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Transmission Routes of HTLV-I: An Analysis of 66 Families

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HTLV-I transmission routes were found for 66 carrier pregnant women by studying sera, from the carrier pregnant women, their mothers, and their husbands, and by obtaining detailed family histories at interview. Forty-one cases (62.1%) were considered to be instances of vertical transmission, 15 (22.8%) of sexual transmission, 6 (9.1%) of blood transfusion, and 4 (6.1%) undecided. To date, most cases of adult T-cell leukemia (ATL) have been considered to result from vertical transmission. Our results therefore imply that about 30% (22.8%+9.1%) of the carrier pregnant women are at minimal risk of ATL. Moreover, in case of presumed husband-to-wife transmission, more than half (6/11) were infected between one year and four years after marriage.

Key words: HTLV-I — Family study — Vertical transmission — Sexual transmission

Human T-lymphotropic virus type I (HTLV-I) is transmitted via three routes, vertical transmission, sexual transmission, and blood transfusion.[1-3] HTLV-I is the first human retrovirus found to be causally related to adult T-cell leukemia (ATL). However, the development of ATL after adult infection with HTLV-I is still in question.[4] In addition, the frequency of each transmission route has been unknown, although one group of investigators has estimated the probability of HTLV-I transmission from husband to wife as 60.8% over a 10-year period.[3]

HTLV-I seropositivity in healthy adults in Kagoshima Prefecture is reported to be 11.9%,[5] which is the second highest rate in Japan. As a result, there is also a high incidence of ATL (approximately 100 cases each year[5]). At present, the most effective measure to control HTLV-I endemicity is the prevention of infection.[6] These facts prompted us to study the routes of transmission of HTLV-I. To do so, we examined the sera of family members of HTLV-I antibody-positive pregnant women who visited Kagoshima City Hospital in the 6 years beginning in September 1986. We also investigated the latency for sexual transmission.

MATERIALS AND METHODS

Subjects for study We examined 7330 pregnant women who visited our hospital from September 1986 to October 1992. Three hundred and twenty-nine of these women (4.7%) were found to be HTLV-I antibody-positive. All of the seropositive women (index subjects) were asymptomatic and there was no case of ATL.

In 66 families, we were able to examine sets of sera, which included index subjects, mothers, and husbands, with informed consent. The average age of index subjects was 28.5 years (range: 18 to 40 years), of mothers 57 years (range: 43 to 72 years), and of husbands 32.5 years (range: 18 to 49 years). History of blood transfusions, extramarital sexual relationships, and drug addiction were obtained by interview.

Assay methods Antibody to HTLV-I was assayed by a particle agglutination (PA) method (Fujirebio, Tokyo)[7] and ELISA (Eisai, Tokyo).[8] Individuals who were seropositive by both methods were considered to be virus-infected.

RESULTS

Routes of transmission We found the HTLV-I transmission routes to the pregnant women (Table I) to be as follows: (1) 41 cases (62.1%) out of 66 carriers were considered to be "mother-to-child" transmission. In this group, the mother of the pregnant woman was seropositive, the husband was seronegative, and the index-subject had no history of blood transfusion, extramarital sexual relationship, or drug use. (2) In the 11 cases (16.7%) of "husband-to-wife" transmission, the husband of the pregnant woman was proved to be seropositive, the mother was seronegative, and she had no history of blood transfusion, extramarital sexual relationship, or drug use. (3) If both mother and husband were seronegative, there was a history of blood transfusion, and the index-subject had no history of extramarital sexual relationship or drug use, we presumed blood transfusion was the route of infection (6 cases, 9.1%). (4) There were 4 cases in which both the mother and husband were negative for HTLV-I antibody and there was no history of blood transfusion or drug use. However, each of these subjects acknowledged that she had had an extramarital sexual relationship with men who were born in Kagoshima Prefecture (a highly en-

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demic area), that lasted for some period of time. We considered these 4 cases (6.1%) to be the "extramarital sexual" transmission group. (5) There were 4 cases (6.1%) where both the mother and the husband were seropositive. These cases are included in the undecided group.

Latency in sexual transmission The intervals of time from marriage to the day when seropositivity of the pregnant women was established (Table II) were as follows: < one year: one case, 1–4 years: 6 cases, 4–6 years: 2 cases, > 6 years: 2 cases. Here the time of marriage is defined as the start of sexual life with the spouse. The shortest interval was 11 months (0.9 year). Thus, more than half of the cases (6/11) were infected between one year and four years after marriage.

DISCUSSION

The number of HTLV-I carriers and the annual incidence of cases of ATL in Japan has been estimated at 1.2 million and 700, respectively.[9] While there have been reported cases of ATL with a familial disposition,[10, 11] to date it has not been reported that sexual and hematogenous transmission of HTLV-I may induce an overt manifestation of ATL. Thus the development of ATL after adult infection with HTLV-I has still not been reported.[4] More than 90% of all patients of ATL were older than 40 years; their average age was 58 years.[9] It is therefore assumed that ATL due to adult infection by HTLV-I is relatively rare, that most cases of ATL result from vertical transmission and that the average latent period is about 50 or more years.

From our study, the rate of vertical transmission to pregnant women was shown to be 62.1%. This means that more than half of the carrier pregnant women may be at risk for ATL. The cumulative incidence of ATL among carriers of HTLV-I was calculated to be 1–3% in females in Japan.[12] From our study, the cumulative incidence of ATL in our pregnant carriers whose transmission routes are vertical is estimated to be 2–5% (1–3%/0.62). Thus, about 30% (22.8%+9.1%) of the carrier pregnant women, i.e. those infected in adult life, can be assumed to be at minimal risk of ATL.

It has been reported that another route of natural transmission of HTLV-I, namely from husband to wife after marriage, is via infected T-lymphocytes in the semen and that infection from wife to husband is relatively rare.[1] This seems to explain why the relative incidence of HTLV-I carriers in females is higher than that in males in the older age-group. However, heretofore an accurate estimate of the sexual transmission rate has not been available because the size of the sample studied has been too small; moreover, a contributing factor, based on the experience of our study, is that it is fairly difficult to obtain serum for analysis from both mother and husband of the index subject. Approximately 22.8% (16.7%+6.1%) of our carrier pregnant women were infected sexually. This transmission rate is expected to increase with age with cumulative exposure to HTLV-I

Table I. Routes of Transmission of HTLV-I

Supposed transmission routes	No.	(%)
Mother to child	41	(62.1)
Husband to wife	11	(16.7)
Blood transfusion	6	(9.1)
Extramarital sexual relationship	4	(6.1)
Both mother and husband were seropositive for HTLV-I[a]	4	(6.1)
Total	66	(100.1)

a) The transmission routes were undecided.

Table II. Transmission from Husband to Wife[a]

Case	Interval from marriage to the day when seropositivity was determined (years)	Age of pregnant woman (years)	Age of husband (years)
1	0.9	27	31
2	1.8	25	28
3	1.8	28	33
4	1.9	26	33
5	2.5	39	44
6	3.9	31	38
7	3.9	31	35
8	5.3	39	49
9	5.8	21	33
10	11	33	40
11	16	39	41

a) Intervals from marriage to the day when seropositivity of the pregnant women was determined.

through repeated sexual contact between spouses. In general, the prevalence among husbands of carrier pregnant women has been estimated as approximately 5%.[5] The discrepancy between this figure (5%) and our data (16.7%; 11 of 66 husbands were seropositive probably reflects the fact that our study was conducted in an HTLV-I endemic area, where any woman is more likely to be married to a carrier than is the case in a non-endemic area.[13]

On the other hand, the latency between initial infection and antibody development was unknown except in the case of blood transfusion, where the mean interval was between 3 and 4 weeks.[2] Seroconversion by blood-borne infections or by oral infection of marmosets suggests that IgG class antibodies usually appear within 2 months of infection.[14] Our findings suggested that more than half of the wives (6/11), who were supposedly infected by their husbands, were infected between one year and four years after marriage. When we studied the birth order of pregnant women who were positive for HTLV-I, women born later in the birth order were found to be more efficiently infected with HTLV-I than those born early.[13] This finding may reflect the time required for husband-to-wife transmission of HTLV-I.

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