Flow Cytometric Distinction of Pure Erythroid Leukemia from Conventional Acute Myeloid Leukemia: A Single-Institution Experience

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Introduction

Pure erythroid leukemia (PEL) is a rare and aggressive subtype of acute myeloid leukemia (AML) characterized by a predominance of immature erythroid precursors.

PEL accounts for roughly 1% of AML. The 2022 WHO classification (5th edition) defines it as acute erythroid leukemia, with at least 80% erythroid precursors, including at least 30% proerythroblasts. The International Consensus Classification places most cases under AML with mutated TP53.

PEL carries a very poor prognosis. In a recent large series, TP53 alterations and a complex karyotype were present in all cases, and median survival was only about 2 months.

Diagnosis is difficult in practice. Aspirates are often suboptimal, and proerythroblasts can form cohesive clusters that mimic metastatic tumor. They lack the usual myeloblast markers, making flow cytometry and immunohistochemistry (CD71, E-cadherin) important.

Morphologic distinction between neoplastic erythroid precursors (pronormoblasts) and myeloid blasts can be challenging, particularly in cases with poorly differentiated cells, overlapping cytologic features, or limited bone marrow material.

These challenges can make it difficult to distinguish PEL from conventional AML or other acute leukemias. Multiparameter flow cytometry is a valuable adjunct that identifies lineage-specific and aberrant antigen expression patterns, facilitating accurate classification in diagnostically challenging cases.

Objective: To describe our institutional experience comparing the flow cytometric immunophenotypic features of PEL with conventional AML and to define the characteristics that help distinguish them.

Design/Sample

We retrospectively reviewed patients with PEL at our institution (n = 5) and compared their multiparameter flow cytometric findings with those of a cohort of non-PEL AML cases evaluated during the same period (n = 15).

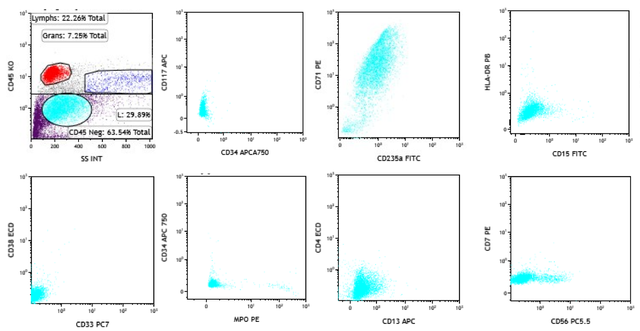
Analysis

Expression patterns of **erythroid-associated markers** (CD71, CD117, CD235a, CD38, CD4, CD45) and **myeloid-associated antigens** (CD34, CD13, CD33, CD117, HLA-DR, CD7, CD56, MPO) were analyzed.

Results

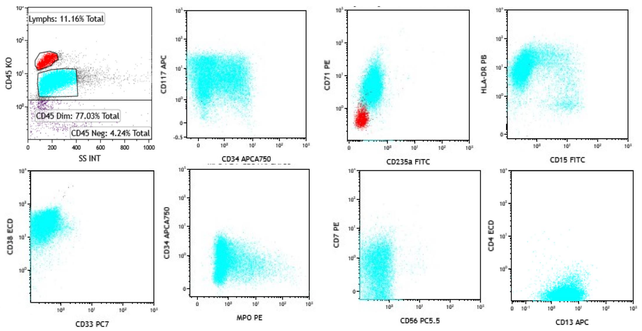
- Neoplastic erythroid cells in all PEL cases showed uniform CD71 expression with dim-to-negative CD45 expression relative to granulocytes. CD117 expression ranged from partial to uniform, while CD235a expression was largely restricted to the more differentiated CD117-dim/negative erythroid subset
- Compared with conventional AML blasts, PEL erythroid precursors consistently lacked CD34, HLA-DR and myeloperoxidase (MPO) expression despite their immature morphology. Markedly decreased or absent CD38 expression was characteristic of PEL and uncommon in AML blasts. Aberrant CD4, CD7, and CD13 expression on erythroid precursors represented lineage-inappropriate antigen expression
- In contrast, conventional AML blasts typically express CD34, CD13, CD33, CD117, HLA-DR (subtype-dependent), and/or MPO without erythroid-associated coexpression of CD235a and CD71
- Notably, despite the absence of CD34 on neoplastic erythroid cells, we identified a distinct population of CD34-positive myeloid blasts in most PEL cases. These blasts were not numerically increased but exhibited aberrant immunophenotypic features, including asynchronous antigen expression and abnormal maturation patterns
- Aberrant CD4 and CD7 expression is usually seen in PEL. The representative case shown in Figures 1 and 2 was diagnosed as PEL but lacked CD4 and CD7 expression; the diagnosis rested on CD71 and E-cadherin expression

Figure 2. Flow cytometry, PEL



The bone marrow flow cytometry study shows an approximately 30% CD45-negative population with the immunophenotype listed in Table 1, most likely representing the erythroid population. Slides from the bone marrow aspirate and biopsy show increased immature cells. Myeloblasts (CD34+/CD117+) are not increased (<1%).

Figure 3. Flow cytometry, AML



The bone marrow flow cytometry study shows a large population of abnormal myeloblasts (~38%) with the immunophenotype listed in Table 1, consistent with AML.

Figure 1. Morphology, PEL

The bone marrow is hypercellular (>95%) with marked erythroid predominance (over 80% of aspirate cellularity) and numerous proerythroblasts (35% by manual differential) that are E-cadherin positive, a subset weakly positive for CD117, and negative for CD34 and MPO.

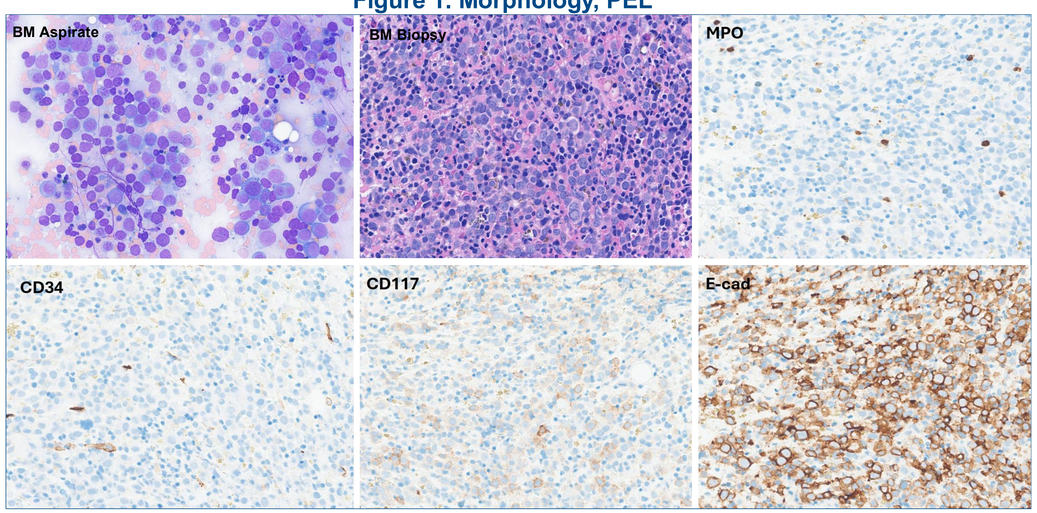


Table 1. Flow cytometry markers

	PEL case	AML case
Positive (+)	CD71, dim CD235a, subset dim CD13, minor subset dim CD14	CD117, subset CD34, CD19, CD38, HLA-DR, CD13, subset CD11c, small subset MPO, subset TdT, subset CD15
Negative (−)	CD45, cCD3, CD19, CD22, CD79a, CD5, CD10, CD56, CD7, CD4, CD15, CD16, CD64, TdT, CD20, CD34, CD117, CD33, CD38, CD11c, CD123, kappa, lambda, CD138	CD33, CD56, CD3, CD5, CD10, CD22, CD79a, CD20

Conclusions/Further Study

Our institutional experience demonstrates that PEL exhibits a distinctive flow cytometric immunophenotype characterized by aberrant antigen expression on neoplastic erythroid precursors and a phenotypically abnormal but quantitatively non-expanded CD34-positive myeloid blast population.

PEL can be distinguished from conventional AML by flow cytometry. Key features include uniform CD71, dim-to-negative CD45, and absence of CD34, HLA-DR, and MPO, with decreased or absent CD38.

Aberrant CD4 and CD7 expression supports the diagnosis when present. In our representative case, these markers were absent, and CD71 and E-cadherin established the diagnosis.

The CD34-positive myeloid blasts in PEL were not increased but were phenotypically abnormal. Recognizing both populations may help avoid misclassification as conventional AML.

Further study: Larger multi-institutional cohorts are needed to validate this marker pattern and define sensitivity and specificity.

Future work should test whether flow cytometry can reliably distinguish PEL from AML when aspirates are limited. It should also correlate flow findings with TP53 status and clinical outcome and compare flow-based distinction with immunohistochemistry.