

# Conjugal Transmission of HTLV-III and Lymphadenopathy in Christmas Disease

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## Key words

AIDS – HTLV-III/LAV – Lymphadenopathy – Coagulation factor – Hemophilia

The risk of conjugal transmission of the HTLV-III/LAV virus, associated with the acquired immunodeficiency syndrome (AIDS), in patients with hemophilia is unknown. To date, only a few instances of proven exposure to HTLV-III have been reported among sexual or family contacts of patients with hemophilia (1–4). However, seropositivity to a related virus, HTLV-I, has been reported in spouses in geographic areas with an increased incidence of human T-cell leukemia/lymphoma (5). As a part of a long-term study of hemophiliacs with lymphadenopathy, we discovered a patient with Christmas disease (factor IX deficiency) who developed lymphadenopathy, immunodeficiency, and evidence of exposure to HTLV-III/LAV. His wife developed similar physical findings eight months later.

A 31 year old man with moderate Christmas disease developed asymptomatic generalized lymphadenopathy in July, 1983. During the prior six years he had used a total of 29,000 units of nonheated, commercial, lyophilized factor IX concentrates but no other blood products. In the three years immediately preceding the development of lymphadenopathy he had used approximately 4,000 units/year (63 U/kg/yr). A lymph node biopsy in December, 1983, showed follicular hyperplasia, reminiscent of the pattern seen in patients with factor VIII deficiency (6). He remained clinically well but stable lymphadenopathy persisted. In February, 1984, his 28 year old wife noted the onset of lymph node enlargement. She was otherwise asymptomatic and continued to work.

Both husband and wife took part in a study of the seroprevalence of HTLV/LAV antibodies among family contacts of hemophiliacs in February, 1985. At that time both had extensive generalized lymphadenopathy although the wife's nodes were rather uniformly enlarged to 3 × 4 cm while her husband's were 2 × 3 cm. Neither person had fever, splenomegaly, nor other findings to warrant concern.

They had not traveled outside of Louisiana and did not share razors. The patient was not on self-infusion therapy and his wife had not helped him prepare his factor concentrate nor recalled any needle stick exposure. They had been married for seven years and practiced only vaginal intercourse. They both denied extramarital sexual activities and recreational or illicit drug use. Their 5½ year old daughter was conceived five months before her father was first exposed to factor IX concentrates. When

Table 1 Laboratory findings in a couple with concordant lymphadenopathy

Laboratory test	Husband	Wife
T4 (Helper/inducer)	20% (477*)	24% (737*)
T8 (Suppressor)	44% (807*)	33% (1,014*)
T4/T8 ratio	0.6	0.7
LAV antibody	(+)	(+)

\* Absolute numbers/mm are given in parentheses

examined in February, 1985, she had no palpable lymph nodes and had experienced no reportable illnesses. Laboratory findings in both husband and wife included evidence of immunodeficiency and seropositivity to HTLV-III/LAV by the Western blot technique as shown in Table 1 (7). The p18, p24, p32, p41, p51, p65, and p110 antibody reactivities were positive in each of the two study subjects. The p41 antibody and the p18 and p24 antibodies recognize, respectively, proteins encoded by the *envelope* and *gag* (core) regions of the viral genome. ELISA assays for disrupted viral antigens were also strongly positive.

Most patients with hemophilia and AIDS have had factor VIII deficiency (8). Each instance to date in which sexual partners or children of hemophiliacs have developed AIDS or lymphadenopathy has involved family contacts of patients with factor VIII deficiency. However, factor IX deficient patients are known to have developed AIDS and seropositivity has been documented among such patients (9). Furthermore, LAV has been cultured from two siblings with Christmas disease; one of the two had AIDS and the other had lymphadenopathy (10). The clinical and laboratory findings in our patient and his wife demonstrate that conjugal exposure can be associated with the development of seropositivity and lymphadenopathy in the spouse of a recipient of factor IX. The absence of other risk factors for the wife and the development of her lymphadenopathy subsequent to that of her husband, support the concept of disease transmission from husband to wife.

This report suggests strongly that viable virus was transmitted sexually, following infection of the hemophiliac through his factor IX concentrate. No other documentation exists to date that spouses of factor IX recipients have antibody to HTLV-III/LAV or symptoms of the AIDS related complex. Sexual abstinence or the use of barrier contraceptives, and heat-treated factor concentrates may spare hemophilic couples a similar experience.

## References

- 1 Pitcher A E, Shafron R D, Glasser R M, Spira T J. The acquired immunodeficiency syndrome in the wife of a hemophiliac. *Ann Intern Med* 1984; 100: 62–5.
- 2 Melbye M, Ingerslev J, Biggar R J, Alexander S, Sarin P S, Goedert J J, Zachariae E, Ebbesen P, Stenbjerg S. Anal intercourse as a possible factor in heterosexual transmission of HTLV-III to spouses of hemophiliacs. *N Engl J Med* 1985; 312: 857.

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- 3 Kreiss J K, Kasper C K, Fahey J L, Weaver M, Visscher B R, Stewart J A, Lawrence D N. Nontransmission of T-cell subset abnormalities from hemophiliacs to their spouses. *JAMA* 1984; 251: 1450-4.
- 4 Ratnoff O D, Lederman M M, Jenkins J. Lymphadenopathy in a hemophiliac patient and his sexual partner. *Ann Int Med* 1984; 100: 915.
- 5 Hinuma Y, Nagata K, Hanaoka M, Nakai M, Matsumoto T, Kinoshita K I, Shirakawa S, Miyoshi I. Adult T-cell leukemia: Antigen in an ATL cell line and detection of antibodies to the antigen in human sera. *Proc Natl Acad Sci USA* 1981; 78: 6476-80.
- 6 Andes W A, de Shazo R D, Reed R J, Harkin R J, Wang N S. Studies of lymph nodes from patients with classical hemophilia. *Blood* 1984; 64: 768-73.
- 7 Tsang V C W, Peralta J M, Simons A R. Enzyme-linked immunoelectrotransfer blot techniques (EITB) for studying the specificities of antigens and antibodies separated by gel electrophoresis. *Methods Enzymol* 1983; 92: 377-91.
- 8 Centers for Disease Control. Changing Patterns of Acquired Immunodeficiency Syndrome in Hemophilia Patients - United States. *MMWR* 1985; 34: 241-3.
- 9 Jason J M, McDougal J S, Holman R C et al. T-Lymphotropic retrovirus, type III/Lymphadenopathy-associated virus (HTLV-III/LAV) antibody: Association with hemophiliac immune status and blood component usage. *J Am Med Assoc* 1985; (in press).
- 10 Vilmer E, Barre-Sinoussi F, Ronzioux C et al. Isolation of a new lymphotropic retrovirus in two hemophiliac B siblings, one presenting with acquired immunodeficiency syndrome. *Lancet* 1984; 1: 753-7.

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