we cannot provide sufficient information on HTLV-1 transmission prevention. Therefore, the information in this case is important, and even more information is needed. At present, the information that we can provide for discordant couples is limited, but mothers should be advised to retest for HTLV-1 at the end of pregnancy, even if HTLV-1 test during the first trimester of pregnancy was negative. Confirmation of HTLV-1 infection at that time can prevent mother-to-child transmission through breast milk.

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Disclosure

The authors declare no conflict of interest.

Author contributions

All authors have contributed to data interpretation and have critically reviewed the manuscript. The final version of the manuscript was approved by all authors.

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Splenectomy resolves hemolytic anemia caused by adenylate kinase deficiency

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Key words adenylate kinase 1 deficiency, non-spherocytic hemolytic anemia, psychomotor impairment, splenectomy.

Human adenylate kinase (AK) deficiency (OMIM 103000) is a rare genetic disorder associated with hereditary non-spherocytic hemolytic anemia, which is caused by the absence of normal human AK type 1 (AK-1) protein.[1] Human AK (or ATP-AMP phosphotransferase, EC 2.7.4.3) is a ubiquitous monomeric enzyme that catalyzes the reversible transfer of a phosphate moiety between ATP, ADP, and AMP.[2] AK also plays important roles in maintaining cellular energy homeostasis. Several families with a history of AK deficiency and hemolysis have been described in the literature (Table S1), and some of these patients had associated psychomotor impairments.[3] In this study, we discuss the case of a Japanese girl with AK deficiency caused by a novel missense mutation in *AK1*. Splenectomy was dramatically effective to treat the hemolytic anemia, but long-term observation was required to evaluate a slow-onset psychomotor impairment.

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