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Content

DETECTION OF PRELEUKEMIC CLONES IN NEONATAL BLOOD SPOTS OF CHILDREN WITH B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Childhood B-cell precursor acute lymphoblastic leukemic (BCP-ALL) can be traced back to birth using leukemic clone-specific immunoglobulin heavy chain (*IGH*) rearrangements, implying prenatal origin of this disease. The aim of this study was to analyze neonatal blood spots (Guthrie cards) of childhood BCP-ALL patients for the presence of clonotypic *IGH* rearrangements.

Methods: The study enrolled 24 patients aged 1 to 9.6 years. Based on the sequences of *IGH* rearrangements identified in diagnostic lymphoblasts, 2 patient-specific primers were designed for each patient and used in semi-nested PCR for the detection of preleukemic clones at birth.

Results: Clonotypic *IGH* rearrangements were detected in neonatal blood spots of 54.2% of patients. In two cases that had double *IGH* rearrangements at diagnosis, only one rearrangement was present at birth, while in the third case both leukemic rearrangements were detected in neonatal blood. Guthrie card-positive findings were significantly more frequent in children ≤5 years of age than in older children (p=0.011). Regarding patients' characteristics at birth and at diagnosis, Guthrie card-positivity was not associated with sex, birth weight and mother's age, as well as with white blood cell count, percentage of bone marrow blasts, immunophenotype and the presence of *ETV6/RUNX1* and *TCF3/PBX1* fusion genes at diagnosis.

Conclusion: Our study confirms that a large proportion of childhood BCP-ALL originates *in utero*, regardless of the molecular subtype defined by chromosomal aberrations. The latency period to the overt leukemia depends on the presence of preleukemic clone at birth, as well as on the postnatal transforming genetic events.

Key words: childhood acute lymphoblastic leukemia; prenatal origin; Guthrie cards; immunoglobulin heavy chain rearrangements

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