CASE REPORT

CD5 Positive B Lymphoblastic Leukemia: Report of a Case with Review of Literature

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Abstract We report a rare CD5 positive B cell acute lymphoblastic leukemia (B-ALL) with a review of the clinopathological features and prognosis of previously reported cases in the literature. The aberrant expression of CD 5 antigen is uncommon in B-ALL; the morphological differential diagnosis includes blastic mantle cell lymphoma, denovo CD5⁺ diffuse large B cell lymphoma and secondary diffuse large cell lymphoma/Richter's transformation. CD5⁺ B cell ALL is commonly reported in younger patients (<18 years). Though the expression of T cell antigens is reported to have poor prognosis, the experience with CD5⁺ B-ALL is limited to draw any firm conclusion regarding its prognosis.

Keywords Leukemia associated abnormal immunophenotype (LAIP) · B acute lymphoblastic leukemia · Aberrant T cell antigen

Introduction

Leukemia associated abnormal immunophenotype (LAIP) is an important character of acute leukemias of which an aberrant expression of an antigen of different cell lineage is well characterized and identified with increasing sensitivity

due to use of multiparameter flow cytometry with larger and newer panel of antibodies [1]. The identification of LAIP has important diagnostic as well as prognostic values and its helps in the identification of minimal residual disease. The aberrant expression of various myeloid and T cell related antigens in B cell acute lymphoblastic leukemia (B-ALL) is reported to occur at different frequencies. Here we report a relatively rare CD5⁺ B-ALL with a compilation of previously reported cases in the literature.

Case Report

A 50-year-old male presented with fever and fatigue of 1-month duration. Physical examination revealed pallor, hepatomegaly (6 cms below right costal margin) and a splenomegaly (10 cms below the left costal margin). Haemogram revealed anemia (hemoglobin—70 g/l), leukocytosis with presence of blasts (total leukocyte count— $85 \times 10^9/l$; 95 % blasts) and thrombocytopenia (platelet count— $28 \times 10^9/l$). Bone marrow examination revealed cellular smears with 90 % blasts and suppression of normal hematopoietic elements. The blasts were two to four times the size of mature lymphocyte and had scant basophilic cytoplasm. There were no cytoplasmic granules or Auer rods (Fig. 1a). The blasts were negative for myeloperoxidase (MPO) (Fig. 1b) and Periodic acid schiff (PAS) stain on cytochemistry. A multiparametric flow cytometry (FCM) was performed. The cells were acquired on BD FACS Canto II and analysis was done using BD FACS Diva software. The antibodies used were CD1a, CD2, CD3 (cytoplasmic and surface), CD4, CD5, CD7, CD8, CD10, CD11c, CD13, CD14, CD19, CD20, CD22, CD33, CD34, CD38, CD45, CD64, CD117, HLA-DR, kappa, lambda (surface), TCR $\alpha\beta$, TCR $\gamma\delta$, TdT (BD Biosciences, USA). The cells with dim

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Fig. 1 **a, b** Bone marrow aspirate smear showing blasts ($\times 100$, May Grunwald Giemsa stain) which were negative for myeloperoxidase in cytochemistry ($\times 100$, myeloperoxidase stain). **c–i** Multiparametric flow cytometry finding performed from bone marrow aspirate. The singlets and further blasts ($CD45^{\text{dim}}$ low side scatter) were gated.

They showed $CD10^+ CD19^+ CD20^+ CD5^+ CD34^-$ Surface kappa $^-$ surface lambda $^-$ immunophenotype. The blasts were also negative for other T cell markers (CD7, CD2, surface and cytoplasmic CD3), myeloid, monocytic markers and TdT (not shown in the figure)

CD45 positivity and low side scatter (blast region) constituted 80 % of the cells. These cells were positive for CD19, CD10, CD20, CD38 and HLA-DR while negative for myeloid and monocytic markers as well as surface immunoglobulins. CD34 and TdT were also negative. In addition 60 % of the blasts were also aberrantly positive for CD5 (Fig. 1h). Morphology together with dim positivity for CD45 and the absence of surface immunoglobulin favored a diagnosis of B-ALL. Multiplex reverse-transcriptase polymerase chain reaction (RT-PCR) and gel electrophoresis performed for various fusion transcripts like *BCR-ABL1* [t(9;22)(q34;q11.2)], *E2A-PBX1* [t(1;19)(q23;p13.3)], *TEL-AML1* [t(12;21)(p13;q22)], *AF4-MLL* [t(4;11)(q21;q23)], *RUNX-RUNX1T1* [t(8;21)(q22;q22)] and *CBF β -MYH11* [inv(16)] did not show any recurrent cytogenetic abnormalities. The patient was treated using modified BFM protocol. A bone marrow performed after induction therapy did

not show any excess of blasts suggesting the remission status of the disease. He received consolidation followed by delayed intensification therapy and bone marrow was in morphological remission before starting maintenance treatment. The patient is on maintenance therapy and is in complete hematological remission till this report.

Discussion

Acute leukemias are characterized by the expansion of cells blocked at a particular stage of maturation. They may show morphologic and immunophenotypic resemblance to their normal counterpart but often shows immunophenotypic aberrations collectively referred to as LAIP [2]. LAIP includes aberrant expression or cross lineage expression, asynchronous expression, under/over expression of

antigens, abnormal spectrum of expression and ectopic phenotype [1, 3]. In a particular case, the number of LAIPs and the percentage of blasts expressing a particular LAIP can vary [1, 3]. Aberrant expression of T or NK cell antigens on B-ALL are uncommon with isolated case reports and recently in two large studies by Seegmiller et al. and Hussein et al. compared to myeloid antigens, T cell antigenic co-expression occur more frequently in adults than in children [3, 4]. Our case is exemplified by uncommon expression of CD5 on B-ALL. CD5 also known as Leu-1 and is a cell surface antigen seen on T cells, NK cells and a subpopulation of B cells called B1 cells [5]. CD5⁺ B cells are seen in peritoneal cavity, pleural cavity, fetal spleen, cord blood and marginal zone of lymphoid follicles in spleen [6]. They are identified by CD19^{hi}CD23^{neg}CD43^{pos}IgM^{hi}IgD^{variable} immunophenotype [7]. These cells are involved in auto-antibody production and is increased in rheumatoid arthritis [5]. With the exception of B1 cells, CD5 antigen expression is not usually seen on B cells. Expression of CD5 is common in B cell lymphoproliferative disorders like chronic lymphocytic leukemia/small lymphocytic lymphoma and mantle cell lymphoma; uncommonly in marginal zone lymphoma, diffuse large B cell lymphoma, prolymphocytic leukemia and lymphoplasmacytic lymphoma; and very rarely in follicular lymphoma and burkitt lymphoma [8]. The expression of CD5 on B-ALL is rare with only few reports in the literature. Subira et al. reported a case of 15-year-old young man with CD19⁺/CD5⁺ ALL in 1998. The cytogenetic analysis was normal. He died of disease within 17 months of diagnosis [9]. In 2007, Peterson et al. reported two cases of CD5⁺ B-ALL, one 16-year-old male and one 15-year-old female. One of them revealed trisomy 22 and both had poor outcome [10]. Ahmed et al. reported a case of 23-year-old female in 2008. This patient showed t(9:22) and achieved morphological remission in 2 weeks; but long term follow up is not known [6]. In a study by Seegmiller et al. who characterized the immunophenotypic aberrancies in 200 cases of B-ALL, CD5 expression was noted in four cases (2 %). Three of them were children and

one was an adult. There was no association with any particular recurrent cytogenetic abnormality. Follow up of cases is not available [3]. Recently in a study by Hussein et al., 6 out of 134 cases of B-ALL (4.5 %) showed aberrant expression of CD5. Four of them were males and one was a female. Five out of six patients were <18 years of age. All but one reached remission. They have shown that the aberrant expression of T cell markers were associated with poor prognosis and increased risk of relapse in B-ALL; however correlation with CD5 aberrant expression as such is not available [4]. Mutreja et al. recently reported aberrant expression of CD5 in a case of B-ALL with a small supernumerary marker chromosome. The patient died of pancreatitis before starting induction chemotherapy [11]. Compiling all the cases in the literature, aberrant expression of CD 5 is reported only in 15 cases [3, 4, 6, 9–11]. They are summarized in Table 1.

In addition to the relative rarity of aberrant expression of CD5 on B-ALL, the available literature suggests this to be associated with an overall poor prognosis. In our patient also, its expression was associated with other poor prognostic factors like older age (50 years), high total leukocyte count ($85 \times 10^9/l$) and expression of CD20. The expression of CD20 on B-ALL is also being explored as a therapeutic target for rituximab [12]. Though our patient had responded to chemotherapy and is in maintenance phase; the prognosis will be clear only on long term follow up. Another important issue is the lack of immaturity markers like CD34 and TdT. Liu et al. reports that, TdT can be negative in up to 3 % of B-ALL which are also frequently associated with high total leukocyte count and CD34 negativity [13]. The expression of CD20 along with the lack of CD34 and TdT lead to a differential diagnosis of a mature B cell neoplasm. However, the dim expression of CD45 and lack of surface immunoglobulins helps to rule out a CD5 expressing mature B cell neoplasm with blastic morphology like blastic mantle cell lymphoma, denovo CD5⁺ diffuse large B cell lymphoma and secondary diffuse large cell lymphoma/Richter's transformation. Blastoid

Table 1 Summary of CD5⁺ B cell ALL cases reported in the literature

	No: of cases	Age (years)	No: of males and females	Cytogenetic abnormality	Prognosis
Subira et al. [9]	One	15	Male	46XY	Poor
Peterson et al. [10]	Two	15, 16	1:1	Trisomy 22 in one case	Poor
Ahmed et al. [6]	One	23	Female	t(9:22)	Long term follow up not known
Seegmiller et al. [3]	Four	Three children, one adult	Not available	No specific abnormality	Not available
Hussein et al. [4]	Six	Five children and one adult	2:1	Not available	Remission in 5; relapsed in 3
Mutreja et al. [11]	One	20	Male	Supernumerary marker chromosome	Died prior to induction therapy
Present report	One	50	Male	No specific abnormality	Remission at 11 months

morphology together with lack of expression of CD45 can create diagnostic confusion with other malignant blue cell tumours especially in children. The expression of B lymphoid markers helps in exclusion of such entities.

To conclude, the aberrant expression of CD 5 antigen is uncommon in B-ALL. CD5⁺ B cell ALL is commonly reported in patients less than 18 years and is thought to have a poor prognosis. Our patient differs from other cases because of presentation at an older age, absence of immaturity markers like CD34 and TdT and early response to chemotherapy. Hence we believe that the experience with this entity is limited to draw any firm conclusion regarding its prognosis. The identification of such aberrancies in ALL helps in distinction from hematogones and in detecting minimal residual disease.

Conflict of interest The authors declare that there is no conflict of interests.

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