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Neutralizing Antibody to Vesicular Stomatitis Virus (HTLV-I) Pseudotype in Infants Born to Seropositive Mothers

Yoshihito Iwahara,[1] Takashi Sawada,[1] Hirokuni Taguchi,[1] Hiroo Hoshino,[2] Masakazu Umemoto,[3] Hiromichi Take,[3] Steven Foung[4] and Isao Miyoshi[1,5]

[1]Department of Medicine, Kochi Medical School, Oko-cho, Nankoku, Kochi 783, [2]Department of Hygiene, Gumma University School of Medicine, Showa-cho, Maebashi, Gumma 371, [3]Department of Pediatrics, Kagoshima Municipal Hospital, Kajiya-cho, Kagoshima 890 and [4]Department of Pathology, Stanford University School of Medicine, Stanford, California 94305

Breast feeding is the major route of mother-to-child transmission of human T-cell leukemia virus type I (HTLV-I). Our experiments with rabbits have shown that passive immunization is capable of blocking cell-to-cell infection of HTLV-I by blood transfusion or breast feeding. In this study, sera were collected serially from 3 infants born to seropositive mothers and were tested for the presence of neutralizing antibody to vesicular stomatitis virus (HTLV-I) pseudotype as well as antibodies to viral structural proteins. There was a good correlation between neutralizing and viral antibody titers, both of which were detectable until 3–6 months after birth. Whether maternally transmitted neutralizing antibody is protective against perinatal infection of HTLV-I remains to be studied.

Key words: HTLV-I — Mother-to-child transmission — Neutralizing antibody

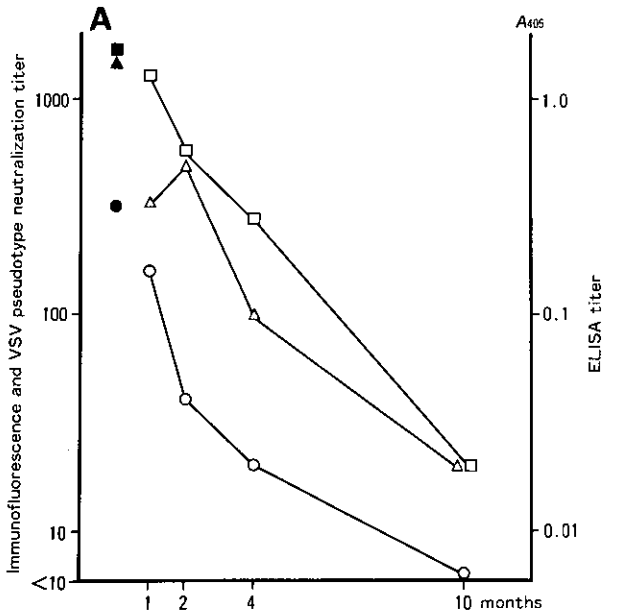
Human T-cell leukemia virus type I (HTLV-I) can be transmitted by blood transfusion,[1,2] breast feeding,[3,4] and sexual intercourse.[5,6] We have found that passive immunization of rabbits with HTLV-I immune globulin containing high-titer neutralizing antibody prevents blood-borne and milk-borne transmission of HTLV-I.[1,7,8] This prompted us to examine the presence of neutralizing antibody in infants born to HTLV-I-infected mothers.

Sera were collected from 3 seropositive mothers aged 21–32 years and their bottle-fed infants. Blood samples were obtained from all 3 infants 4 times during the first year of life. Sera were titrated for HTLV-I antibodies by indirect immunofluorescence against the MT-2 cell line as previously described.[1] Sera were also tested for antibodies by whole-virus ELISA according to the manufacturer's instructions (Eisai, Tokyo). Western blot analysis was done with an MT-2 cell lysate and 2 recombinant envelope proteins MTA-1[9] and p21E[10] as antigens. Neutralizing antibody was assayed using vesicular stomatitis virus (VSV) bearing envelope antigens of HTLV-I as previously described.[11] Serum dilutions that inhibited plaque formation of VSV (HTLV-I) pseudotype by more than 80% were taken as neutralizing antibody titers against HTLV-I.

The immunofluorescence antibody titers of the 3 mothers were 1:320, 1:160, and 1:80, and those of their respective infants were 1:160, 1:40, and 1:40 at 1 month after birth and became undetectable within several months (Fig. 1). The antibody titers as determined by ELISA declined in parallel with a half-life of about 1 month. The higher the mother's antibody titer was, the longer the infant's antibodies were detectable. The neutralizing antibody titers also declined gradually to the background levels of less than 1:50, being concordant with the viral antibody titers. Western blot analysis indicated the presence of antibodies not only to *gag* proteins (p28, p24, and p19) but also to *env* proteins (MTA-1 and p21E) (Fig. 2). Reactivities with at least one of the proteins were detected until 3–6 months after birth. In particular, the reactivities with MTA-1 correlated well with the neutralizing antibody titers.

The present study demonstrates for the first time transplacental transfer of neutralizing antibody as well as antibodies to HTLV-I viral structural proteins from seropositive mothers to fetuses. The maternally transmitted antibody titers reflected the mother's antibody titers and diminished sooner or later depending upon the antibody levels at birth. By analogy to immunoglobulin prophylaxis in rabbits,[8] it is conceivable that infants will be protected from milk-borne transmission of HTLV-I, as long as they carry neutralizing antibody of sufficient titer, although the minimum protective level of neutralizing antibody is unknown. This concept is supported by the observation that the majority of postnatal HTLV-I infections by breast feeding occurred after the decline of maternally acquired antibodies.[12] The occurrence of intrauterine or intrapartum infection of HTLV-I is a

[5] To whom correspondence should be addressed.



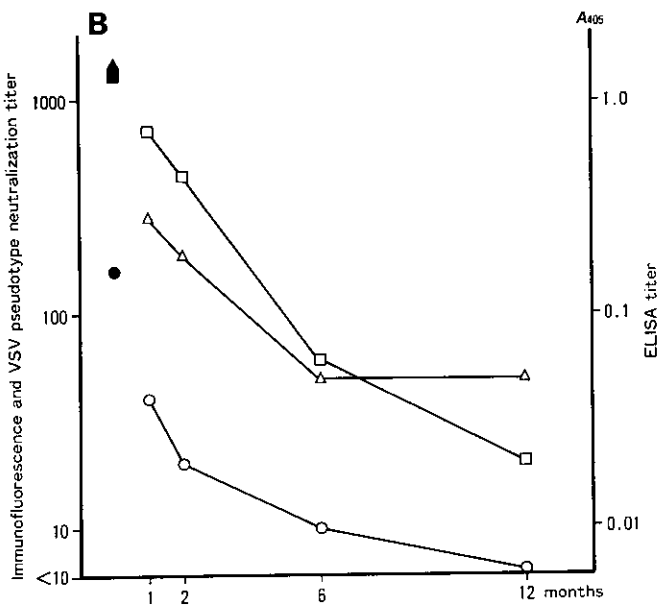
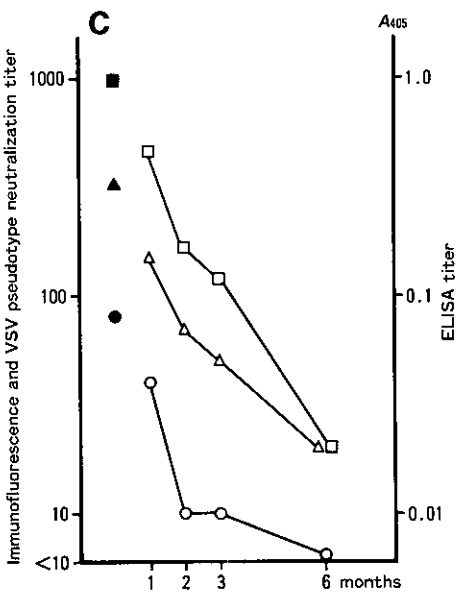


Fig. 1. Three mother-and-child pairs (A, B, and C) were tested for HTLV-I antibodies by immunofluorescence assay (circles), ELISA (squares), and VSV (HTLV-I) pseudotype neutralization assay (triangles). Note a concordant decline of neutralizing and viral antibody titers. Solid and open symbols denote mother and child, respectively.



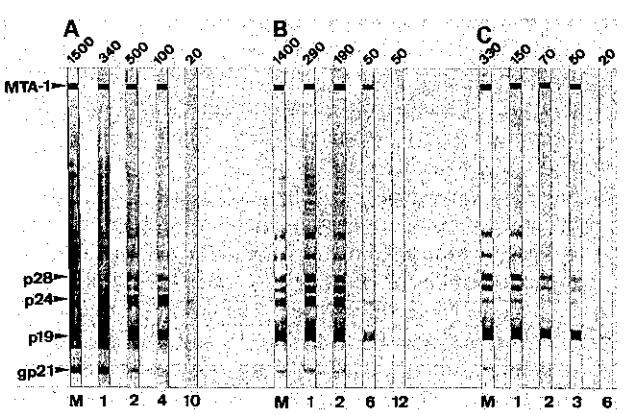


Fig. 2. Western blot analysis in the 3 mother(M)-and-child pairs (A, B, and C), showing antibodies to HTLV-I core proteins p28, p24, and p19 and recombinant envelope proteins MTA-1 and p21E. Numbers above lanes denote VSV (HTLV-I) pseudotype neutralizing antibody titers and numbers below lanes denote months after birth.

controversial issue. Although some cord blood samples were shown to contain a small number of HTLV-I-infected cells by polymerase chain reaction,[13] this does not necessarily lead to anti-HTLV-I seroconversion of the children.[14] It is possible that the genome-positive cord blood cells may be mother's lymphocytes that are prevented from transmitting HTLV-I by maternal neutralizing antibody.

MTA-1 used in the Western blot strips is a gp46 recombinant protein (residues 162–209)[9] and contains amino acids 191–196, thought to be a putative HTLV-I neutralizing epitope.[15] The fact that there was a good correlation between the reactivities with MTA-1 and VSV (HTLV-I) pseudotype neutralizing antibody titers suggests that MTA-1 may be useful for the analysis of neutralizing antibody against HTLV-I. If so, it would supplement VSV (HTLV-I) pseudotype neutralization assay, which is difficult to perform routinely.

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