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GENETIC AND IMMUNOPHENOTYPIC PROFILING REVEALS DISTINCT MEASURABLE RESIDUAL DISEASE BIOMARKERS IN OF B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Background B-cell acute lymphoblastic leukemia (B-ALL) presents marked genetic and immunophenotypic heterogeneity. Specific genetic subtypes, such as Philadelphia chromosome-positive (Ph^+) ALL, may present distinctive leukemia-associated immunophenotypes (LAIPs) that can be used for measurable residual disease (MRD) monitoring by flow cytometry. **Objectives:** To compare flow cytometric immunophenotypic patterns across B-ALL genetic subtypes, focusing on LAIPs associated with Ph^+ ALL and their prognostic relevance. **Material and methods:** We retrospectively studied 106 B-ALL cases diagnosed between 2017 and 2024, integrating cytogenetic/molecular profiles with flow cytometric data from EuroFlow™ diagnostic and MRD panels. T-ALL and MPAL cases were excluded. Immunophenotypic patterns were evaluated using 8-color panel (two tubes, seven backbone markers: CD81, CD34, CD19, CD10, CD20, CD38, CD45; and four LAIP markers: CD66c, CD123, CD73, CD304). Leukemia-associated immunophenotype (LAIP) and different-from-normal (DfN) approaches were applied. Survival analyses were performed according to genetic subtypes, LAIPs, and MRD kinetics. **Results:** The cohort included 27 Ph+ patients, twelve hyperdiploidy, five ETV6::RUNX1, two E2A::PBX1, ten KMT2A-rearranged, seven other abnormalities, 24 normal karyotypes, and 17 without genetic results. Immunophenotypic profile: Ph^+ ALL displayed a distinct profile, with $CD34^{++}$/$CD38^-$/dim blasts in 77.7% vs. 20.2% of other B-ALL ($p < 0.0001$), and frequent $CD66c^+$ (70%), $CD304^+$ (80%), and $CD66c^+$/$CD304^+$ (52.9%) expression. CD66-negative Ph^+ cases expressed $CD73^+$ and/or $CD304^+$. Ph^+ ALL also exhibited higher co-expression of $CD66c^+$/$CD73^+$ (94.0% vs. 56.9%), $CD66c^+$/$CD304^+$ (58.8% vs. 6.9%), and $CD73^+$/$CD304^+$ (75.5% vs. 15.5%) ($p < 0.001$ for all). In non-Ph^+ B-ALL, specific genetic subtypes correlated with marker expression: TEL::AML1 correlated with $CD73^+$/$CD73^+CD304^+$ ($p = 0.002$), E2A::PBX1 with $CD73^+$ ($p < 0.001$), hyperdiploidy with triple positivity ($p = 0.05$), and KMT2A rearrangements with CD10 loss and absence of CD66c, CD73, CD304. Normal karyotype correlated with $CD66c^+$ ($p = 0.006$). Survival: Children had higher OS than adults (89.0% vs. 49.3%, $p < 0.001$). Low-risk genetics correlated with better OS (80.3% vs. 57.2%, $p = 0.02$), while Ph^+ and KMT2A-rearranged cases had the worst outcomes ($p < 0.01$). $CD66c^+$ showed a trend toward lower OS (63.7% vs. 80.3%, $p = 0.11$). MRD Kinetics: Day 15 MRD >0.01% was not prognostic ($p = 0.58$), but day 33 MRD >0.0001% predicted inferior OS (55.0% vs. 87.0%, $p = 0.001$). Combined MRD kinetics showed OS of 81.0% ($D15^-$/$D33^-$), 79.8% ($D15^+$/$D33^-$), and 50% ($D15^+$/$D33^+$) ($p < 0.05$). **Conclusion:** Ph^+ ALL is characterized by a unique LAIP — $CD34^{++}$/$CD38^-$/dim with frequent CD66c, CD73, and CD304 co-expression — ensuring MRD detectability in all cases. Distinctive LAIPs were also identified in non-Ph^+ subtypes, supporting their inclusion in MRD monitoring strategies. Here we confirm that LAIP signatures are promising biomarkers for highly sensitive MRD monitoring and may inform risk-adapted treatment approaches in B-ALL. Furthermore, day 33 MRD levels and MRD kinetics, but not day 15 MRD alone, were strong survival predictors. Integratiting immunophenotypic, genetic and MRD kinetic data refines prognostic stratification, with age, genetic risk category and MRD dynamics being key determinants of overall survival in B-ALL in our setting.

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IMPORTÂNCIA DA CITOMORFOLOGIA ASSOCIADA À IMUNOFENOTIPAGEM NO LABORATÓRIO DE CITOMETRIA DE FLUXO: RELATO DE CASO DE LEUCEMIA PROMIELOCITICA AGUDA VARIANTE MICROGRANULAR

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Introdução: A leucemia promielocítica aguda (LPA) é um subtipo de leucemia mieloide aguda definida por alterações citomorfológicas e translocações cromossômicas específicas e tem como principal característica o aumento de células imaturas com fenótipo de promielócitos anômalos na medula óssea, com ou sem envolvimento do sangue periférico. Sua gravidade está relacionada à suscetibilidade dos indivíduos a apresentarem sangramentos, resultando em uma coagulopatia grave e potencialmente fatal. O diagnóstico da LPA é realizado através da correlação do quadro clínico do indivíduo, que irá apresentar manifestações hemorrágicas, junto aos exames laboratoriais, como a imunofenotipagem, citogenética e biologia molecular. Embora os achados do hemograma sejam importantes, nem sempre são suficientes para orientar uma suspeita diagnóstica, o que torna fundamental a análise citomorfológica da amostra. Este relato de caso tem como objetivo ressaltar a importância do exame de citomorfologia como ferramenta para o direcionamento da pesquisa imunofenotípica. **Descrição do caso:** Paciente feminina, idosa, deu entrada no hospital hematológico apresentando os seguintes sintomas e sinais clínicos: otorragia, equimoses, episódios de epistaxe, hiporexia e hematúria. O material de sangue periférico foi encaminhado ao laboratório de citometria de fluxo com a indicação clínica informando anemia, monocitose e trombocitopenia. A análise citomorfológica foi realizada antes da imunofenotipagem e revelou a presença de células mononucleares atípicas, apresentando alta relação núcleo/citoplasma, núcleo clivado em formato de “asa de borboleta” ou