# DETECTION OF HUMAN T-CELL LEUKEMIA VIRUS CARRIERS IN THALASSEMIA PATIENTS IN SHIRAZ: A BRIEF REPORT

M. Sotoodeh, S.Z. Tabei

Department of Pathology, Shiraz University of Medical Sciences, Shiraz, Iran

ABSTRACT The presence of human T-cell leukemia virus (HTLV-I) carriers in Fars province, southern Iran, was investigated. The sera of 160 randomly selected thalassemia patients, a well-known high-risk group for transfusion-associated viral infections, were screened for detection of antibodies to HTLV-I by the enzymelinked immunosorbent assay method (ELISA), positive results were confirmed by Western blot (WB) analysis. Patients were ages 6 to 24 years, from Shiraz and nearby cities. Four patients were found to be seropositive.

Keywords • HTLV-I • thalassemia • transfusion • Iran

## Introduction

The human T-cell lymphotropic virus type I (HTLV-I) is the first isolated human retrovirus. 2,3,18 This virus is strongly believed to be the causative agent of adult T-cell leukemia/lymphoma and some neurological disorders in the human being, 7,13,15,18,19 infection occurs worldwide but tends to be geographically restricted or clustered.3 Transfusion of blood and its different components is reported to be one of the major routes of transmission in endemic and non-endemic areas. 2.3.7 High-risk groups such as patients with hemophilia are reported to be in great danger of virus transmission.17 We intended to demonstrate the possibility of the presence of HTLV-I carriers by detecting seropositive high-risk patients in our region.

# Materials and Methods

#### Case History

One-hundred and sixty cases aged 6 to 24 years were randomly selected among the patients with thalassemia major, referring for their regular blood transfusion. Three to four ml blood sample was collected from each patient before starting the transfusion.

According to the results obtained by the ELISA method, the sera of 5 out of 160 thalassemia patients showed definite reactivity to HTLV-I antibodies in two repeated assays (Fig. 1) four of which were confirmed by Western blotting (WB) analysis. None of the patients showed any sign or symptoms of HTLV-I associated diseases. The ages of these four patients ranged 9-15 years. Each had received more than 90 blood transfusions.

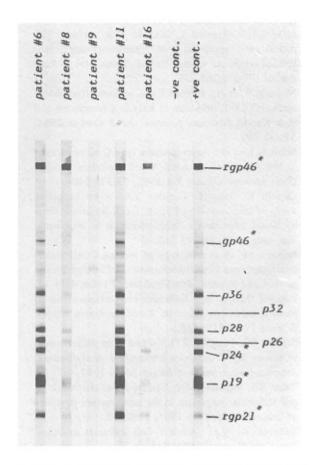


Figure 1. Western blotting results in the five seropositive patients by the ELISA method.

### Discussion

The human T-cell leukemia/lymphoma virus type I (HTLV-I) was the first human retrovirus to be isolated by Gallow in 1978. The vast majority of HTLV-I infected cells derived from patients or obtained from *in-vitro* experimental infection of blood cells are shown to be T4 lymphocytes. The virus is responsible for the malignant transformation of the target cells. The HTLV-I is strongly believed to be the causative agent of the adult. T-cell leukemia/lymphoma (ATL), The project spastic paraparesis and the HTLV-I associated myelopathy. Many studies have shown that healthy individuals with anti-HTLV-I antibodies in their

sera are carriers and are responsible for the virus transmission. 4.9

HTLV-I is an old primate virus, is believed to have originated in Africa, and transferred to other parts of the world by the slave trade and migration of people.<sup>3</sup> Today, the HTLV-I infection occurs worldwide but tends to be geographically more prominent in certain parts of the world such as the Caribbean Islands and southwestern Japan.<sup>3,6</sup> Many cases are reported from Italy,<sup>8</sup> Spain,<sup>5</sup> the United States and Western Europe. Most of these cases are attributed to intravenous drug abuse or blood transfusion.<sup>2,3,7,10</sup> Cases of HTLV-I associated ATL have also been reported from the northeastern province of Iran.<sup>1,14,21</sup>

Transfusion of contaminated blood and its components is the major route of virus transmission in endemic and non-endemic regions. Studies in the United States have identified 2.5 per 10,000 healthy voluntary donors as positive for HTLV-I antibody by ELISA and confirmatory tests. Patients requiring repeated transfusions are certainly of a greater risk of transfusion-associated HTLV-I infection. In a study of a series of 50 Japanese patients with hemophilia, two carriers of the virus were detected. 17

In our study, we investigated the presence of HTLV-I antibodies in the sera of 160 thalassemia patients, a well-known risk group for transfusion-associated viral infections. In this manner, we intended to indirectly demonstrate the possibility of the presence of virus carriers among the blood donors in our region. The initial screening of the sera by the ELISA method detected five patients suspected to be virus carriers. The confirmatory Western blot technique proved four of them to be true virus carriers and showed one false-positive ELISA result (Fig. 1). Considering the age of the 160 thalassemia patients, the age at the first blood transfusion and the average number of required transfusions per month, a total number of 17,600 transfusions were estimated to have been given in these patients. If we do not consider the possibility of multiple blood donations by a voluntary donor, this pilot study indicates the necessity for investigating at least 4,400 blood donors for the likelihood of detecting one virus carrier. This figure indicates the possibility of presence of 2.3 carriers per 10,000 donors, a figure near that obtained in the United States. However, a large-scale sero-epidemiological study of blood donors (and possibly the general population in our region) is needed to investigate the accuracy of this estimation. We believe that such a study may include southern Iran as a new geographical region potentially endemic for the HTLV-I infection.

# Acknowledgement

The authors wish to express their gratitude to A. Ghaderi, Ph.D., for his kind technical assistance in performing the Western blotting. The kits used in this study were supplied as a gift from the Organon Technika, Belgium.

### References

- Farid R, Shirdel A, Tabei SZ: Clinical manifestation of adult T-cell lymphoma/leukemia associated with HTLV-I in north-eastern Iran. Irn J Med Sci 1992; 17: 105-108.
- 2 Gallow RC: The first human retrovirus. Sci Amer 1986: 255:88-98.
- 3 Gallow RC: The human T-Cell leukemia/lymphotropic retroviruses (HTLV) family: Past, present and future. Cancer Res 1985; 45:4524-4533.
- 4 Gotoh Y, Sugamma K, Hinuma Y: Healthy carriers of a human retrovirus, T-cell leukemia virus (HTLV), demonstration by clonal culture of HTLV carrying Tcells from peripheral blood. Proc Natl Acad Sci USA 1982; 79: 4780-4782.
- 5 Guroff RM, Gallow RC: Immunology of human Tcell leukemia/lymphoma (lymphotropic viruses, the HTLV family), in RB Herberman (ed), Basic and
- 6 Clinical Tumor Immunology. Vol 2, The Hague, Martinus Nijhoff Publishers, 1985.
- Hjelle B: Human T-cell leukemia/lymphoma viruses.
  Life cycle, pathogenecity, epidemiology and diagno-

- sis. Arch Pathol Lab Med 1991; 115:440-450.
- 8 Jaffe ES, Crossman J, Blattner WA, et al.: The pathologic spectrum of adult T-cell leukemia/lymphoma in the United States. Am J Surg Pathol 1984; 8:263-275.
- 9 Manzari V, et al.: Human T-cell leukemia/lymphoma virus (HTLV-I) detection in Italy in a lymphoma and in a Kaposi Sarcoma patients. Int J Cancer 1984; 34:891-892
- 10 Miyoshi I, et al.: Asymptomatic type C virus carriers in the family of an adult T-cell leukemia patient. Gann Monogr Cancer Res 1982; 73:339-340.
- 11 Okochi K, Sato H, Hinuma YA: A retrospective study of transmission of adult T-cell leukemia virus by blood transfusion: Seroconversion in recipients. Vox sang 1984; 46:245-252.
- 12 Popevic M, et al.: Biology of human T-cell leukemia/lymphoma virus transformation of human T-cells in vivo and in vitro. Adv Virol Oncol 1984; 4:45-70.
- 13 Popevic M, et al.: Isolation and transmission of human retrovirus (Human T-cell leukemia virus). Science 1983; 219: 856.
- 14 Sandler SG, Fang C: HTLV-I and other retroviruses. In Moore SB: Transfusion transmitted viral diseases. American Association of Blood Banks 1987.
- Tabei SZ, Rajabian MH, Shirdel A, et al.: Adult T-cell leukemia/lymphoma in the northeastern province of Iran. Irn J Med Sci 1986; 13:85-86.
- 16 Takasuki K, et al.: Adult T-Cell leukemia in Japan. Top Curr Hematol 1976; 415;73-77.
- 17 Takatsuk K, et al.: Adult T-cell leukemia: Proposal as a new disease and cytogenetic, phenotypic and functional studies of leukemic cells. Gann Monogr Cancer Res 1982; 28:13-22.
- 18 Takeshi A, Tadttoshi K, Juso M, et al.: Detection of antibodies to HTLV-I and III in sera from Japanese hemophiliaes. Cancer Research (Suppl) 1985;45:462
- 19 American Association of Blood Banks; Technical Manual. 10th ed., 1990.
- 20 Vernant JC, Maurs L, Gessain A, et al.: Endemic tropical spastic paraparesis associated with human Tlymphotropic virus type I: A clinical and seroepidemiological study of 25 cases. Ann Neurol 1987; 21: 123-130.
- 21 Williams AE, et al.: Seroprevalence and epidemiological correlates of HTLV-I infection in US blood donors. Science 1988; 240:243-246.
- Yechezkei S, Dina M, Batia S, et al.: Adult T-cell lymphoma in Israeli patients of Iranian origin. Cancer 1990; 65: 590-593.