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Aberrant expression of CD5 in a B-lineage Acute Lymphoblastic Leukemia (ALL): a case report



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ABSTRACT

Background: CD5 is expressed in several B-lymphocyte malignancies, including Chronic Lymphocytic Leukemia (CLL), Mantle Cell Lymphoma (MCL), but CD5 positive B-cell lineage Acute Lymphoblastic Leukemia (ALL) is extremely rare. Aberrant T-cell antigen expression is associated with poor prognosis and is a useful marker to identify patients at increased risk. This case report aims to elaborate on the aberrant expression of CD5 in B-lineage ALL.

Case Presentation: A 16-years-old male presented

with a history of gum bleeding and abdominal pain of 7 days with associated fever, weakness and bone pain of 2-month duration. The bone marrow aspiration showed lymphoblast 30 % with the positive vacuole. In addition, the immunophenotyping test indicates for leukemia B-lineage with expression CD19, CD10, HLA-DR, CD 34, and there is the aberrant expression of CD5.

Conclusion: Aberrant expression CD5 in cases of ALL B lineage is very rare. This can be associated with a poor prognosis.

Keywords: CD5, Aberrant Expression, B-lineage, ALL.

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INTRODUCTION

Acute leukemia is defined as the presence of over 30% of blasts cells in the blood or bone marrow at diagnosis.¹ Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) are the 2 main types of acute leukemias.^{1,2} Classification of acute leukemia is necessary to make a diagnosis related to the selection of the right therapy. ALL is the most common leukemia in children, comes from the initial form of lymphocytes, both B cells and T cells.³ The incidence of ALL is 1 every 60,000 people per year, with the highest incidence in children aged 2 to 3 years and at the age of 50 years.^{3,4}

Recent developments in immunology, molecular biology, and cytogenetics can increase understanding of the biological markers that differentiate between normal hematopoietic cells and leukemic cells, differentiation of leukocytes and cellular origins from acute leukemia, and allow

accurate classification of malignant clones such as myeloid, B lymphoid, T lymphoid, or phenotypic B-lineage in most cases.⁵ Approximately 80% of ALL cases originate from the B-cell lineage (BL), while 15–20% of cases ALL originate from T-cell lineage. Patients are classified as ALL B-lineage if $\geq 30\%$ of isolated lymphoblast cells positive for CD19 and $<30\%$ positive for CD10, CD20 and CD22.⁵ Patients were classified as T-lineage (TL) if $\geq 30\%$ of isolated lymphoblasts were positive for CD2, CD5, or CD7 and $<30\%$ were positive for CD19. BL and TL patients are classified as positive myeloid (My+) if $\geq 30\%$ of isolated lymphoblast cells are positive for CD13 or CD33, or both.⁵

This report will present a case of acute lymphoblastic leukemia (ALL)-L2, B lineage with aberrant CD5. It is hoped that this case report can add a broader insight into ALL and also immunophenotyping which is useful in diagnosing ALL.

CASE REPORT

A 16-years-old male presented with a history of gum bleeding and abdominal pain of 7 days duration with associated fever, weakness, and bone pain of 2-month duration on admission. On physical examination, he was febrile with a temperature of 38.3°C, anemic in both conjunctivae, examination of the heart and lungs within normal limits, no liver or lymph enlargement, and no edema in the extremities. Laboratory tests showed a decrease in Hb levels, a decrease in the number of leukocytes and platelets.

During patient care, several investigations are carried out. The complete blood count showed leukopenia with neutropenia and lymphocytosis, anemia and thrombocytopenia (Table 1). In addition, the patient also underwent bone marrow aspiration with results in hypocellularity, decreased activity in erythroid, myeloid, and megakaryocyte.

Table 1. Hematology results

Variables	05/27/2019	06/02/2019	06/26/2019	Reference range
WBC (10 ⁶ /μL)	3.84	0.82	8.35	4.1-11.0
% Neu	33.30	66.41	64.41	47-80
%Lym	57.87	26.80	23.41	13-40
%Mono	6.74	4.97	9.89	2.0-11.0
%Eos	1.06	0.26	1.72	0.0-5.0
%Baso	1.03	1.57	0.71	0.0-2.0
RBC (10 ⁶ /μL)	3.31	3.69	4.08	4.5-5.9
Hb (g/dL)	9.07	10.10	10.67	13.5-17.5
HCT (%)	26.55	30.29	30.29	41.0-53.0
MCV (fL)	80.26	82.07	84.68	80.0-100.0
MCH (pg)	27.43	29.22	26.13	26.0-34.0
MCHC (g/dL)	34.17	34.52	34.52	31-36
RDW (%)	11.21	12.36	12.97	11.6-14.8
PLT (10 ⁶ /μL)	12.89	9.43	89.68	150-440

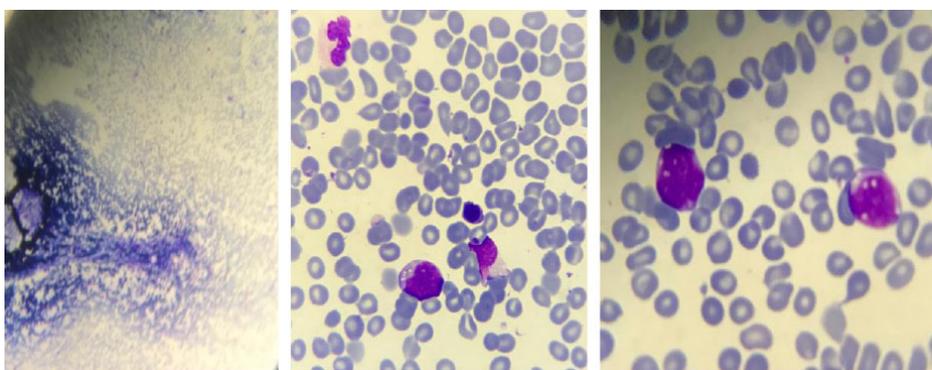


Figure 1. Bone marrow aspirate smear.

Lymphoblast count was found at 30% with vacuole (+) (Figure 1). The clinical chemistry found that all parameters were within a normal range (Table 2).

The patient was diagnosed with acute lymphoblastic leukemia (ALL) L3 from the history, physical examination, and bone marrow aspiration smear. From the immunophenotyping result, the patient was diagnosed with acute lymphoblastic leukemia B Lineage with an aberrant expression CD5 (Figure 2).

DISCUSSION

Acute lymphoblastic leukemia (ALL) is the most common leukemia in children, originating from the initial form of lymphocytes, B cells and T cells. The incidence of ALL is 1 every 60,000 people per year, with the highest incidence in children aged 2 to 3 years and at the age of 50 years.⁴

Some of the risk factors that influence the incidence of leukemia include genetic factors, such as mutations in

chromosomes, chronic infectious factors, like Human T lymphocyte (HTLV-1) infection in T-cell leukemia, Epstein-Barr virus infection in Burkitt's lymphoma and environmental factors such as radiation, pesticides, alcohol, cigarette smoke, and drugs.⁶

The clinical manifestations of ALL in children vary widely and appear at varying times. The most common complaints are pallor and fever.⁷ Other symptoms that appear are bleeding, bone pain, and an enlarged stomach. On physical examination, an enlarged liver or spleen is found in 70% of cases of ALL. Diagnosis of leukemia is based on clinical features and investigations.⁷ Supporting examinations include blood tests, bone marrow aspiration (cell morphology), immunophenotyping, cytochemistry, and cytogenetics.⁸ On complete blood count, ALL shows various degrees of anemia and thrombocytopenia. The leukocyte count may be high, normal, or low, with neutropenia present. On the evaluation of the peripheral blood smear, lymphoblasts

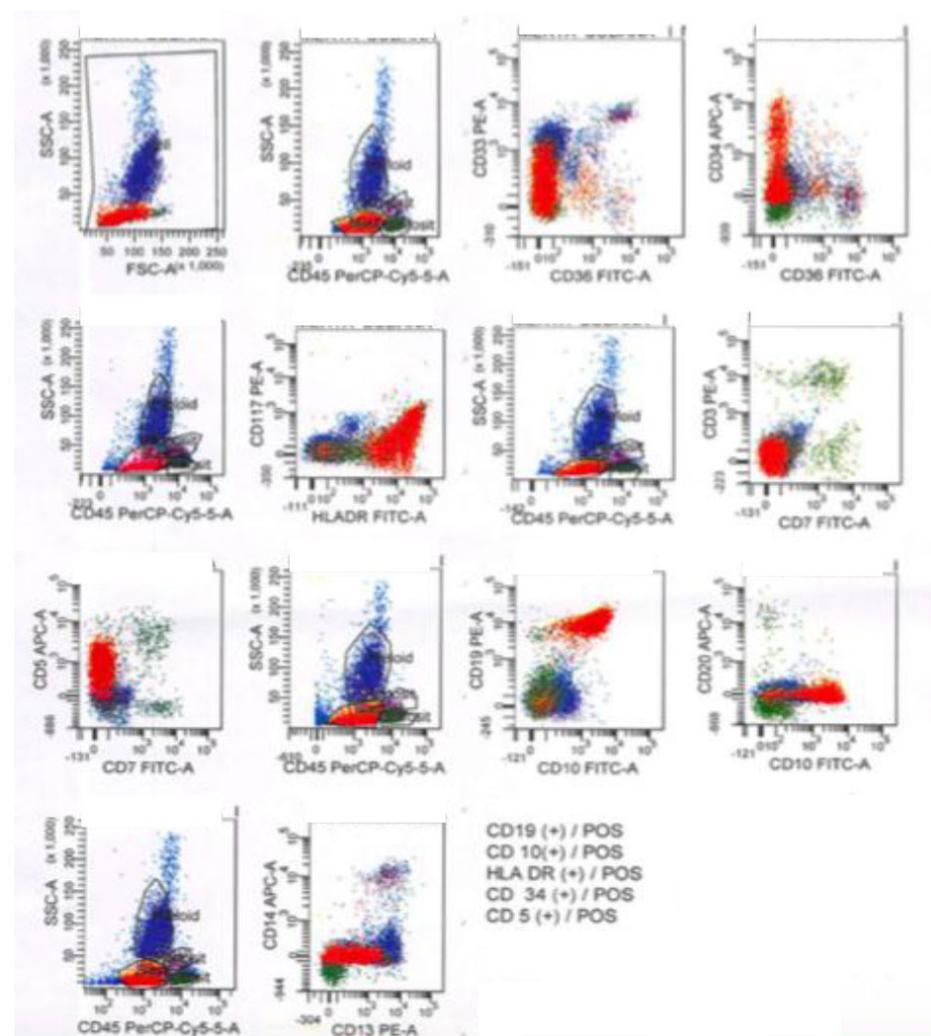
are usually found, although the number is not large.⁸

In this patient, the main complaint is gums bleeding, abdominal pain accompanied by fever and joint pain. On physical examination, there was fever with a temperature of 38.3°C, anemic in both conjunctiva and no enlarged liver or lymph nodes. Complete blood count results showed a decrease in the number of leukocytes, Hb and platelets. On the peripheral blood examination, there is an impression of normochromic anemia with leukopenia and thrombocytopenia, but blast cells are not found. The symptoms in this patient are consistent with the clinical manifestations of ALL according to a previous study.⁷

The first classification of ALL was based on the morphological criteria of the French-American-British (FAB) classification, which includes the nucleus-cytoplasm ratio, nucleoli, size of the cell, vacuoles, and the bone marrow must contain at least 30% of blast cells.⁹ FAB divides the ALL classification into three types: ALL-L1, which is most common in children with small lymphoblast cells, regular-shaped nuclei, homogeneous chromatin, indistinct nucleoli or, if present, usually only one, with a little cytoplasm.⁹ ALL-L2 found in 10 percent of children usually affects adults, lymphoblasts are small and large, the shape of the nucleus with irregular grooves and various nuclear chromatin, relatively large cytoplasm. ALL-L3 or also known as Burkitt type leukemia, cell form from medium to large with moderate cytoplasm, clear basophilic picture with dominant cytoplasmic

Table 2. Clinical chemistry result

Parameters	06/27/2019	Reference range
BUN (mg/dL)	22.40	8.00-23.00
Creatinine (mg/dL)	0.44	0.50-0.90
Kalium (mmol/L)	5.1	3.50-5.10
Natrium (mmol/L)	139	136-145
Chloride (mmol/L)	95.3	94-110
Calcium (mg/dL)	9.3	9.20-11.0
Bilirubin total (mg/dL)	1.18	0.30-1.30
Bilirubin direct (mg/dL)	0.08	0.00-0.30
Bilirubin indirect (mg/dL)	1.10	0.20-1.20
Albumin (g/dL)	4.40	3.20-4.50
SGOT (U/L)	26.3	11.00-33.00
SGPT (U/L)	20.20	11.00-50.00

**Figure 2.** Bone marrow flowcytometry immunophenotyping with ALL B lineage with aberrant expression CD 5.

vacuoles, smooth and homogeneous chromatin.^{9,10}

Nowadays, immunophenotyping for acute leukemia cases has become more important in determining the lineage of leukemia. Acute leukemia

showed characteristic patterns of surface antigen expression through Clusters of Differentiation (CD) antigen, facilitating their identification and proper classification and playing an essential role in instituting adequate treatment

plans.¹¹ World Health Organization (WHO) included immunophenotype and cytogenetic and cytomorphologic and cytochemistry in the current WHO criteria for diagnosis and classification of leukemia.¹² This examination can be used to differentiate the differentiation of myeloid or lymphoid leukemia cells, determine the classification of ALL B cells or T cells, identify undifferentiated blasts that appear morphologically or cytochemical as ALL, detect expression of aberrant antigen, and determine the presence of minimal residual disease. B cells and T lymphocytes have similarities when viewed under a microscope. On flowcytometry, the locations of these two cells are on the same axis and ordinate. Still, these two cells have different membrane proteins that allow them to be distinguished by immunophenotyping with special marks on B cells that have CD20, whereas T cells have CD3.^{5,8}

In certain circumstances, leukemia cells can express two or more different lineages, called Biphenotypic Acute Leukemia (BAL) and Acute Bilineal Leukemia (ABL).^{13,14} European Group for the Immunological Classification of Leukemias (EGIL) defines biphenotypic leukemia as a group in which blast express simultaneously myeloid and lymphoid antigens with a score \geq of 2 points present in two different lineages.¹⁵ B-lineage leukemia is defined as a heterogeneous group of hematopoietic malignancies with blasts that cannot be classified as myeloid or lymphoid or blasts from both lineages.¹⁶ But some leukemias also showed antigen expression of two cellular lineages but not all biphenotypic, bilinear, or mixed phenotype criteria. The expression of these antigens has been termed abnormal or aberrant. Another definition of aberrant immunophenotypes is the antigen expression pattern in the neoplastic cell that differs from the normal antigens in the maturation process of hematopoietic cells, such as myeloid antigens in ALL, B cell antigens in T cell ALL or vice versa.¹⁷

The bone marrow aspiration smear results in this patient showed 30% lymphoblast infiltration with vacuolization (+) in the cytoplasm. According to FAB criteria, this appearance supports ALL-L3 that usually occurs in 2-3% of all children

with a characteristic of vacuolization in their cytoplasm. However, the patient's immunophenotyping results showed ALL B-lineage that expressing CD19+, CD10+, HLA-DR+, CD 34+, and the expression of aberrant CD5+.

B- Acute Lymphoblastic Leukemia (B-ALL) is a neoplasm of hematopoietic precursor B cells characterized by the expression of various B-cell lineage-associated antigens. CD 5 is a T-cell membrane glycoprotein expressed on T-cells and a subset of T-independent and memory B-cells survival and IL-10 production. CD 5 expression in B-cell neoplasm is relatively confined to Chronic Lymphocytic Leukemia (CLL) or small lymphocytic lymphoma, Chronic Myeloid Leukemia (CML), and rare other B cell lymphomas. However, it's nearly always negative in B-ALL. The immunophenotypic expression of T-cells in B lymphoblastic leukemia can sometimes be asynchronous and aberrant. The expression of T-cell antigens in B lymphoblastic leukemia may sometimes complicate the lineage assignment in leukemia and raises concern for ambiguous lineage acute leukemia. Based on a previous study, T-cell lineage assignment requires CD3 expression, and in the absence of CD3, the other T-cell antigens (e.g., CD2, CD5, and CD7) are generally considered aberrancies.¹⁸ Previous studies reported that aside from CD3, CD5 and CD7 were the most sensitive antigens in cases of T-ALL.^{19,20} Aberrant expression of CD5 in B-ALL is uncommon, seen in 2 % in a series of 200 cases of B-ALL cases and 4.5% cases in a series of 134 cases. A previous study also reported a case of a 15-years-old boy with a CD5 expression, but this patient died 17 months after diagnosis.²¹ In a study conducted by Hussein S et al on 134 cases of B -ALL, 6 cases expressed CD5 with 5 male patients, aged less than 18 years and one female patient; only one of these 6 patients achieved remission.²² This shows that the expression of CD 5 in the B-ALL case is associated with a poor prognosis.¹⁹⁻²²

CONCLUSION

The case of a 16-years-old male patient with ALL-L2 based on the FAB classification has been reported, with a

phenotypic B lineage picture accompanied by an aberrant expression of the T lineage, namely CD5+. Aberrant expression CD5 in cases of ALL B lineage is very rare, which can be associated with a poor prognosis.

CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

ETHICS CONSIDERATION

This case report has obtained informed consent from the patient as well as the following COPE for publication ethics guidelines.

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None.

AUTHOR CONTRIBUTIONS

All authors equally contribute to the study from selecting a case, evaluating the laboratory results until interpreting the case study through publication.

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