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Case report ■

Hyperlymphocytosis in a Patient with T-prolymphocytic Leukemia Not Responding to Therapy: Case Report

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SUMMARY

A 64-year-old patient with extremely high number of white blood cells was diagnosed with T prolymphocytic leukemia. After the initiation of chemotherapy with Cyclophosphamide, Oncovin, Doxorubicin and Prednisone (CHOP), there was no improvement and the patient died within two months. Authors have made a review of the current therapy of this rare disorder of mature T-lymphocytes and discussed various therapeutic aspects of hyperlymphocytosis.

Key words: **T-cell prolymphocytic leukemia, hyperlymphocytosis, therapy**

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INTRODUCTION

T-cell prolymphocytic leukemia (T-PLL) is a rare aggressive lymphoproliferative disease with a mature T-cell phenotype. The median age at presentation is 63 years (1). Its clinical course is generally aggressive with poor response to chemotherapy and median survival periods ranging from five months to two years. For a long time, the CHOP (Cyclophosphamide, Oncovine, Doxorubicine and Prednisone) was among the main therapeutic options for the treatment of this disease (1, 2). Here we report a case of a patient poorly responding to CHOP therapy with a review of the literature in a search for more appropriate therapeutic approaches.

CASE REPORT

A 64-year-old man presented with malaise, weakness, and tinnitus lasting ten days. On physical examination, purple-reddish skin infiltrates covering the whole body were observed (Figure 1).

A left pleural effusion was found on standard chest radiography. Abdominal ultrasound was normal except mild splenomegaly (135mm in diameter). Laboratory investigations revealed hemoglobin of 107 g/l, thrombocytopenia $31x10^9$/l, and hyperleukocitosis with $593x10^9$/l cells. Blood chemistry was normal except for elevated activity of serum lactic dehydrogenase 1891, 1 IU/l, high acid uric levels 661.7 and high β2 microglobulin reaching 13,9 μmol/l. Peripheral blood smear showed 92% of atypical lymphoid cells, which were medium-sized with regular nuclear outline, single nucleolus and scant agranular cytoplasm (Figure 2).

Cells in the peripheral blood as well as in the bone marrow showed high activity of α-naphthyl acetate esterase stain, but remained negative to myeloperoxidase and periodic acid schiff. Flow cytometry showed CD4+ lymphocytes phenotyped as $CD2^+CD3^+CD7^+$ CD5-$HLADR^-$, $CD1a^-CD56^-$ and $CD56^-/CD16^-$. Lymphocytes were considered mature post-thymic (Figure 3).

Immediate therapy with CHOP was administered. During the next control examination, extreme hyperlymphocytosis was still present. Since general condition was very poor, other therapies could not be used and patient died within two months since the diagnosis was established.

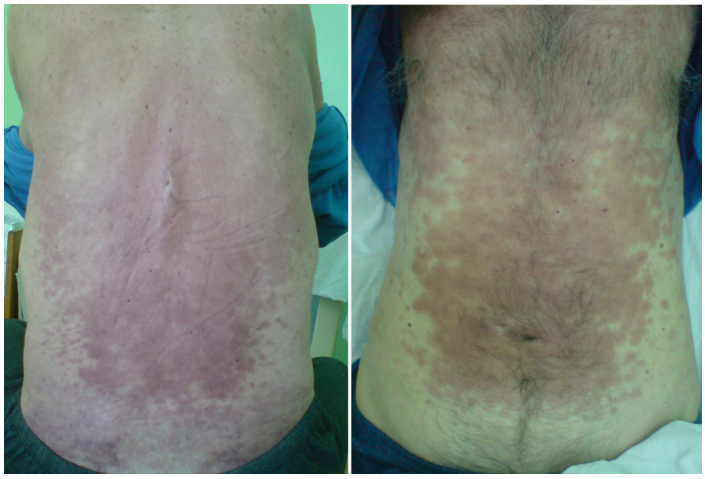

Figure 1. *Composite photograph of skin eruptions in a patient with T-cell prolymphocitic leukemia*

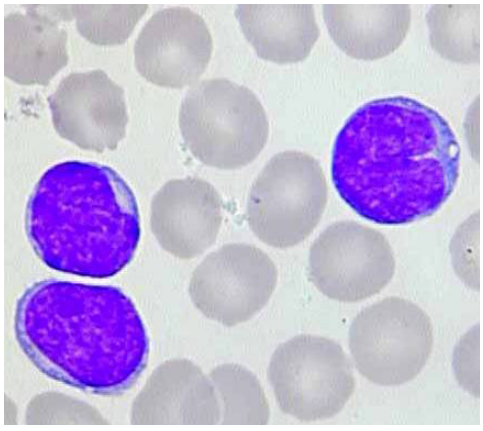

Figure 2. *The diagnosis of T-PLL could be made by light microscopy examination of blood films in most cases. May-Grunwald Giemsa x 100*

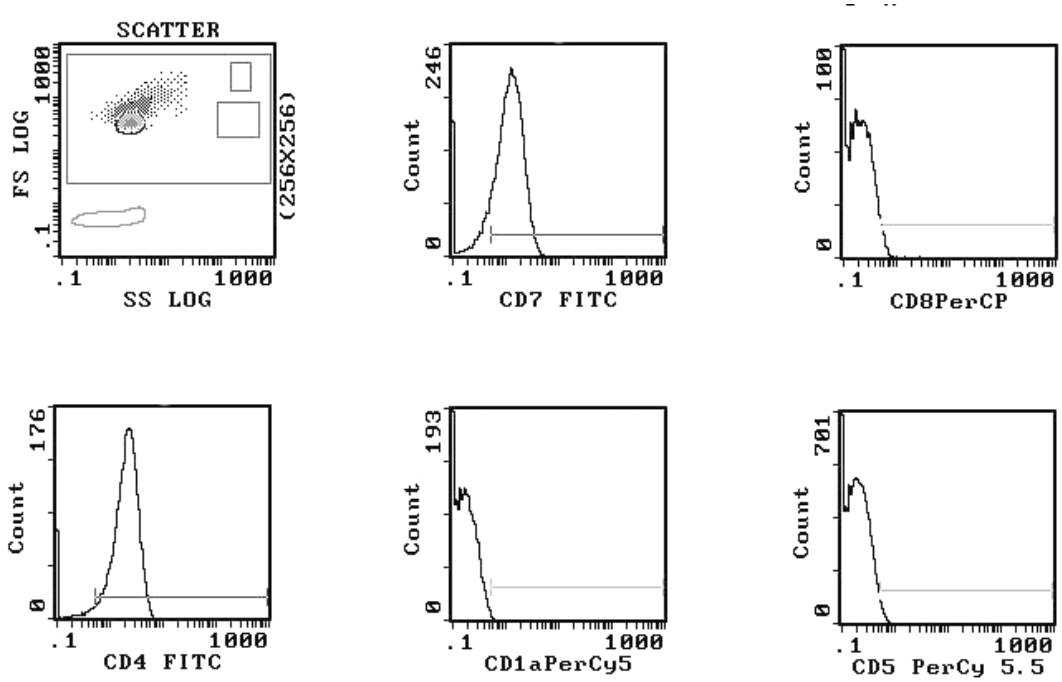

Figure 3. *A composite photograph of the most relevant immunophenotypic characteristics found on malignant T-cell prolymphocytes in our patient (performed on Beckman coulter, EPIX-XL flow cytometer, using System II software).*

DISCUSSION

We present a case of T-PLL, a rare disease, which accounts for approximately 3% of all T-cell lymphoproliferative disorders. Although white blood cell counts in T-PLL are classically higher than those seen in B-CLL, lymphocytosis in excess of 500,000 cells/μL has been rarely reported; only one of 39 patients in a recently published case series have had a lymphocyte count of that magnitude (3). Our case is noteworthy because it appears to represent among the highest recorded white blood cells in T-PLL, together with a case reaching 1,052,000 cells/μL (4).

Hyperleukocytosis is defined as a WBC count in excess of 100,000 cells/μL (5). The incidence of hyperviscosity and/or leukostasis syndromes in lymphocytic leukemias is rare. The cells in B- and T-CLLs are small and mostly well-differentiated. Hence, to reach a leukocrit of 20%, where, in vitro, the whole-blood viscosity increases, the cell count has to reach 1,000,000 cells/μL (4). This could explain the absence of leukostatic and hiperviscosity symptoms in our patient. Nevertheless, we might expect that rheological characteristics of patient's blood were abnormal. Although the case we presented is not a candidate for leukopheresis, it might benefit the use of medications that are able to improve rheological characteristics of blood (6).

T-PLL frequently demonstrates an aggressive course and resistance to conventional therapeutic measures (1). In a series of 15 patients treated with CHOP by Matutes et al.

Only one patient achieved complete remission (CR) lasting three months (1). Besides unresponsiveness to CHOP, which was also the case in our patient, modest therapeutic results were obtained using 2' deoxycoformycin (7). In a study of 55 T-PLL patients, only 5 (9%) reached complete remission, 20 (40%) had partial response with median response duration of six months (range 3-16 months) (8). More encouraging treatment results were reported with alemtuzumab an anti CD52 monoclonal antibody. The largest group was that of 76 patients with T-PLL treated with alemtuzumab recently reported by Keating et al. The response rate to alemtuzumab was 51%, with 39.5% of patients achieving CR. The median duration of CR was 8.7 months. The median time to progression was 4.5 months, with 14.8 months for patients with CR (9).

Finally, high - dose chemotherapy followed by allogenic stem cell transplantation (allo-STC) seems to be an effective, probably curative strategy for the treatment of selected patients with T-PLL (10). The use of umbilical cord blood UCB as a stem cell source can broaden the number of eligible patients who would benefit from allo-SCT (11).

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HIPERLIMFOCITOZA KOD BOLESNIKA SA T-PROLIMFOCITNOM LEUKEMIJOM KOJA NE ODGOVARA NA TERAPIJU: PRIKAZ SLUČAJA

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Sažetak

Prezentovan je slučaj muškarca starog 64 godine sa ekstremnim vrednostima leukocita i dijagnozom T-prolimfocitne leukemije. Nakon započete terapije Ciklofosfamidom, Onkovinom, Doksorubicinom i Pronizonom (CHOP) ne dolazi do poboljšanja, usled čega dolazi do smrtnog ishoda u periodu od dva meseca. Autori analiziraju savremenu terapiju ove retke bolesti zrelih T limfocita i razmatraju različite aspekte lečenja hiperlimfocitoze.

Ključne reči: **T-prolimfocitna leukemija, hiperlimfocitoza, terapija**