

Aberrant B-Cell Marker Expression in RUNX1::RUNX1T1-Positive Acute Myeloid Leukemia

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Dear Editor,

Acute myeloid leukemia (AML) is a biologically heterogeneous clonal hematopoietic malignancy in which cytogenetic and molecular abnormalities play a pivotal role in disease classification, prognostication, and therapeutic decision-making. AML with t(8;21)(q22;q22.1), resulting in the RUNX1::RUNX1T1 fusion, represents a biologically distinct subtype characterized by disruption of normal myeloid differentiation due to altered RUNX1-mediated transcriptional regulation^[1,2]. According to the European Leukemia Network (ELN) 2017 recommendations, this entity is classified as a favorable-risk subgroup^[3].

AML with t(8;21) is associated with distinctive morphologic and immunophenotypic features, including aberrant expression of B-cell-associated antigens such as CD19 and CD79a^[4,5]. These aberrancies are believed to reflect transcriptional deregulation induced by the RUNX1::RUNX1T1 fusion protein. With the widespread availability of multiparameter flow cytometry in routine diagnostic laboratories, recognition of such immunophenotypic patterns may provide an early clue to underlying cytogenetic abnormalities during initial diagnostic evaluation^[6].

In this retrospective analysis, we evaluated the predictive value of aberrant B-cell marker expression for identifying RUNX1::RUNX1T1 fusion in newly diagnosed AML cases. A total of 98 consecutive AML cases diagnosed between January 2022 and December 2024 were analyzed using morphology and flow cytometry immunophenotyping. Aberrant B-cell marker expression was defined as CD19 and CD79a expression of $\geq 1+$ intensity. Cases demonstrating such aberrancies underwent cytogenetic evaluation by conventional karyotyping and fluorescence in situ hybridization for t(8;21), with selected cases further assessed by next-generation sequencing for associated molecular abnormalities.

Aberrant co-expression of CD19 and CD79a was identified in 11 of 98 cases (11.2%). Among these 11 cases, RUNX1::RUNX1T1 fusion was confirmed in 5 cases, yielding a positive predictive value of 54.5% (Table 1). Within the RUNX1::RUNX1T1-positive subgroup, CD19 expression was detected in all 5 cases (100%), while CD79a expression was present in 3 cases (60%). Notably, two additional AML cases lacking aberrant B-cell marker expression were found to harbor t(8;21), underscoring the limited sensitivity of immunophenotypic prediction alone. Molecular analysis revealed an associated *c-KIT* mutation in one case and *ASXL2* mutations in two cases within the RUNX1::RUNX1T1-positive subgroup^[7].

These findings are concordant with previous reports demonstrating that aberrant B-cell antigen expression, particularly CD19 and CD79a, is commonly observed in AML with RUNX1::RUNX1T1 but is neither universal nor sufficiently specific to serve as a surrogate diagnostic marker. Duployez et al. reported that RUNX1::RUNX1T1-positive AML frequently harbors additional cooperating mutations that contribute to biological heterogeneity and may influence clinical outcomes^[7]. Similarly, Eisfeld et al. highlighted the molecular and clinical diversity of this AML subtype and emphasized the importance of integrated molecular characterization^[8]. Furthermore, Kayser et al. demonstrated that cooperating mutations in core-binding factor AML significantly affect disease behavior and prognosis^[9].

In conclusion, flow cytometry serves as a valuable frontline screening tool in AML diagnostics. Awareness of aberrant B-cell marker expression can facilitate early suspicion of RUNX1::RUNX1T1-positive AML and prompt timely genetic evaluation, particularly in resource-limited settings. However, integration of

immunophenotypic, cytogenetic, and molecular data remains essential for accurate diagnosis and optimal patient management.

Keywords: Acute myeloid leukemia, t(8, 21), RUNX1: : RUNX1T1 fusion, Flow cytometry, Immunophenotypic aberrancy

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Table 1. Predictive Value of Aberrant B-Cell Marker Expression for RUNX1::RUNX1T1 Fusion

Parameter	Number of Cases
Total AML cases analyzed	98
Cases with aberrant CD19 and CD79a expression	11
RUNX1::RUNX1T1-positive among aberrant cases	5
RUNX1::RUNX1T1-negative among aberrant cases	6
Positive predictive value	54.5%