Coinfection With HIV-1 and Human T-Cell Lymphotropic Virus Type II in Intravenous Drug Users Is Associated With Delayed Progression to AIDS

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Summary: Human T-cell lymphotropic virus (HTLV) type II has spread among intravenous drug users (IDUs), many of whom are coinfected with HIV-1. We have investigated the rate of HTLV-II infection in 3574 Italian IDUs screened for HIV-1, HTLV-I, and HTLV-II from 1986 to the present. HTLV-II proviral load was determined by a real-time polymerase chain reaction specifically designed for *tax* amplification. The frequency of HTLV-II infection was 6.7% among HIV-1–positive subjects and 1.1% among HIV-1–negative subjects ($P < 0.0001$). For examination of AIDS progression, a group of 437 HIV-1–monoinfected subjects and another group of 96 HIV-1/HTLV-II–coinfected subjects were monitored. Enrollees were matched at entry by CD4 cell counts and followed for an average of 13 years. HIV-1/HTLV-II coinfection was associated with older age ($P < 0.0001$) and higher CD4 ($P < 0.0001$) and CD8 ($P < 0.001$) cell counts compared with monoinfected IDUs. The number of long-term nonprogressors for AIDS was significantly higher ($P < 0.0001$) among coinfected patients (13 [13.5%] of 96 patients) than HIV monoinfected patients (5 [1.1%] of 437 patients), showing that HTLV-II exerts a protective role. An increased incidence of liver disease and hepatitis C virus positivity among coinfected IDUs was observed. Five coinfected subjects undergoing antiretroviral therapy showed a significant ($P < 0.05$) increase in HTLV-II proviral load concomitant to a decrease in HIV-1 viremia, suggesting that the treatment is ineffective against HTLV-II infection.

Key Words: human T-cell lymphotropic virus infection, HIV infection, intravenous drug user, antiretroviral therapy, human T-cell lymphotropic virus type II proviral load, long-term nonprogressor

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Human T-cell lymphotropic virus (HTLV) types I and II are closely related members of the Retroviridae family and infect $CD4^+$ and $CD8^+$ T lymphocytes in human beings.[1,2] HTLV-I is the causative agent of adult T-cell leukemia and is associated with an inflammatory myelopathy, termed *HTLV-associated myelopathy/tropical spastic paraparesis* (HAM/TSP). Although HTLV-II was originally isolated from patients with hairy cell leukemia and was reported in subjects suffering from neurodegenerative and lymphoproliferative disorders,[2,3] a causative role for this virus in specific syndromes has not been substantiated.

In Europe, HTLV-I infection is found mainly in individuals originating from endemic areas, principally the Caribbean and South America, whereas HTLV-II has been introduced since the second half of the 20th century and has mainly spread among intravenous drug users (IDUs).[3]

Because a significant proportion of IDUs are infected with HIV-1, most HTLV-II–positive cases show evidence of dual HIV-1/HTLV-II infection. The possible influence of HTLV-II on HIV-1 infection is still a matter of debate, with some authors suggesting an acceleration to AIDS[4–7] and others showing a delay or no influence on HIV-1 disease development.[8–12]

Prospective monitoring of 2 HIV-1/HTLV-II–coinfected patients showed an increase in HTLV-II proviral loads after beginning highly active antiretroviral therapy (HAART), followed later by a slight decline.[13] A more recent analysis of 2 coinfected patients undergoing HAART suggested that HTLV-II proviral expansion may be pronounced in the context of antiretroviral therapy.[14]

In this study we have analyzed the relation between coinfection and AIDS. We screened 3574 Italian IDUs for HIV-1 and HTLV-I/II from 1986 to the present. We studied virologic, clinical, and immunologic parameters in relation to AIDS progression for an average of 13 years in 2 distinct groups that included 96 HIV-1/HTLV-II–coinfected IDUs and 437 HIV-1–monoinfected IDUs. The proviral loads of HTLV-II in 5 HIV-1 subjects coinfected with HTLV-II were studied before and during antiretroviral therapy. The clinical and virologic features of 13 HTLV-II–monoinfected untreated subjects were also followed.

METHODS

Study Population

Beginning in 1986 and up to the present, approximately 3600 Italian IDUs of white origin were screened for HTLV and

HIV-1 seropositivity as well as for other viral infections. At 6-month intervals, each patient was given a physical examination and underwent hematologic and microbiologic analyses, including $CD4^+$ and $CD8^+$ T-cell counts. The stage of HIV-1 infection was classified according to the Centers for Disease Control and Prevention guidelines.[15] The subjects were selected on the basis of their availability in regional hospitals and treatment centers located in the north and center of Italy and their willingness to undergoing clinical examination and blood analyses over an extended period. At the time of entry, the age, sex, and self-reported history of injection drug use were documented.

At enrollment in the study, monoinfected and coinfected individuals had the same seroprevalence for herpes simplex virus (HSV) types 1 and 2; cytomegalovirus (CMV); hepatitis B, C (HCV), and D viruses; and *Toxoplasma gondii*.

For examination of the progression to AIDS, HIV-1–monoinfected (n = 437) and HIV-1/HTLV–II coinfected (n = 96) patients were selected from the same study population and matched by date of clinical entry and average CD4 cell counts. Patients were followed for an average of 13 years; during that time, age, CD4 and CD8 T-cell counts, and HIV-1 viral load were compared. At each visit, patients were evaluated for myelopathy, peripheral neuropathy, thrombocytopenia, bronchitis, urinary tract infection, liver disease, and HCV infection, because all these clinical complications have been reported to be prevalent among HTLV-infected individuals.[16]

Laboratory Methods

Serologic and Virologic Assays

HIV antibodies in serum were assayed by enzyme immunoassays (EIAs; Abbott Laboratories, North Chicago, IL and Wellcozyme, London, UK), and positive results were confirmed by Western blot (WB) analysis (DuPont, Wilmington, DE). HIV-1 RNA in plasma was quantitated using the Amplicor Monitor system (Roche Molecular Systems, Branchburg, NJ), and results were reported as copies/mL of serum. The assay had a sensitivity of 50 copies/mL.

HTLV antibodies in serum or plasma samples were assayed according to the HTLV European Research Network (HERN) algorithm.[17] Briefly, preliminary screening was performed by passive particle agglutination (Fujirebio, Tokyo, Japan), and positive samples were confirmed by EIA assays (Murex Biotech, Dartford, England). Samples repeatedly reactive to tests were assayed by quantitative WB (Generlabs Diagnostics, Singapore) and classified as positive for HTLV-I or HTLV-II according to their reactivity against virus-specific recombinant envelope protein. HTLV infection type was confirmed by polymerase chain reaction (PCR) on patient peripheral blood mononuclear cells (PBMCs).[18]

Quantitative Polymerase Chain Reaction

The HTLV-II proviral load was measured by real-time quantitative PCR using an ABI PRISM 7000 Sequence Detection System (TaqMan Applied Biosystems, Foster City, CA). The HTLV-II *tax* region (Genbank reference sequence M10060) was amplified using primers MGBT2 forward (nt 7260–7282), MGBT2 reverse (nt 7384–7402), and probe Tax2MGB (nt 7298–7313) with FAM (6-carboxy-fluorescein) as dye reporter. The human albumin gene (Genbank reference sequence M12523) was amplified using Alb-S (nt 16283–16304), Alb-AS (nt 16442–16421), and probe Alb 1 (nt 16340–16366) containing the 5′ reporter dye JOE and 3′ quencher 6-carboxy-tetramethylrhodamine.

The 50-μL PCR mixtures contained 100 ng of DNA purified from patient PBMCs; primers MGBT2fw, MGBT2rv, Alb-S and Alb-As (300 nM each); 200 nM of Alb1 and Tax2MGB TaqMan probes; and TaqMan universal master mix (Applied Biosystems). The PCR conditions were 50°C for 2 minutes, 95°C for 10 minutes, and 50 cycles at 95°C for 15 seconds and 60°C for 1 minute.

Standard curves for the albumin and HTLV-II *tax* genes were generated using DNA extracted from the HTLV-II–positive cell line C344. All assays on patient samples were performed in duplicate, and quality control standards were done in triplicate. The cutoff value for coefficient of correlation (r^2) was set at >0.99. To determine the exact HTLV-II copy number in C344 cells, a fragment of the *tax* gene was PCR amplified, cloned into the plasmid pCR 4-TOPO, and used as a standard together with control DNA from uninfected subjects. Two copies of HTLV-II provirus per C344 cell were found. The lower limit of detection for the assay was 1 copy/10^5 cells.

The HTLV-II proviral load was calculated as copy number of HTLV-II (pX) per 10^6 PBMCs = [(copy number of pX)/(copy number of albumin)/2] $\times$ 10^6.

For graphic presentation, proviral load values were $\log_{10}$ transformed. Undetectable proviral loads were assigned the value of 1 copy/10^6 cells before $\log_{10}$ transformation, as suggested by Murphy et al.[19]

T-Lymphocyte Subsets

Lymphocytes were obtained from samples of whole blood that were lysed by the standard lysis method and subsequently stained using subtype-specific monoclonal antibodies (Beckman Coulter, Fullerton, CA). $CD4^+$ and $CD8^+$ cell percentages were determined by flow cytometry (FACSCalibur; Becton Dickinson Pharmingen, San Diego, CA), and absolute numbers of each were calculated using total and differential white blood cell counts as well as the percentage of lymphocytes.

HTLV-II Subtyping

Molecular characterization of the HTLV-II genotype was carried out by nested PCR and restriction analysis.[20]

Statistical Analyses

Comparisons between mean values were calculated by the nonparametric Mann-Whitney *U* test. For analysis of differences between HTLV-II proviral loads before and after treatment, the Wilcoxon signed rank test was used.

For contingency analysis between HIV-1–monoinfected and HIV-1/HTLV-II–coinfected subjects, the Fisher exact test was used. The StatView statistical software package (SAS Institute, Cary, NC) was used for all analyses.

RESULTS

Screening of Italian Intravenous Drug Users for Human T-Cell Lymphotropic Virus Infection and Its Relation to AIDS Progression

A total of 3574 IDUs from locations throughout Italy were screened for HTLV-I/II. Of these, 2371 patients belonged to a cohort of HIV-1–positive IDUs and 159 of 2371 were positive for HTLV-II, resulting in an average HIV-1/HTLV-II coinfection rate of 6.7%. The highest percentages of HTLV-II–positive patients were found in large metropolitan areas, and lower percentages were detected in small centers. After screening of 1203 HIV-1–negative IDUs, 13 HTLV-II–monoinfected cases were identified, representing a positive rate of 1.1%. It is noteworthy that HTLV-II seropositivity was significantly higher in HIV-1–positive IDUs (6.7%) than in HIV-1–negative IDUs (1.1%) ($P < 0.0001$). None of the IDU subjects scored positive for HTLV-I.

To analyze whether a relation between coinfection and AIDS progression existed, 2 distinct study groups of IDU patients were monitored for an average of 13 years. One group consisted of 437 HIV-1–monoinfected subjects, and the second group included 96 HIV-1/HTLV-II–coinfected subjects. The 2 study groups were selected from the initially described study population of 3574 IDUs and matched on the basis of date of clinical entry, average CD4 counts (682 ± 246 cells/μL for HIV-1 and 654 ± 269 cells/μL for HIV-1/HTLV-II), and history in years of drug abuse (4.6 ± 2.7 years for HIV-1 and 5.8 ± 4.3 years for HIV-1/HTLV-II). The clinical, immunologic, and virologic features were monitored, and the data obtained at the end of the 13-year monitoring period are reported in Table 1. The data corresponding to T-cell counts and HIV-1 load were categorized into different subgroups, according to the number of cells/μL or copies/mL. Compared with HIV-1–monoinfected IDUs, those coinfected with HTLV-II were significantly older ($P < 0.0001$) and CD4 ($P < 0.0001$) and CD8 ($P < 0.001$) cell counts were significantly higher. Neither HIV viral loads nor average HIV infection time was significantly different between the 2 groups.

Within the coinfected group, we were able to identify a subgroup of patients with the typical features that define long-term nonprogressors (LTNPs) for AIDS.[21] Specifically, this subgroup of patients with CD4 counts >500 cells/μL and a stable HIV viremia between 1000 and 1500 copies/mL did not develop opportunistic infections or require treatment with antiretrovirals during a follow-up period of at least 10 years. The number of LTNPs in the coinfected group (13 [13.5%] of 96 patients) is significantly higher ($P < 0.0001$) than in the HIV-1–monoinfected patients (5 [1.1%] of 437 patients) followed for the same period. We studied the distribution of HTLV-II proviral loads in 8 coinfected subjects belonging to the LTNP subgroup and compared it with that of 18 coinfected subjects with a CD4 count ranging between 300 and 400 cells/μL and HIV infection stage A2 or A3, designated as AIDS slow progressors (SPs), and 14 coinfected subjects with a CD4 count <200 cells/μL and HIV infection stage from B2 to C3, designated as AIDS progressors (Ps). The distribution of the proviral values for the 3 subgroups shows that the LTNPs have a significantly lower number ($P < 0.02$) of undetectable values when compared with the SP and P subgroups (Fig. 1).

The medians and the means of HTLV-II proviral loads calculated for the 3 subgroups (LTNP, SP, and P; see Fig. 1) do not differ significantly.

TABLE 1. Clinical, Virologic, and Immunologic Parameters of IDUs With HIV Infection and Coinfected With HIV and HTLV-II at the End of a 13-Year Follow-Up Period

Characteristic	HIV-1–Monoinfected Patients (n = 437)	HIV-1/HTLV-II–Coinfected Patients (n = 96)	*P*
Sex			
Male	313 (71.6)	57 (59.4)	
Female	124 (28.4)	39 (40.6)	
Age (y)			<0.0001
<35	302 (69.1)	44 (45.8)	
>35	135 (30.9)	52 (54.1)	
$CD4^+$ T-cell count (cells/μL)			<0.0001
<200	203 (46.4)	20 (20.8)	
200–500	180 (41.2)	51 (53.1)	
>500	54 (12.4)	25 (26.0)	
$CD8^+$ T-cell count (cells/μL)			<0.001
<500	76 (17.4)	9 (9.3)	
500–1000	241 (55.2)	42 (43.8)	
>1000	120 (27.4)	45 (47.9)	
HIV-1 viremia (copies/mL)			
<50	212 (48.5)	49 (51.0)	
50–10,000	64 (14.7)	12 (12.5)	
>10,000	28 (6.4)	5 (5.2)	
Data missing	133 (30.4)	30 (31.2)	
AIDS diagnosis	71 (16.2)	13 (13.5)	

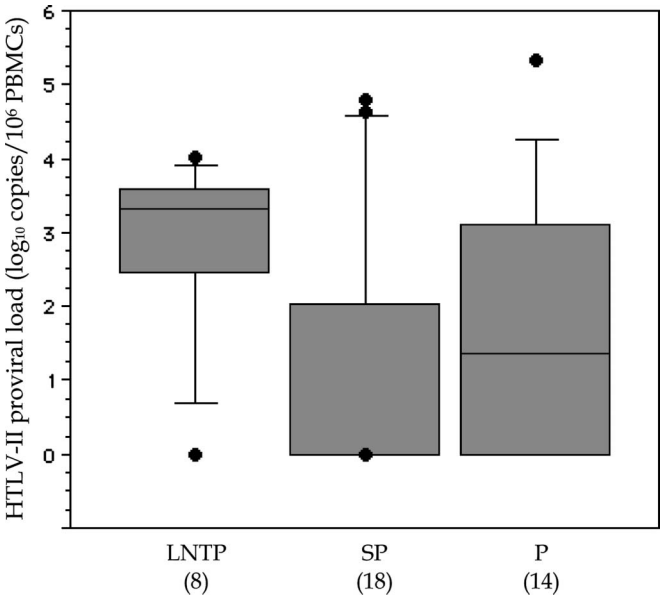

FIGURE 1. Distribution of HTLV-II proviral loads in HIV-coinfected LTNPs, SPs, and Ps for AIDS. The number of cases is indicated in parentheses.

Prospective Clinical Monitoring of Coinfected Patients

The results of clinical monitoring at 6-month intervals gave the following incidences of clinically significant events for the respective monoinfected and coinfected groups; specifically, myelopathy (0.45% and 0%), peripheral neuropathy (3.2% and 2%), bronchitis (20.1% and 22.9%), urinary tract infection (6.2% and 5.2%), liver disease (7.8% and 11.4%), and HCV infection (11.7% and 44.8%). Significant differences ($P < 0.0001$) were observed only for higher frequencies of positivity to HCV infection and presence of liver disease in the coinfected group.

Changes in Human T-Cell Lymphotropic Virus Type II Proviral Load in Coinfected Subjects Exposed to Antiretroviral Therapy

To understand the effect of antiretroviral therapy on HTLV-II infection, 5 coinfected subjects belonging to HTLV-II subtypes IIa and IIb and with an average CD4 count of 210 ± 200 cells/μL were followed before and during antiretroviral therapy (Table 2). A considerable variation among the different subjects in HTLV-II proviral load was observed. Comparison of the time point before initiation of antiretroviral therapy with the time point approximately 1 year after initiation of treatment revealed a significant increase ($P < 0.05$) of approximately 3-fold in HTLV-II proviral loads. The HTLV-II subtype did not seem to influence the proviral load increase.

The increase in HTLV-II proviral load was concomitant to a decrease in HIV-1 viremia and an increase in CD4 cell count, thus confirming a similar observation of Murphy et al.[14] The increase in proviral load was accompanied by an increase in CD8 cells, which are known to be selectively infected by HTLV-II.

Clinical Features and Proviral Load of Human T-Cell Lymphotropic Virus Type II–Monoinfected Subjects

The general and clinical features of 13 IDUs infected with HTLV-II alone are shown in Table 3. The population consisted of 12 men and 1 woman, with a mean age of 42 years and an average history of more than 20 years of intravenous drug use. Most of these subjects were also infected with HCV. With the exception of 1 patient treated for HCV with interferon, the subjects were not undergoing any specific therapy. No clear symptoms of pathologic manifestations directly related to HTLV-II infection were detected in these individuals. The quantitation of HTLV-II proviral loads revealed high variability, with approximately 40% of the cases having less than 500 copies per 10^6 cells.

Comparison of Human T-Cell Lymphotropic Virus Type II Proviral Loads in Human T-Cell Lymphotropic Virus Type II/HIV-1–Coinfected and Human T-Cell Lymphotropic Virus Type II–Monoinfected Individuals

The mean HTLV-II proviral load (2914 ± 3354 copies/per 10^6 cells) in coinfected subjects not undergoing treatment, composed primarily of the LTNP subgroup of 96 coinfected patients, was not significantly different from that (8817 ± 13048 copies/mL) of the HTLV-II–monoinfected subjects (see Table 3).[22,23]

TABLE 2. Effect of Antiretroviral Therapy in Coinfected IDUs on HIV and HTLV-II Before and 1 Year After Starting Therapy

Subject	HTLV-II Subtype	Antiretroviral Therapy	CD4		HIV*		CD8		HTLV-II†	
			Before	After	Before	After	Before	After	Before	After
PR-19	II-b	AZT, ABC	530	764	500	121	1172	1225	44,230	136,640
PR-39	II-a	AZT, d4T, 3TC	256	440	4457	58	770	968	5110	14,700
PR-44	II-b	IDV, d4T, 3TC	25	479			135	876	90	5330
PR-41	II-b	IDV, d4T, 3TC	168	476	1234	113	2332	2898	3550	5520
PR-42	II-a	RTV, d4T, 3TC	69	173			593	1053	14,370	59,680
Mean ± SD			210 ± 200	466 ± 210	2064 ± 1105	97 ± 34	1000 ± 832	1404 ± 845	13,470 ± 1799	44,340 ± 56,260

The following inhibitors were used: AZT, 3TC, ABC, d4T, RTV, and IDV.
*HIV-1 viremia (copies/mL).
†HTLV-II proviral load (copies/10^6 PBMCs).
ABC indicates abacavir; AZT, zidovudine; d4T, stavudine; IDV, indinavir; RTV, ritionavir; SD, standard deviation; 3TC, lamivudine.

TABLE 3. Features of HTLV-II–Monoinfected IDUs

Subject	Sex	Age	Year Initiated Intravenous Drug Use	Other Infections	Therapy	HTLV-II Proviral Load (copies/10^6 PBMCs)
PR-60	M	46	1978 (26)	HCV	Interferon	—
PR-53	M	34	1984 (20)	HCV, HBV	No	—
PR-49	M	43	1980 (24)	HCV	No	—
PR-51	M	32	1990 (14)	HCV	No	1000
PR-46	M	33	1992 (12)	HCV	No	1090
PR-54	M	42	1979 (25)	HCV	No	—
PR-56	M	44	1977 (27)	HCV	No	40
PR-59	M	31	1999 (5)	HCV	No	470
PR-55	M	48	1972 (32)	HCV	No	330
PR-47	M	47	1972 (32)	HCV	No	20
PR-23	M	55	1970 (34)	None detected	No	29,940
PR-43	F	47	1971 (33)	None detected	No	29,690
PR-6	M	47	1980 (24)	HCV	No	16,770
Average ± SD		42 ± 8	1980 ± 9 (24 ± 9)			8817 ± 13,048

F indicates female; HBV, hepatitis B virus; M, male; SD, standard deviation.

DISCUSSION

In this study, we have documented HIV-1/HTLV-II coinfection in Italian IDUs and studied the relation between coinfection and AIDS progression. The HTLV-II infection rate showed notable variations among the study population, with the highest percentage found in large metropolitan areas. The 6.7% frequency of HTLV-II in HIV-1–infected individuals versus the 1.1% frequency in HIV-1–negative IDUs confirms similar data reported in other countries.[24] The higher seroprevalence of HTLV-II in HIV-1–positive IDUs might reflect a longer history of injection drug use. Our data also confirm the previously reported low prevalence of HTLV-I, confirming reported data showing low prevalence among Italian IDUs.[25,26]

When emphasis was placed on monitoring T-lymphocyte CD4 and CD8 subsets as well as HIV-1 viral loads, our data showing that there were elevations in CD4 and CD8 cells but not HIV-1 viral load in coinfected subjects as compared with those who were monoinfected extend and corroborate the findings recently reported by Beilke et al.[16] In addition, our coinfected patients as well as those of Beilke et al[16] were older than monoinfected individuals.

After 13 years of monitoring, approximately 13.5% of LTNP IDUs were coinfected and never required treatment as compared with the 1.1% frequency of LTNPs in the monoinfected patients. In a much larger database of monoinfected HIV-1–infected cases, a close percentage of approximately 1.5% LNTPs was observed (Adriano Lazzarin, MD, S. Raffaele Hospital, personal communication, 2004). The median value of HTLV-II proviral loads tended to be higher in the LTNP patients who were coinfected. This subgroup also presented a much lower number of undetectable values than in the AIDS SP and P groups. Our data point to a protective role of HTLV-II infection by preventing loss of CD4 T cells and delaying AIDS progression in some coinfected individuals. A possible mechanism of this effect may relate to our finding that HTLV-II induces expression of the LD78β isoform of macrophage inflammatory protein (MIP)-1α, which is the most potent known ligand for CCR5 and a dominant HIV-suppressive chemokine.[27,28] The overrepresentation of C-C chemokine ligand 3-like 1 gene (CCC3L1, also known as MIP-1αP and LD78β) copy number that is associated with reduced HIV/AIDS susceptibility[29] supports a role of HTLV-II in delaying AIDS progression that involves induction of LD78β expression. The role of HTLV-II is likely to influence HIV infection at more than a single level. Specifically, spontaneous production of C-C chemokines by individuals infected with HTLV-II has been reported.[30] In addition, studies from our laboratory have shown that HTLV-II interferes with STAT1 activation induced by HIV-1.[31]

Our clinical monitoring revealed significant differences only in an increased incidence of liver disease and an increased frequency of positive HCV serology in coinfected patients compared with monoinfected patients. No increase was found for incidence of thrombocytopenia, bronchitis, or urinary tract infection in coinfected subjects. A possible explanation of these differences in reported results[16] could be related to our study population, which is rather homogeneous, being uniquely composed of Italian IDUs of white origin.

Our data indicate that antiretroviral therapy does not inhibit but, instead, has an enhancing effect on HTLV-II proviral load. The impact of antiretroviral therapy on HTLV-II proviral load was studied in a group of 5 coinfected subjects who were monitored for an average period of 2 years. The significant increase in HTLV-II proviral load in our patients after 1 year of treatment is consistent with the observations of Machuca et al.[13] The increase in proviral load correlated with the decline in HIV-1 viremia and the increase in CD4 and CD8 cell numbers. In HIV patients undergoing potent antiretroviral therapy, CD4 cell rescue is related to a decrease of apoptosis in the $CD8^+$ subset, suggesting that the treatment is preferentially preserving the cells infected by HTLV-II.[32]

These data are consistent with the observation that HTLV-II proviral load is amplified by expansion of infected cells.[33] A clear effect of antiretroviral therapy on HTLV-II proviral loads in a coinfected patient was recently reported by Murphy et al,[14] who suggested that HTLV-II–infected lymphocyte clones may expand selectively during immune reconstitution.

The clinical and molecular analysis of 13 HTLV-II–monoinfected individuals revealed extensive variation in the HTLV-II proviral load. Values ranged from a few to several thousands of copies per 10^6 PBMCs. No clear pattern of pathogenesis related to HTLV-II infection could be detected in this group, however. These data are not completely unexpected, because almost all the HTLV-II–infected individuals with neurologic disorders reported to date are female.[3] In our group, all but 1 of the subjects were male. An increased incidence of respiratory and urinary infections, asthma, and arthritis has been reported in a large cohort of HTLV-II–infected subjects.[34] The association of HTLV-II infection with a disorder clinically similar to HAM/TSP, as recently reviewed by Araujo and Hall,[35] needs to be confirmed by prospective monitoring of large populations of HTLV-II–monoinfected subjects.

Reports differ as to whether HTLV-I and HTLV-II infectivity increases with HIV-1 coinfection.[7,22,36] Our data showing that HTLV-II proviral loads in LTNPs within the coinfected group are not significantly different from those in HTLV-II–monoinfected patients suggest that HIV-1 infection has no influence on HTLV-II proviral load. Our finding is consistent with the observation that HTLV-II is tropic in vivo for CD8 T lymphocytes in HTLV-II–infected and HIV-1/HTLV-II–coinfected individuals.[37]

In conclusion, the evidence presented in this study points to a protective role of HTLV-II infection against AIDS progression. A significant proportion of HIV-1/HTLV-II–coinfected IDUs maintained elevated CD4 cell counts for a long period. Antiretroviral treatment in coinfected patients is successful in controlling HIV-1, the result of which is an expansion of CD4 and CD8 cells, but is ineffective against HTLV-II infection.

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