

De-novo CD5 + B- prolymphocytic leukemia (PLL) presenting at younger age with favourable outcome

Küçük yaşta olumlu prognoz ile seyreden de-novo CD5 + B- prolenfositik lösemi (PLL)

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Abstract

B-cell prolymphocytic leukemia (B-PLL) comprises 1% of chronic lymphocytic leukemias. CD5 positivity is seen in 1/3rd of cases which generally arise from pre existing CLL. They have longer median survival compared with de novo B-PLL which are commonly CD5 negative and are more aggressive with an older age of presentation. Herewith, we describe a 48-year-old male of de-novo CD5+ B-PLL presenting with minimal lymphadenopathy and massive splenomegaly with 90% atypical lymphoid cells in the peripheral smear and bone marrow. Immunophenotyping was strongly positive for CD5, CD45, CD19, CD22, FMC-7, S-Ig and CD38, moderately positive for CD 11c, weakly positive for CD23 and negative for CD-103 and ZAP 70. The patient responded well to fludarabine and cyclophosphamide and had an uneventful hospital course. Our case illustrates a de-novo B-PLL with aberrant CD5 positivity who had a short duration of illness, younger age at presentation and favourable treatment outcome. (*Turk J Hematol 2008; 25: 149-51*)

Key words: CD5+, prolymphocytic leukemia, splenomegaly, prognosis.

Received: February 22, 2007 Accepted: October 11, 2007

Özet

B-hücreli prolenfositik lösemi (B-PLL), kronik lenfositik lösemilerin %1'ini oluşturur. CD5 pozitifliği vakaların 1/3'ünde görünmekte olup genellikle önceden var olan CLL'den ileri gelmektedir. Genellikle CD5 negatif olan ve ileri yaşta görüldüğünde daha agresif olan de novo B-PLL'e nazaran daha uzun ortalama sağkalımları bulunmaktadır. Burada, de novo CD5+B-PLL hastası olan, minimal lenfadenopati ve masif splenomegaliye sahip, periferik yaymasında ve kemik iliğinde %90 atipik lenfoid hücre olan 48 yaşındaki bir erkeği sunuyoruz. İmmünofenotipleme, CD5, CD45, CD19, CD22, FMC-7, S-Ig ve CD38 için güçlü derecede, CD 11c için orta derecede ve CD23 için zayıf derecede pozitif ve CD-103 ve ZAP 70 için de negatiftir. Hasta fludarabin ve siklofosfamide iyi yanıt vermişti ve hastanede kaldığı sürede herhangi bir olay ortaya çıkmamıştı. Aberan CD5 pozitifliği olan de novo B-PLL olgumuz, kısa hastalık süresi, genç yaşta başvuru ve tedaviye iyi cevap göstermektedir. (*Turk J Hematol 2008; 25: 149-51*)

Anahtar kelimeler: CD5+, prolenfositik lösemi, splenomegali, prognoz.

Geliş tarihi: 22 Şubat 2007 Kabul tarihi: 11 Ekim 2007

Introduction

Polymorphocytic leukemia (PLL) was first described in 1974 as a rare variant of chronic lymphocytic leukemia (CLL) [1]. By definition, prolymphocytes must exceed 55%, and cases with 11-54% prolymphocytes are designated CLL/PLL [1,2]. In 60-70% of cases, PLL is of B-cell lineage, and the rest constitute T-PLL. De novo B-PLL is a rare and progressive disease comprising 1% of CLLs [3] with a median survival of 65 months [4]. It has an older age of presentation, with median age at 70 years [3] and poor outcome. The usual immunophenotype is strong surface IgM, FMC 7 and B-cell antigen CD19, CD20, CD22, and CD79a and b. CD5 is present in one-third of cases and CD23 is typically absent [3]. Herein, we report a case of B-PLL with younger age of presentation, indolent clinical course and strong CD5 positivity.

Case Report

This 48-year-old male presented to us with weight loss for 4 months and fever, headache and easy fatigability for 1 month. On examination, he had pallor, nontender lymphadenopathy (B/L axillary and right inguinal 0.5-1 cm), hepatomegaly palpable 3 cm and massive splenomegaly palpable 10 cm below respective costal margins. Routine hemogram showed low hemoglobin ranging from 74-83 g/L, persistent high total leukocyte counts (TLC) ranging from 55-75 $\times 10^9/L$ and sustained platelet counts ranging from 214-244 $\times 10^9/L$.

Peripheral smear and bone marrow aspirate showed a predominant population (90%) of medium-sized cells with moderate amount of light basophilic agranular cytoplasm with occasional cytoplasmic blebs, and slightly eccentric nucleus with relatively regular nuclear margins, less condensed chromatin and a single centrally placed nucleolus (Figure 1). Cytochemically, these cells were negative for myeloperoxidase, Sudan black, acid phosphatase and periodic acid Schiff, while few cells showed granular and dot positivity with non-specific esterase as described in an older literature [5]. The bone marrow trephine biopsy was cellular and showed diffuse as well as

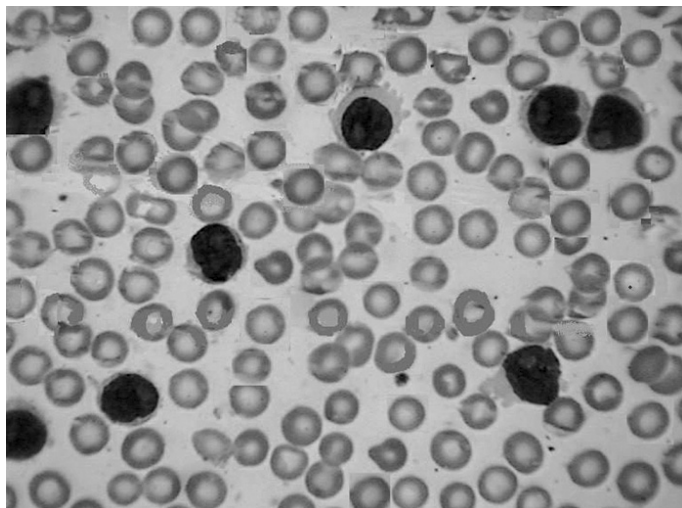


Figure 1. Peripheral smear ($\times 1000$) showing CD5+ prolymphocytes

nodular pattern of infiltration by immature cells. With this morphology, a diagnosis of chronic lymphoproliferative disorder with possibilities of PLL and hairy cell leukemia (HCL)-variant was made and immunophenotyping was advised. Immunophenotyping was strongly positive for CD5, CD45, CD19, CD22, FMC-7, S-Ig and CD38, moderately positive for CD11c, weakly positive for CD23, and negative for CD-103 and ZAP 70. Cyclin D1 staining was not available. With this phenotype, a diagnosis of CD5+ B-cell PLL was made.

During hospitalization, the patient received supportive care and a first cycle of chemotherapy with fludarabine and cyclophosphamide for 3 days, which he tolerated well with reduction in total blood counts from $63 \times 10^9/L$ (pre-chemotherapy) to $43 \times 10^9/L$ (post-chemotherapy). He was subsequently discharged and developed fever after a few days of discharge, for which he was re-admitted and received antibiotics. His TLC had declined to $6 \times 10^9/L$ with 29% prolymphocytes. He subsequently underwent all six cycles of chemotherapy uneventfully. At 6 months post-chemotherapy, he had one episode of community-acquired pneumonia of the left lower lobe requiring hospitalization, which was treated successfully. Now at 14 months post-chemotherapy, he has no pallor or organomegaly and his counts have normalized with Hb 130 g/L, TLC $6.3 \times 10^9/L$ and platelet count $142 \times 10^9/L$, and with bone marrow showing remission.

Discussion

Patients with B-PLL typically have massive splenomegaly, minimal lymphadenopathy, very high TLC with distinct morphology, resistance to chemotherapy, and poor prognosis [1,5]. The treatment in PLL has progressed from splenectomy, splenic irradiation, leukapheresis and alkylating agents to purine nucleoside analogs (fludarabine, cladribine and pentostatin) with prolonged progression-free survival with fludarabine [6]. More recently, the monoclonal antibodies alemtuzumab [7] and rituximab [8] have proved useful in treating B-PLL.

Aberrant CD5 expression is a characteristic feature of small lymphocytic lymphoma/CLL (SLL/CLL) and mantle cell lymphoma (MCL), which can be distinguished reliably by CD23, being positive in the former and negative in the latter [9]. In B-PLL, CD5 expression is variable and seen in up to one-third of cases. Thus, B-cell PLL may be divided into CD5+ PLL (arising in CLL) and CD5- PLL (de novo PLL). CD5+ PLL has a longer median survival than CD5- PLL [9]. In contrast, our case represents a de novo B-PLL with CD5 positivity rather than CLL in transformation, who had a short duration of illness, younger age at presentation and good response to chemotherapy. In another study [10], no significant difference between de novo PLL and prolymphocytoid transformation of CLL was found, but patients with p53 mutations had worse prognosis irrespective of the presentation. B-PLL has also been sub-classified into two groups based on cytogenetic findings, namely t(11; 14) positive group and t(11; 14) negative group. CD5 expression was more frequent in the former [11]. The authors have retrospectively re-classified these cases as MCL. Although leukemic phase of blastoid MCL can be a difficult differential diagnosis of B-PLL, in

the index case, the monomorphic population of atypical lymphocytes with characteristic morphology and immunophenotyping characteristics tilted our diagnosis in favor of B-PLL short of cyclin D1 staining and cytogenetics.

The other differential diagnosis entertained was HCL-variant. The immunophenotype differs somewhat from classical HCL in that there is variable expression of CD103 and lack of CD25 [9]. Since HCL is typically CD5- and 23- negative, we ruled it out as a possibility in this case. A study [12] evaluating CD11c+ CD5+ chronic B-cell leukemias found that these represent forms of either CLL or PLL rather than HCL.

In conclusion, this case illustrates the importance of immunophenotyping as an adjunct to morphology in the diagnosis of chronic lymphoproliferative disorders. It also underscores the fact that de novo cases of B-PLL may have aberrant CD5 positivity may not be as aggressive as previously believed.

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