A new case of Sézary cell leukemia: a morphologic variant of prolymphocytic leukemia

We report the clinical, ultrastructural, immunophenotypic and cytogenetic features of a patient with Sézary cell leukemia (SCL) without cutaneous lesions. The findings might support a relationship between SCL and T-cell chronic prolymphocytic leukemia as suggested by other authors and argues against the assumption that SCL is a distinct T-cell disorder.

Sir,

Sézary cell leukemia (SCL) has been described as a very rare variant of T-prolymphocytic leukemia (T-PLL)[1-4] with 11 cases reported. T-PLL is usually an aggressive, mature T-cell disorder accompanied by progressive lymphocytosis, splenomegaly, skin lesions and poor outcome.[4] However, a few cases with an indolent course have been reported.[3] Prolymphocytes of T-PLL show an irregular nuclear shape, deep basophilic cytoplasm with protrusions and a single prominent nucleolus. Several morphologic variants, cases with cerebriform (Sézary-like cells), multilobated (flower-cells) nuclei and other cells which are indistinguishable from the B-PLL small variant have been described.[5,6] We report the clinical, ultrastructural, immunophenotypic and cytogenetic features of a SCL detected in a routine screening examination.

A 94-year old woman was referred to our division because of a mild lymphocytosis. Peripheral blood count showed: Hb 134 g/L, platelets 263×10^9/L and WBC 12.2×10^9/L with 21% segmented neutrophils, 1% band forms, 2% eosinophils, 1% monocytes, 12% lymphocytes and 63% Sézary-like and Lutzner cell types (Figure 1). Blood chemistry values were within normal ranges and serology to HCV, HBV and HIV was negative. Physical examination was unremarkable, without cutaneous lesions, organ or lymph node enlargements. The atypical lymphocytes found in peripheral blood were $CD3^+$, $CD4^+$, $CD5^+$, $CD7^-$, $CD8^-$, and were negative for pan B-cell markers. Electron microscopy revealed lymphocytes resembling Sézary cells with a cerebriform nuclear shape, heterochromatin marginated at the periphery and a prominent nucleolus. Combining conventional cytogenetic studies, using a 72-hour culture of peripheral blood stimulated with PHA, with the cross-species color banding fluorescence in situ hybridization (RxFISH) technology, the following complex karyotype was detected: 46,XX [5] 44⇒45, XX,der(2)t(2;12)(p25;q11),der(5)t(1;5)(q25;q35),-9,-10,-13,der(14)t(6;14)(p21;p11),der(15)t(8;15)(q?;q26),der(17)t(13;17)(q?;q25),i(17)(q10), add(20) (q13), +21[9]/44⇒45,XX,der(2)t(2;12)(p25;q11), der(3)(1qter→1q32::3q22→3q29: :3p26→3qter), del(5)(q13),+der(8)(8pter→8q21::4q25→4q35::8p21→8pter), -9,-10, der(14)t(6;14) (p21;p11), -15,-17,i(17)(q10),+21[6].

A diagnosis of SCL was established. The patient has remained stable since her diagnosis 12 months ago.

T-PLL is typically associated with a short survival and a resistance to chemotherapy;[5] however, a relatively frequent presentation of T-PLL with an indolent course has been described. In a series of 78 cases, Garand et al.[3] reported that one third of patients showed isolated, moderate and stable lymphocytosis and among them, 2% had Sézary-like cells, a post-thymic phenotype and an abnormal karyotype. The majority of these cases eventually progressed after a mean of 33 months in a stable phase. The progression phase was characterized by B symptoms, splenomegaly, lymphadenopathy, skin lesions, rapidly increasing leukocytosis (often $>100x10^9$/L) and thrombocytopenia. Median survival after progression was as short as that of T-PLL (9 months) and response to treatment was very poor.

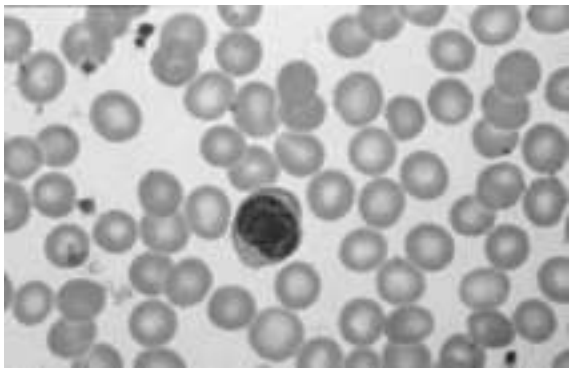

Figure 1.

The karyotype of T-PLL is often complex showing multiple rearrangements.[7-9] The most significant finding is involvement of chromosome 14 at 14q11, where the TCR α/δ locus is mapped. Structural aberrations at 14q11 are present as inv(14)(q11q32), t(14;14)(q11;q32) or t(X;14)(q28;q11) with similar incidence in all forms of T-PLL. Chromosome 8 abnormalities, usually as i(8)(q10) or t(8;8)(p21;q11), are also frequently observed.[10] In the present case, we found a complex karyotype with chromosomal abnormalities common in T-PLL and Sézary syndrome.

The clinical, morphologic, immunophenotypic and cytogenetic findings in our patient might support a relationship between SCL and T-PLL as suggested by other authors[2,3] and argues against the assumption that SCL is a distinct T-cell disorder.

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Keywords

T-PLL, Sezary Cell Leukaemia, Cerebriform nuclei, Cytogenetics, RxFISH

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Modifications of lymphocyte subsets in autoimmune thrombocytopenic purpura patients submitted to splenectomy

We studied the behaviour of blood subset lymphocytes in 25 adult patients with autoimmune thrombocytopenic purpura (ATP) submitted to splenectomy. An increase of absolute concentrations of T-subset lymphocytes was observed in the different groups of splenectomized patients; in no responding/relapsing subjects an activation of T lymphocytes was demonstrated.

Sir,

Several studies have noted modifications in the cellular immunity in ATP patients.[1-7] We studied 25 patients (18 females, 7 males) with chronic ATP (thrombocytopenia lasting for more than 6 months), who had undergone splenectomy due to their unresponsiveness to corticosteroid therapy. These patients did belong to a more wide group of 94 splenectomized ATP subjects, recently evaluated as long-term follow-up.[8] Lymphocyte subset analysis was performed at a median time from the splenectomy of 10^8 months (12-252 months). By employing a Cytoron Absolute flow cytometer (Ortho Italia SpA, Milan, Italy) and Ortho monoclonal antibodies, the following parameters were evaluated: white blood cell count; lymphocyte and platelet count; absolute blood concentrations of T (CD3-positive), B (CD19-positive), helper-inducer (CD3/CD4-positive), suppressor-cytotoxic (CD3/CD 8-positive), activated T lymphocytes (CD3/HLA-DR-positive), T lymphocytes which express the receptor for interleukin-2 (IL-2) (CD3/CD25-positive) and natural killer (NK) cells (CD16-positive).

The data obtained were analyzed by comparing the groups of responding and non responding/relapsing patients to normal subjects (Table 1). The group of responding patients showed significant increases in the absolute count of lymphocytes, in the total number of T lymphocytes and in the main subsets of CD3-lymphocytes (CD3/CD4, CD3/CD8, CD3/HLA-DR-positive lymphocytes), compared to normal subjects. Similar results were obtained in the group of non responding/relapsing patients. A significant increase in the CD3/CD25-positive lymphocytes was also noted in no responding/relapsing patients as compared to the normal subjects. A more significant increase in the absolute values of

Table 1. Lymphocyte subsets in ATP patients.

	Normal subjects (n = 25)	*Splenectomized responding pts.* (n = 14)	*ATP pts. non responding and relapsing* (n = 11)	*Non splenect. pts.* (n = 15)
Lymph. total	1771±535.8	3,030.9±1,100.9 § #	3,100±674.7 *	1,700±544.4 °
CD3+	1364±422.4	2,347±784.4 § #	2,325±334.4 *	1,240±425.6 °
CD3/CD4+	798±262.9	1,301±412.8 § #	1,458±593.1 *	750±256.6 °
CD3/CD8+	544±190.4	855±364.1 § #	893±322.7 *	435±191.3 °
CD3/HLA-DR+	153± 81.4	253±215.9 § ^	451±256.5 *	184±90.5 ° #
CD3/CD25+	61±61.5	54±72.1 ^	147±164 *	60±80.8 °
CD16+	176±83.7	244±330.4	257±185.2	189±145
CD19+	231±106.6	191± 342.7	248±195.9	168±74.5
CD4/CD8	1.5±0.4	1.4±0.4	1.5±0.9	1.6±0.5

*Blood lymphocyte subset concentrations are expressed as cells/mL. Statistically significant differences: *normal subjects vs no responder patients; §normal subjects vs responder patients; ^responder vs no responder patients; °no splenectomized patientsvs no responderpatients or †vs. normalsubjects or #vs.responder patients.*