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Unusual Finding of HTLV-I Infection among Amazonian Amerindians

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Human T-cell lymphotropic virus type II is a retrovirus endemic in Amerindian communities throughout the American continent, although some Amerindian groups that apparently emerged from the same ethnic root as HTLV-II carriers do not secrete antibodies against the virus and show very low prevalence for human T-cell lymphotropic virus type I. In this study, sera from 487 Amazonian amerinds were screened for HTLV type I and II antibody by the gelatin particle agglutination assay and ELISA and confirmed by Western blot and indirect immunofluorescence assay. None was positive for HTLV type II. One young healthy male of Waiãpi ethnicity was reactive with HTLV-I and was confirmed by Western blot assay and indirect immunofluorescence test. The absence of HTLV type II infection among these Amerindian communities would suggest a behavior pattern distinct from other groups in the American continent. Also, the very low prevalence of HTLV type I infection among these ethnic groups probably indicates contamination by blood transfusion (external transmission route). © 2007 IMSS. Published by Elsevier Inc.

Key Words: HTLV-I, HTLV-II, Amerindians, Waiãpi, Amazon.

Introduction

Human T-cell lymphotropic virus types I and II (HTLV-I and II) are retroviruses of the deltaretrovirus genus, Oncovirinae subfamily (1). Both viruses were initially isolated from patients with hematological disorders (2,3), but to date there is no conclusive evidence linking HTLV-II to a human disease (4). In contrast, HTLV-I has been shown to cause adult T-cell leukemia/lymphoma (ATLL), neurodegenerative disorders, and HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP) (3,5,6). Whereas HTLV-I is mainly endemic in the Japanese archipelagos (7), the Caribbean basin (8) and Central Africa (9), HTLV-II is spread out among Amerindians throughout the American continent, especially among Amazonian natives. Some years ago, an HTLV-II epidemic developed among intravenous drug users in the U.S. (10). As reviewed by Menna-Barreto et al. (11), HTLV-II infection was found in Amerindians from Canada to Chile, and in Brazil, all Amerindian communities investigated presented high or low incidence of HTLV-II infection.

Among Amerindians located in Brazil, HTLV-II prevalence is very high among Kayapo, Kraho, Mundurukus, Tiriyo, and Arara, varying from 8.1–57.9% (11). This widespread HTLV-II infection among Amerindians would suggest a common route of origin, Africa and through Asia, as pointed out by some authors (12,13).

Anthropological and genetic evidence point to Africa as the probable homeland of HTLV and also of the human host, who dispersed in various ways to other continents (12–15). Gallo et al. (16) proposed that HTLV-I was disseminated to Japan, the Caribbean basin, and the America continent by African slave traders. Even though the Ainu HTLV-I isolate would be claimed by Ishida et al. (17) as an indicator of ancient origin of the virus among prehistoric populations in Japan, Yamashita et al. (18) reported that the HTLV-I strain isolated from the Ainu population is a member of the Cosmopolitan group and belongs to the Transcontinental subgroup, which also predominates among Ryukyuans ethnicity. The idea that both viruses, HTLV-I and HTLV-II, followed human evolution from Africa to other continents, particularly to the New World, has been hypothesized by some authors (12), but the reasons of

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predominance of these viruses in distinct populations is not so clear, although HLA restriction would explain the segregation of these viruses in different ethnic populations (19).

The Nivkhi are native, isolated people in the Nogliki region of Sakhalin, Far East Russia, found to be infected by HTLV-I. It is interesting to note that the Nivkhi are intermediately related to the Inuit, Tlingit, and Andean Amerindians. HLA analyses have shown that the Japanese Ainu are remotely related to Asian Mongoloids (20,21). Also, there is a relatively high prevalence of HTLV-I in areas where African slaves were brought as in the Caribe islands and in Brazil, particularly in Bahia State, which has the largest concentration of African descendents in the country (22).

The pattern of HTLV-I and HTLV-II distribution among human populations in the world appears to be ethnically determined based on genetic background, but due to the intense miscegenation among different ethnic groups, this pattern is being lost.

Although HTLV-II is widely spread among Amazonian amerinds, we could not find HTLV-II among Waiãpi Amazonian amerinds. One case of HTLV-I among them (23) was recently confirmed by French researchers in French Guyana (24,25) and by Shindo et al. (26) among the same Waiãpi group.

Materials and Methods

Blood samples of 487 amerinds from six different ethnic communities (Table 1) were collected by venopuncture in 1987, after informed consent, and kept frozen at −20°C. Serum samples were screened for the detection of HTLV-I and HTLV-II antibodies by the gelatin particle agglutination test (PA; Fujirebio Inc., Tokyo, Japan) and the enzyme-linked immunosorbent assay (ELISA; Embrabio, São Paulo, Brazil) according to manufacturer's instructions (27,28). Reactive samples were confirmed by Western blot (WB; Embrabio) and immunofluorescence assay (IFA) as described elsewhere (23,29). In the WB analysis, samples that reacted for one of the *gag* peptides (p19, p24, p29, p34 and p36) or *env* glycopeptides (gp46 or gp61/68) were considered positive. Samples reacting solely to *gag* or *env* petides/glycopeptides are considered indeterminant. In the IFA, discrimination between HTLV-I and HTLV-II infection is comprised by serum titration on the HTLV-I- and HTLV-II-infected prototype cells, MT2 and Mo-T (clone 19) respectively, the one that showed stronger reaction in low homologous titrated serum being positive.

Table 1. Amazonian amerind communities from Brazil tested for HTLV type I and II antibodies

Amerind ethnic groups	Male (%)	Female (%)	Total (%)
Galibis	48 (48.48)	51 (51.51)	99 (20.32)
Kubenkroke	20 (32.78)	41 (67.21)	61 (12.52)
Mundurukus	43 (46.23)	50 (53.76)	93 (19.09)
Palikur	26 (53.06)	23 (46.93)	49 (10.06)
Yanomami	42 (46.15)	49 (53.84)	91 (18.68)
Waiãpi	48 (51.06)	46 (48.93)	94 (1930)
Total	227 (46.61)	260 (53.38)	487 (100.0)

The Brazilian Indian Protection Agency, FUNAI, which oversees legal affairs of Native Brazilian Amerinds, gave consent for this project.

Results

Of all the samples screened by PA and ELISA and confirmed by WB and IFA for HTLV-I and HTLV-II antibodies, one young healthy male of Waiãpi ethnicity was positive for HTLV-I (Figure 1), and two other members of the Waiãpi community yielded indeterminant results by the WB assay and weak reaction by the IFA.

Discussion

According to Talarmin et al. (30), HTLV-I antibodies were detected in 1/54 (1.8%) of Arawaks, 2/78 (2.6%) of Palikurs, and 2/138 (1.4%) of Wayãpis. However, none of 56 Emerillons, 385 Wayanas, and 136 Galibis was reactive with either HTLV-I or -II in a serosurvey of Amerindian population of French Guyana conducted in 1997. Shindo et al. (26), in an epidemiological survey conducted with samples collected in 1997, detected HTLV-I antibodies among Waiãpi amerinds inhabiting Amapa State, Brazil. HTLV-I antibodies among Waiãpi Amerindians were initially detected by our group in 1989 in one subject. Later, in an amplified sample collected and tested in 1996, we again obtained the same result, analyzing the same subject. Members of the Waiãpi community in both Brazil and French Guyana visit each other and have relatives in both countries. Despite different periods of HTLV screening, there were apparently no changes in the dynamics of HTLV-I spread among Waiãpi Indians in spite of cultural background and behavioral patterns that would favor virus transmission among them.

The low HTLV-I prevalence among some Amerindian groups in South America and the high prevalence of HTLV-II among the majority of Native Americans in both continents suggest at least two hypotheses. One would suggest a different origin of these ethnic groups, which is hard to explain as the HTLV-negative groups possess linguistic and genetic characteristics similar to other groups presenting high prevalence of HTLV-II (15). On the other hand, the geographic isolation of these communities would favor the genetic dominance of MHC haplotypes and clearance of HTLV-II infection and contamination by HTLV-I by different routes such as blood transfusion or sexual contact.

It is noteworthy to mention that in Brazil, the Amerindians are protected and, especially in the Waiãpi communities, are isolated and carefully studied and monitored by

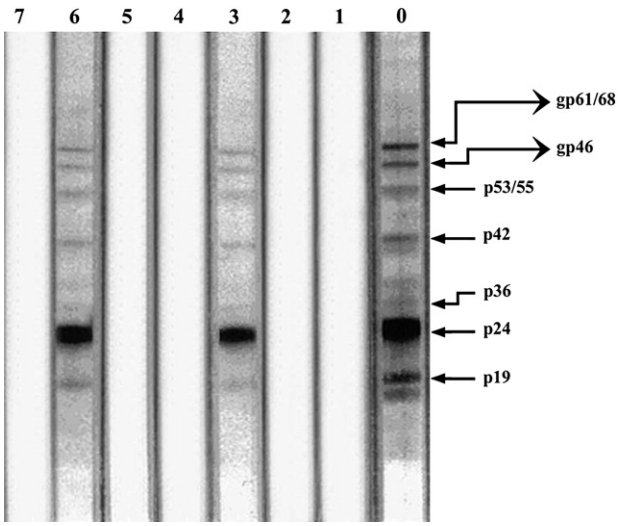

Figure 1. Western blot profiles of a reactive HTLV-I Waiãpi Amerindian (Lane 6) and negative controls (Lanes 1, 2, 4, 5, and 7) and positive control (Lanes 0 and 3).

anthropologists. The Waiãpi communities are isolated in locations of difficult access, and the entrance of any person into the area is restricted and only allowed by written permission from the Ministry of Justice (FUNAI). In French Guyana, Amerindians have the same civil rights as any French citizen, which enables them to be free and responsible for their own acts. This may more easily allow for close relationships between Amerindians and non-Amerindians, contrary to the conditions in Brazil. Another contributing factor may be the fact that communities of descendants of African origin are located near where Amerindians live in French Guyana as pointed out by Talarmin et al. (30), suggesting that the Amerindian HTLV-I strains are of Africa origin. In these circumstances, HTLV-I contamination on the Brazilian side would be more difficult than on the French side.

Also, there is information that when Waiãpi people became ill in the past, they were treated at Serra do Navio Hospital (Amapá, Brazil) and sometimes transported to Macapa (Amapá, Brazil). Screening for HTLV in blood banks was not mandatory before 1990 and the Amapa State in Brazil and French Guyana have communities of African descendents, which might be a source of HTLV-I contamination of the blood supply.

Another plausible hypothesis would be that serological screenings do not detect HTLV-I/II genome integration in host chromosomes (31) and under certain stressful conditions or exposure to some environmental factors would favor virus expression (32).

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