



Abnormal expression of CD79a, CD56 and CD7 in acute myeloid leukemia

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Abstract

Background: Flow cytometric analysis of leukemias improves accuracy for distinguishing acute leukemias of myeloid and lymphoid origin. In rare cases, both myeloid and lymphoid antigens are expressed, creating ambiguity for lineage assignment and difficulties in diagnosis of leukemia. Aberrant antigen expression in acute myeloid leukemia (AML) is recognized to be a poor prognostic indicator. CD79a is a highly lineage-specific marker of B lymphoid cells and plays an important role in the diagnosis of acute leukemia.

Methods: We report an unusual case of acute myeloid leukemia in which CD79a is clearly expressed along with other lymphoid antigens (CD7 and CD56) in addition to antigens denoting myeloid lineage. The characteristics of morphology, immunophenotype, molecular and cytogenetic of bone marrow samples were analyzed.

Results: This is an unusual case of AML shows that, CD79 expression in acute leukemia is not restricted to B-ALL and is rarely aberrantly expressed in AML.

Conclusions: The high score given to CD79a by EGIL is questionable based on cytogenetic classification. The prognostic relevance of expression of CD79a in AML is unclear and need further studies. The prognostic significance of selected markers of leukemic cells is well known, CD7 and CD56 expression at diagnosis has been associated with low remission rates and biological aggressiveness in a significant proportion of acute leukemias.

Keywords: Acute myeloid leukemia, CD79a aberrant expression, CD56 and CD7

Introduction

Immunophenotyping improves accuracy of acute leukemia classification and is considered particularly useful for identifying aberrant lineage association of acute leukemia, biphenotypic and bilineal acute leukemia, as well as monitoring minimal residual disease [1].

The European Group for the Immunological Characterization of Acute Leukemia (EGIL) developed a scoring system that ranges from 0.5 to 2.0 for the relative significance of cluster of differentiation (CD) antigens in determining the immunophenotype of leukemias **Table 1** [2], use of this scoring system has been used mainly for the identification of leukemias of ambiguous lineage [3]. Two reported large series showed that, approximately 46% of acute lymphoblastic leukemia (ALL) cases and 48% of AML cases have aberrant expression of a single antigen associated with another cell lineage [4,5], most commonly CD20 [3] and CD7 [6] in AML and CD33 in ALL [7].

Aberrant antigen expression in AML is recognized to be a poor prognostic indicator. CD56 and CD7 expression at diagnosis has been associated with low remission rates and biological aggressiveness in a significant proportion of acute leukemias [3].

CD79a is a subunit of an intracytoplasmic protein reported to be specific for B lymphocytes. Few studies demonstrates that CD79a expression in acute leukemia is not restricted to

B-ALL and rarely aberrantly expressed in AML and T-ALL, [8-10]. In the EGIL system, CD79a is believed to be highly specific for B-lymphoid lineage. In fact, some authors have suggested that CD79a positivity is essentially diagnostic of ALL [11].

We report an unusual case of AML in which the blasts express CD79a, an antigen reported to be highly specific for B-lymphoid lineage with other antigens associated with lymphoid lineage (CD56 and CD7), along with antigens of myeloid lineage (CD117, CD33, and CD64).

Materials and methods

Case report

A 42-year-old man, known to be Diabetic, hypertensive, ischemic heart disease and chronic hepatitis (HBV), presented to our Hospital by mild fever, chronic cough, weight loss and loss of appetite 2 months ago, complete blood cell count (CBC) showed leucocytosis, and mild thrombocytopenia with circulating blasts in PB smear. On admission CBC information included the following: white blood cell count (WBC), $21.7 \times 10^9/L$; neutrophils $5.6 \times 10^9/L$; lymphocytes $5.9 \times 10^9/L$; monocytes $2.0 \times 10^9/L$; eosinophils $3.0 \times 10^9/L$; basophils $0.2 \times 10^9/L$; band $0.4 \times 10^9/L$; and 21% blasts ($4.6 \times 10^9/L$), hemoglobin, 13.3 g/dL; and platelet count, $117 \times 10^9/L$. Accordingly, bone marrow aspirate and core biopsy were performed, and the sample

Table 1. Scoring System for the Definition of Acute Leukemias of Ambiguous Lineage [Adapted from Bene et al., [2]].

Score	B-Lymphoid	T-lymphoid	Myeloid
2	cCD79a	cCD3 or sCD3	MPO
	cIgM	Anti-TCR	--
	cCD22	--	--
1	CD19	CD2	CD117
	CD20	CD5	CD13
	CD10	CD8	CD33
	--	CD10	CD65
0.5	TdT	TdT	CD14
	CD24	CD7	CD15
	--	CD1a	CD64

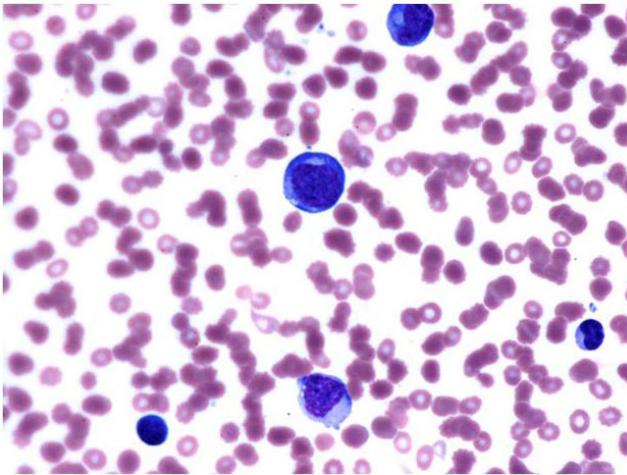


Figure 1. Peripheral blood (Wright-Giemsa stain) showing circulating blast cells which are medium to large size with dispersed chromatin with one or more nucleoli, the cytoplasm is relatively abundant with variable degree of basophilia.

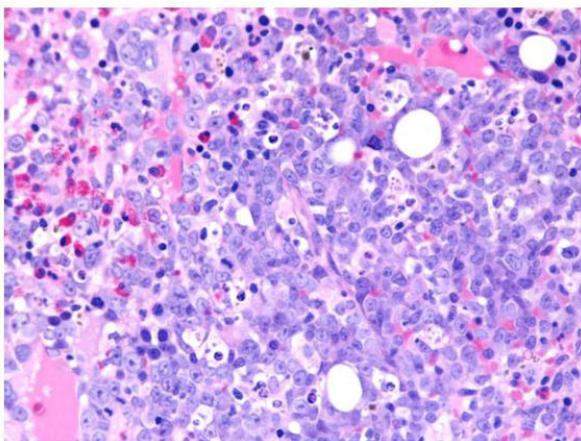


Figure 2. Low power of H&E bone marrow trephine biopsy showing hypercellular marrow with infiltration by immature, mononuclear cells with one or more nucleoli.

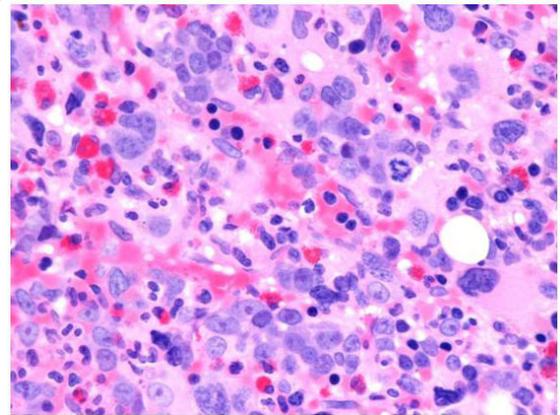


Figure 3. High power of H&E bone marrow trephine biopsy showing hypercellular marrow with infiltration by immature, mononuclear cells with one or more nucleoli.

was submitted for morphologic, cytogenetic, molecular, and flow cytometric immunophenotypic analysis. A diagnosis of acute myeloid leukemia (AML, NOS) according to WHO 2008 classification and AML M5a according FAB classification, with aberrant expression of CD79a, CD56 and CD7 was established. Unfortunately, the patient died from sepsis during standard induction chemotherapy for AML.

Morphologic analysis

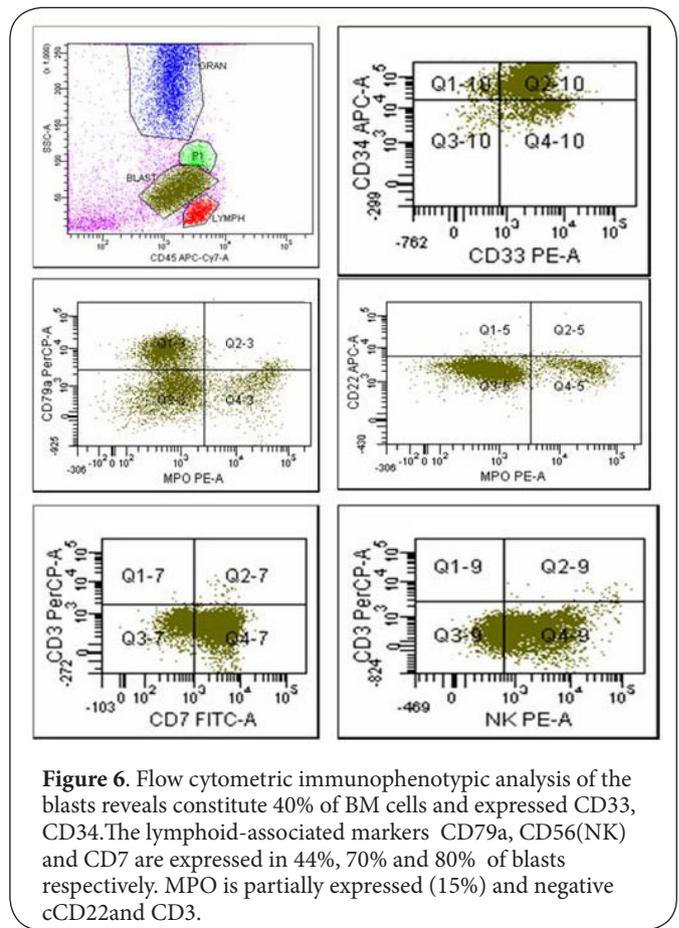
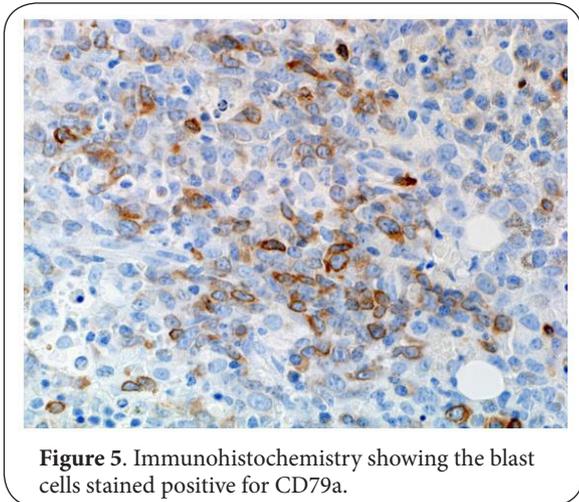
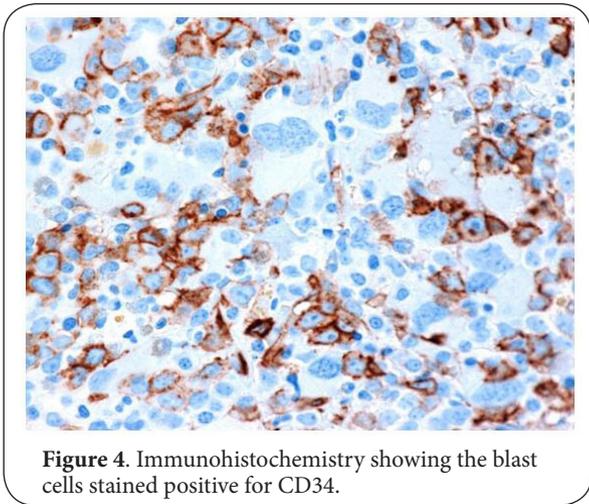
A blast population was identified representing 21% of the white blood cells in the peripheral blood and 40% of the bone marrow nucleated hematopoietic cells. In the peripheral blood film and bone marrow aspirate, the blast cells were medium to large size with dispersed chromatin with one or more nucleoli, the cytoplasm is relatively abundant in the majority of blast cells with variable degree of basophilia (Figure 1). In bone marrow core biopsy, the marrow was hypercellular for age (90-100%) and infiltrated by abnormal immature cells which stain positive for CD34, CD117 and negative for TdT and CD3 (Figures 2,3,4 and 5).

Flow cytometric analysis

Flow cytometric analysis of the patient’s bone marrow demonstrates a discrete blast population gated using side scatter versus CD45. The blast cells showed positivity for CD45, HLA-DR, CD38, CD34, CD33, CD64 (75%), CD117 (22%), MPO is expressed only in 15% of gated cells. CD79a, CD56, and CD7 were expressed in 44%, 70%, and 80% of the blast cells respectively. Terminal deoxynucleotidyl transferase (TdT), CD19, CD20, CD22, CD10, CD13, CD15 and T-cell markers were negative (Figure 6).

Cytogenetic analysis

We performed interphase cytogenetics, fluorescence in situ



hybridization (FISH) to ascertain the presence or absence of ALL and AML specific abnormalities. Cytogenetic/FISH studies were negative for specific abnormalities for both AML and ALL panel including ABL- BCR, ETV6-RUNX1, TCF3-PBX1, MLL and MYC genes for ALL and PML-RARA, AML1-ETO, CBFβ, CEP8/D8Z2 and MLL genes for AML, the result was reported according to ISCN 2009 as follow nuc ish (ABL1,BCR)x2[100]/(ETV6,RUNX1) x2[100]/(5'MLL,3'MLL,5'MLL con 3'MLL x2[100]/(5'MYC, 3'MYC, 5'MYC con 3'MYC)x2[100]/(TCF3,PBX1)x2[100]/ nuc ish (PML) x3(RARA)x2[100]/(AML1,ETO)x2[200]/ (5'CBFβ,3'CBFβ,5'CBFβ con 3'CBFβ) x2[100]/(D8Z2)x2[100]. Trisomy 15 was detected in 47% of the studied cells as solo abnormality.

A PCR-based assay was performed showed no clonal immunoglobulin gene rearrangement.

Discussion

Flow cytometric immunophenotyping has become

an important diagnostic tool for the classification of acute leukemias. The aberrant expression of selected markers in acute myeloid leukemic cells has been associated with relapse and biological aggressiveness [12]. There have been many reports of unusual immunophenotypic expression in AML with the prediction of impending relapses prior to clinical manifestations [13-16].

CD79a is a highly lineage-specific marker of B lymphoid cells and plays an important role in the diagnosis of acute leukemia [17]. Its expression in AML, however, is less extensively described than for CD7 and CD56. The prognostic meaning of CD79a expressions in AML is still a controversial matter; Frater et al., [7] reported four of the 46 patients were CD79a positive, the prognostic significance in these cases is unclear. Another study done by Chung et al., [17], found Five patients among 68 AML with t(8;21)(q22;q22) revealed CD79a positive reaction, the survival probability of the CD79a expression group was significantly lower than classical AML with t(8;21)(q22;q22). However, these results in both studies should be treated with reservation due to relatively small sample sizes and further studies are needed for assessment the prognostic relevance of CD79a expression in AML.

A similar study done by Kozlov et al., [18] showed 2 cases

among 89 cases of AML showed strong coexpression of CD79a, both cases were demonstrated the t(8;21) with cytogenetics and the AML1/ETO rearrangement with FISH, although the immunophenotyping met proposed scoring criteria for a diagnosis of Biphenotypic acute leukaemia (BAL), the cytogenetic and FISH findings indicate that CD79a represented the aberrant presence of a B-cell antigen in leukemias of distinct myeloid lineage. Accordingly, we think that, the high score given to CD79a by EGIL is questionable based on cytogenetic classification.

Apparently, these markers were expressed early in hematopoietic ontogeny in the lesser-differentiated acute myeloid leukemia subtypes, including FAB M0, M1, and M2 [3]. Saxena et al., [6] found that CD7 expression in AML is associated with the immature antigens CD34, HLA-DR, and TdT, these findings are in accordance with our results except for TdT which was negative, they also contend that AML with CD7 may originate from early hematopoietic precursors and indicate biologic aggressiveness in a significant proportion of patients. Tiftik et al., [19] found CD7 positivity in 7 of 12 AML patients and CD56 expression in 3 AML patients and revealed that CD7 and CD56 expression at diagnosis was associated with a low remission rate and biological aggressiveness in AML patients. Suzuki et al., [20] revealed poor prognosis in AML in which CD7 and CD56 were aberrantly expressed. Regardless of CD7 positivity, sole expression of CD56 in AML has been shown to be a predictor of lower complete remission rates and shorter survival [21,22].

Conclusion

This study demonstrates that CD79 expression in acute leukemia is not restricted to B-ALL and may be aberrantly expressed in AML and T-ALL. The high score given to CD79a by EGIL is questionable based on cytogenetic classification. The prognostic significance of selected markers of leukemic cells is well known, CD7 and CD56 expression at diagnosis has been associated with low remission rates and biological aggressiveness in a significant proportion of acute leukemias, however, the prognostic relevance of expression of CD79a in AML is unclear and need further studies. The aberrant expression of CD7, CD56, and CD79a, representing the capacity of these leukemias for trilineal expression of leukocyte differentiation antigens.

List of abbreviations

AML: Acute Myeloid Leukemia
EGIL: The European Group for the Immunological Characterization of Acute Leukemia
CD: Cluster of Differentiation
ALL: Acute Lymphoblastic Leukemia
MPO: Myeloperoxidase
TdT : Terminal Deoxynucleotidyl Transferase
FISH: Fluorescence in Situ Hybridization
FAB: French-American-British

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	GE	KF	AA
Research concept and design	√	√	√
Collection and/or assembly of data	√	√	√
Data analysis and interpretation	√	--	--
Writing the article	√	--	--
Critical revision of the article	√	--	√
Final approval of article	√	√	√
Statistical analysis	√	--	--

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