Case Report

Aberrant Expression of a T-Cell and a Monocytic Antigen in a Newly Diagnosed Precursor B-Cell Acute Lymphoblastic Leukaemia

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Abstract: Background: Aberrant expression of antigens/or loss of some antigens on leukemic cells is sometimes seen. Such expressions may or not affect prognosis of leukaemia. Aberrant co-expression of CD5 and CD64 on precursor B-cell ALL leukemic cells is found first time.

Objective: To report a novel case of precursor B-cell ALL which co-expressed a T-cell lineage (CD5) and a monocytic lineage (CD64) antigens.

Methods: Bone marrow immunophenotyping was performed using FACSCalibur (a four-color flowcytometer) and acute leukaemia panel of antibodies.

Case Presentation: A 4-year old boy with circulating small sized blasts. Immunophenotyping data revealed expression of CD45, CD19, CD79a, TdT, CD34, CD10, CD5 and CD64 while absence of CD3, MPO, CD13, CD33, CD4, CD7 and CD8 antigens.

Conclusion: A diagnosis of precursor B-cell ALL with aberrant CD5 and CD64 expression was made.

Keywords: Aberrant expression of antigens, CD5 and CD64 co-expression, Monocytic, Organomegal, Pre-B-ALL.
doi.org/10.21089/njhs.23.0128

INTRODUCTION

Precursor B-cell acute lymphoblastic leukaemia (Pre-B-ALL) is the most common malignancy in pediatric population. It is characterized by uncontrolled proliferation of an early precursor B-cell, replacing normal hemopoietic tissue in the bone marrow and other lymphoid tissues of the body. This results in symptoms of anaemia, thrombocytopenia and neutropenia. Immunophenotyping is an important tool to identify the cell lineage of leukemic cells. Aberrant expression and/or loss of antigens from a given lineage are not an uncommon finding on leukemic cells. Pre-B-ALL is diagnosed when B-lineage markers *e.g.*, CD19, CD20, CD79a along with markers of immaturity terminal deoxynucleotidyl transferase (TdT), CD34 and HLA-DR are found to be expressed on leukemic cells. Normal T-cell lineage markers include CD3, CD5 and CD7. Expression of CD3 is lineage specific while, CD5 and 7 are not. Expression of CD5 on pre-B-ALL is an extremely rare phenomenon [1]. However, it is expressed on different B-cell lymphomas *e.g.*; chronic lymphocytic lymphoma (CLL), mantle cell lymphoma (MCL) and subset of diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma [2]. CD64, a marker for monocyte lineage was the other marker that was aberrantly expressed in this patient [3]. To the best of our knowledge and after extensive literature review, we were unable to find any other case report or a disease entity with aberrant expression of these two antigens in a case of pre-B-ALL. Here we describe a patient who aberrantly expressed a T-cell and a monocytic antigen in a case of pre-B-ALL.

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CASE REPORT

A 4-year old boy was presented in haematology clinic with a history of pallor and weakness since 3-months. He received pack red blood cell transfusion twice for correction of anaemia. On examination, he was pale, there was no organomegaly or lymphadenopathy appreciated. On presentation, CBC showed bicytopenia with Hb of 5.0 g/dl, WBC 12.7 x 10^9/L and PLT 35 x 10^9/L. Peripheral smear showed 40% blast cells; they were of small sized with regular cellular outline, high nuclear/cytoplasmic ratio, partially clumped nuclear chromatin and 1-2 nucleoli (Fig. **1**). Bone marrow biopsy showed a diffuse infiltration with blast cells, which had similar morphology as described above. Renal and hepatic profile was normal with LDH of 783 I.U and uric acid 3.1 mg/dl. Coagulation profile was within normal limits. Ultrasound abdomen and chest x-ray were normal. Flow-

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cytometry was performed on a four-colour flowcytometer, FACSCalibur (BD USA) (Fig. **2**). Data was analysed using Paint-A-Gate software. It revealed the following immune-phenotype result: CD45, CD19, CD79a, TdT, CD34, CD10, CD5 and CD64 positive while CD3, MPO, CD13, CD33, CD4, CD7 and CD8 were negative. Therefore, a diagnosis of precursor B-cell ALL with aberrant CD5 and CD64 expression was made. Bone marrow cytogenetics revealed a normal male karyotype. Bcr-abl p190 transcript was not detected by PCR. While the family was preparing for treatment of the child, he died at home.

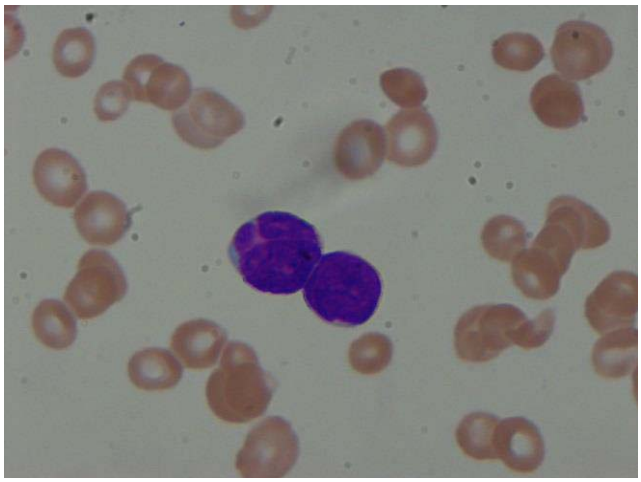

Fig. (1). Peripheral smear showing lymphoblasts.

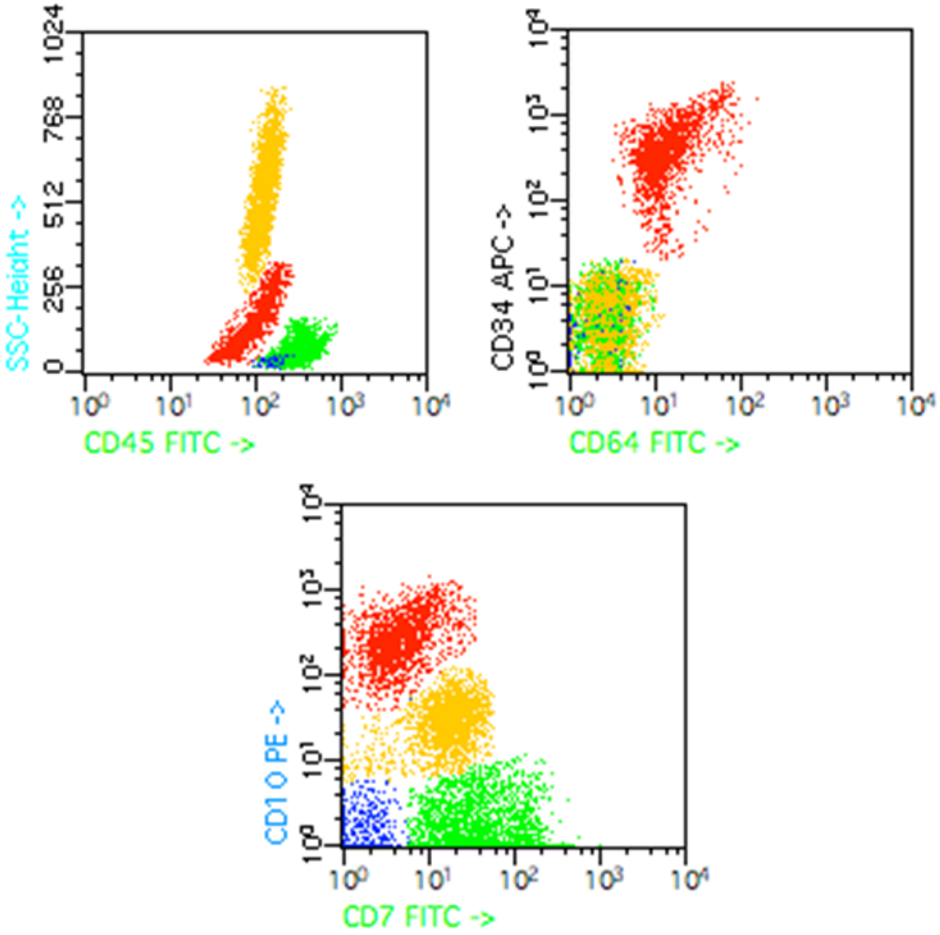

Fig. (2). Cont……

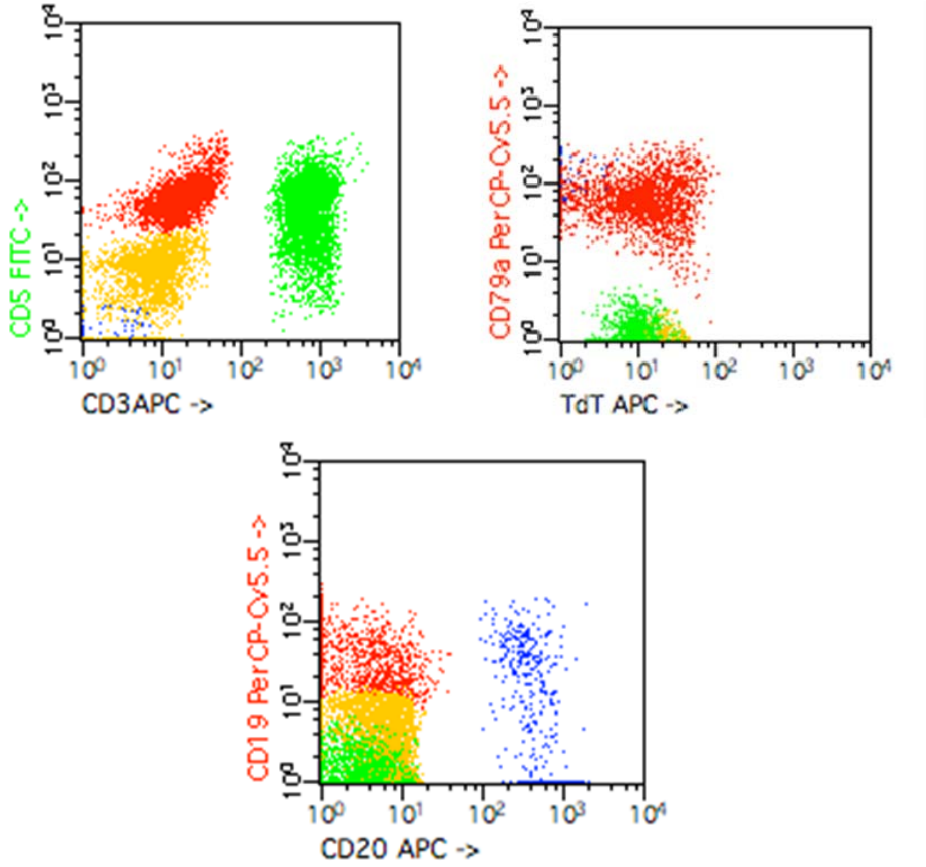

Fig. (2). Immunophenotyping by Flowcytometry: Dot plots showing blasts in red color positive for CD 45, CD 5, CD 34, CD 79a, CD 19, CD 64, CD 10 and Tdt. Benign T-lymphocytes in green color and granulocytes in yellow color.

DISCUSSION

Precursor B-cell ALL is the most common haematological malignancy in children with a high cure rate. Certain biological factors help in prognostication of this disease. Age between 2-10 years, female sex and a WBC count of <50 x 10^9/L predict a favourable outcome. Presence of Philadelphia chromosome and certain other cytogenetic abnormalities (MLL gene) has an adverse outcome. Similarly, expression of other lineage antigens (bi-phenotypic Leukaemia) also adversely affects the treatment outcome. CD5 positive pre-B cell ALL is a very rare entity reported in one case series with only 2% frequency in 200 cases of ALL [4]. All these cases were young. All the patients described in case reports published till now correlate this entity with aggressive behaviour, described a patient of same entity with lymphadenopathy, hepatomegaly and ascites. This patient died before chemotherapy could be initiated [5]. Two patients reported showed aggressive behaviour [6] and reported a Ph positive B-cell ALL patient with aberrant CD 5 expression. Aberrant expression of other T-cell markers is also associated with poor outcome [7].

CD64 was the other marker that was aberrantly expressed in this patient. CD 64 is a marker for monocytes. It is also aberrantly expressed in variable number of B-cell ALL [8]. Co-expression of CD5 and CD64 was not reported in the literature previously. Our patient was in standard-risk group (4 year old, WBC 12 x 10^9/L, male sex, normal cytogenetics). Aberrant co-expression of these antigens resulted in an aggressive disease and a fatal outcome without any treatment.

Immunophenotyping, cytogenetic analysis and other molecular genetic studies are essential for diagnosis, risk stratification and prognostication of patients. Risk-stratified treatment approach helps to select patients to be treated with standard treatment protocol. High-risk category of patients should be treated with risk adapted aggressive strategy in order to benefit majority of patients. Partial work-up in these disease and “one treatment for all” strategy results in disappointment for patients, families and to the treating physicians and other healthcare professionals.

CONFLICT OF INTEREST

Declared none.

ACKNOWLEDGEMENT

Declared none.

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Received: December 15, 2016 Revised: March 23, 2017 Accepted: March 24, 2017

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