CASE REPORT

T-cell prolymphocytic leukemia: a report of two cases with review of literature

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Abstract T-cell Prolymphocytic Leukemia (T-PLL) is a mature post-thymic T-cell malignancy with aggressive clinical course. The principal disease characteristics are organomegaly, skin lesions and raised lymphocyte counts. We report two cases of T-PLL. T-PLL is a rare T-cell malignancy with characteristic clinical and laboratory features and a poor prognosis. It needs to be differentiated from B-Cell prolymphocytic leukemia (B-PLL) and other mature T-cell lymphoproliferative disorders with predominant leukemic pattern. Differentiation can be made by a comprehensive approach taking into account the clinical features, the cell morphology and the immunophenotype of leukemic cells.

Keywords T-PLL · Prolymphocyte · Immunophenotyping

Introduction

T-cell prolymphocytic leukemia (T-PLL) is a mature post-thymic T-cell malignancy with aggressive clinical course. It has distinct clinical and laboratory features and is currently recognized as a distinct T-cell malignancy in WHO classification [1]. T-PLL affects adults and occurs more frequently in men. The principal disease characteristics are organomegaly, skin lesions and a raised lymphocyte count. Immunological markers show a post-thymic T-cell phenotype: TdT negative, CD 2+ CD5+, CD7+ and CD3+/- . T-helper (CD4+CD8-) phenotype is seen in two third of cases and 25% may co-express CD4 and CD8. T-suppressor (CD8+CD4-) phenotype is rare. Here, we present clinico-pathological features of two cases of T-PLL which presented at our center, with emphasis on the diagnostic features and differential diagnosis.

Case report

Case 1

A 42-year-old man presented with fever, weight loss and bilateral red eye since one month. On physical examination, generalized lymphadenopathy and moderate hepatosplenomegaly was noted. There was conjunctival hemorrhage in both the eyes. Laboratory investigations revealed hemoglobin of 11.2 g/dl, total leukocyte count of $230 \times 10^3/\text{cumm}$ and platelet count of $57 \times 10^3/\text{cumm}$. Blood biochemistry was normal except elevated lactate dehydrogenase (LDH) levels. Peripheral blood smear showed 92% atypical lymphoid cells, which were medium sized with regular nuclear outline, single nucleolus and scant, agranular,

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deeply basophilic cytoplasm. Bone marrow aspirate smears showed predominantly atypical lymphoid cells with similar morphology as peripheral blood cells. There was marked reduction of normal hematopoietic cells. On flow cytometric immunophenotyping, the atypical lymphoid cells were positive for CD2, CD3, CD5, CD7, CD8 and CD38; and negative for CD19, CD22, CD4, CD56, CD25, CD30 and TdT (Fig. 1). Taking into account the clinical, morphologic and immunphenotypic features a diagnosis of T-PLL was

made. Patient was put on chlorambucil, prednisolone and allopurinol but was lost to subsequent follow-up.

Case 2

A 77-year-old woman presented with fever and breathlessness since eight months. Physical examination revealed pedal edema, generalized lymphadenopathy and moderate

Fig. 1 Dot plots showing immunoreactivity pattern of prolymphocytes in T-prolymphocytic leukemia

hepatosplenomegaly. Laboratory investigations showed hemoglobin of 7.3 g/dl, total leukocyte count of $430 \times 10^3/\text{cumm}$ and platelet count of $53 \times 10^3/\text{cumm}$. Blood biochemistry was normal except elevated LDH levels. Peripheral blood smear showed 94% atypical lymphoid cells which were small in size, with high nuclear-cytoplasmic ratio, irregular nuclear outline, inconspicuous nucleolus and scanty cytoplasm (Fig. 2). Bone marrow examination was not done because of poor general condition of the patient. On flow cytometric immunophenotyping, the atypical lymphoid cells were positive for CD2, CD3, CD5, CD7, CD4 and CD38; and negative for CD8, TdT, CD34, CD19, CD20, CD22, CD10, CD13, CD33, CD56, CD25, and CD103. Based on the above findings, a diagnosis of T-PLL was made. Patient however refused treatment and was discharged on request.

Discussion

T-PLL is a rare chronic T-cell lymphoproliferative disease and represents 20% of PLL (remaining 80% being B-PLL). Main disease features at presentation are lymphadenopathy, hepatosplenomegaly, skin lesions and marked leukocytosis. It rapidly progresses and is more aggressive than B-PLL. The disease was first recognized in 1973 in a patient presenting with a leukemic picture similar to that of B-PLL but in whom the cells were shown to be E-rosette positive [2].

The clinical features, morphological variations and cytogenetic characteristics were reported by Matutes et al and Brito-Babapulle et al in their studies conducted on a series of patients with T-PLL [3–5]. The lymphoid cells in T-PLL are small to medium-sized with round, oval or irregular

nuclei, non-granular basophilic cytoplasm and cytoplasmic blebs. T-PLL cells show a post-thymic T-cell immunophenotype with expression of CD2, CD3, CD5, CD7 and; absence of TdT and CD1a. Expression of CD4 and CD8 is variable. T-PLL needs to be distinguished from B-PLL and adult T-cell leukemia lymphoma (ATLL) and Sezary syndrome (SS) which have overlapping morphological features and mature T-cell phenotype. Distinction is based on a constellation of clinical and laboratory features which include cell morphology, histology, and immunological markers.

As compared to T-PLL, lymphadenopathy and skin lesions are uncommon in B-PLL. The T-PLL cells differ from B-PLL cells in size (B-prolymphocytes are larger), degree of cytoplasmic basophilia (more in T-prolymphocytes) and nuclear irregularity (irregular in half of the cases of T-PLL). The total leukocyte count is generally below $100 \times 10^3/\text{cumm}$ and massive splenomegaly is uncommon in ATLL and SS. Other features which help in differentiation include erythroderma in SS and; hypercalcemia and positivity for HTLV-I in ATLL. Morphologically, SS is characterized by cells with cerebriform nuclei and ATLL by presence of flower cells which have polylobated nuclei. In Sezary cell-like leukemia, cells are indistinguishable from Sezary cells by light and electron microscopy but, unlike SS, the skin is not involved. Establishing a differential diagnosis of T-PLL and Sezary cell-like leukemia (a rare form of T-cell leukemia) can be difficult [6]. Sezary syndrome, ATLL and T-PLL display a post-thymic T-cell phenotype with SS cells negative for CD7 and CD25, ATLL cells positive for CD25 and negative for CD7, and T-prolymphocytes positive for CD7 and negative for CD25.

Both our cases presented with lymphadenopathy, hepatosplenomegaly and high leukocyte count. The lymphoid cells in first case consisted of monomorphic population of medium sized cells with round to oval nucleus, moderately condensed chromatin, and single prominent nucleolus. Differentiation from B-PLL was made by immunophenotypic characterization of lymphoid cells. Significant nuclear irregularity was observed in second case and differentiation from ATLL and SS was based on clinical features i.e. massive splenomegaly, absence of skin lesions, normal calcium levels and; presence of CD7 and absence of CD25 on leukemic cells. Serology for HTLV-1 was not done in our patients.

One of our patients presented with bilateral conjunctival inflammation. Lee et al. reviewed all case reports of leukemia with conjunctival involvement and reported a case of T-PLL with bilateral perilimbal conjunctival infiltrates of atypical lymphoid cells with immunophenotypic features consistent with T-PLL [7]. In our patient, further workup for conjunctival involvement was not done and therefore,

Fig. 2 Peripheral blood smear showing T-prolymphocytes with irregular nuclear outline (Jenner-giemsa, 1000X)

involvement of conjunctiva by prolymphocytes can not be ruled out.

A precise diagnosis of T-PLL is important for patient management. As a rule patients treated with alkylating agents such as chlorambucil are either resistant to this therapy or achieve only partial and short lived responses. Approximately one-third patients respond to CHOP but most responses are partial [8]. More recently, Campath-1H has been shown to be effective in T-PLL [9]. Both of our patients were lost to follow up, so the clinical course could not be defined in them.

To conclude, we have reported two cases of T-PLL, which is a relatively rare disorder and has characteristic clinical, morphological and immunologic features within the spectrum of post-thymic T-cell malignancies. A precise diagnosis is important for patient management, treatment and prognostication.

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