DESCRIPTIVE STUDY OF KARYOTYPIC PROFILE ACUTE LEUKEMIA IN INFANTS

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Background

Acute leukemias (ALs) are the most frequent neoplasms in childhood, being rare in infants. Rearrangements involving the KMT2A gene represent the most frequent group of abnormalities (about 70% of cases in infant leukemia up to 12 months of life) and present different prognoses, which vary according to the partner gene involved in the translocation. In children over 18 months, the frequency of rearrangements involving KMT2A decreases, and the frequency of other recurrent rearrangements increases, such as the t(1;19)/E2A-PBX1, t(12;21)/*ETV6-RUNX1* and hyperdiploidy >51 chromosomes. Although the presence of KMT2A gene rearrangements is a classic prognostic factor in the infant's ALs, the role of their different partner genes in the prognosis and possible mechanisms of leukemogenesis are still unclear. In this study, we aim to characterize the chromosomal alterations in infant acute leukemias through conventional and molecular high-resolution cytogenetic techniques.

Methods and Results

During the period from June 2017 to July 2018, we assessed 16 samples of bone marrow aspirate / peripheral blood of patients with ages varying from 0 to 24 months, in the laboratory of cytogenetics of INCA, RJ. From these, 3 cases were disregarded, 1 for an insufficient sample and 2 (of the patients) for presenting a congenital syndrome. Among the patients in our sample, 12 were diagnosed with ALL and 1 with AML. From these, 7/13 (~ 53%) could not have the analysis completed because they did not present mitosis. Regarding the cases that presented mitosis, 50% (6) presented rearrangements involving the *KMT2A* gene, and one of these cases presenting an abnormality not yet described in the literature; 15% (2) were negative for *KMT2A* gene rearrangements. One case presented E2A gene rearrangement.

Table 1

Paciente/Sexo	Idade	Diagnóstico	Citogenética	FISH
P1/M	13 m	LLA pro-B	46,XY,dup(11)(q23-qter),t(11;14;9)(q23;q32;p22)	MLL+; CCND1(del); CDKN2A(del)
P2/F	12 m	LLA	46, XX, del(11q)?	BCR/ABL-; MLL-
P3/M	8 m	LLA	46, XX, t(4;11)	MLL+
P4/F	9 m	LMA	46, XX, t(9;11)	MLL+; CBFb/MYH11-
P5/F	15 m	LA	sem condições de análise	MLL-; ETV6/RUNX1-
P6/F	17m	LLA comum	48, XX + 2mar	KMT2A-; ETV6/RUNX1-
P7/M	16 m	LLA	16, XY , t(1;19)(q23;p13)	E2A+
P8/M	13 m	LLAB	sem condições de análise	MLL-
P9/M	6 m	LA	sem condições de análise	sem condições de análise
P19/F	12 m	LLA	Sem mitose	MLL-
P20/M	24 m	LLA	Sem mitose	MLL-
P21/F	24 m	LLA BAL	Análise em andamento	MLL-
P22/F	24 m	LLA	Sem mitose	MLL-

Table 1. del - deletion, ter - terminal chromosome region, dup - duplication, mar - marker chromosome, p - short arm of the chromosome, q - long arm of the chromosome, t - translocation, (-) - negative sign: loss of genetic material, (+) - positive sign: gain of genetic material, ( ) - parentheses: delimits altered chromosomes and breakpoints, (,) - comma: separates number of chromosomes, sex chromosomes and chromosomal abnormalities, (;) semicolon: separates chromosomes and chromosomal regions when structural rearrangements involve more than one chromosome, (/) - slash: separates the clones from a karyotype, (?) - interrogation: questionable identification of chromosome or chromosome structure, X and Y - Sex chromosomes, (:) - two points: break, (: :) - two double points.

Figure 1

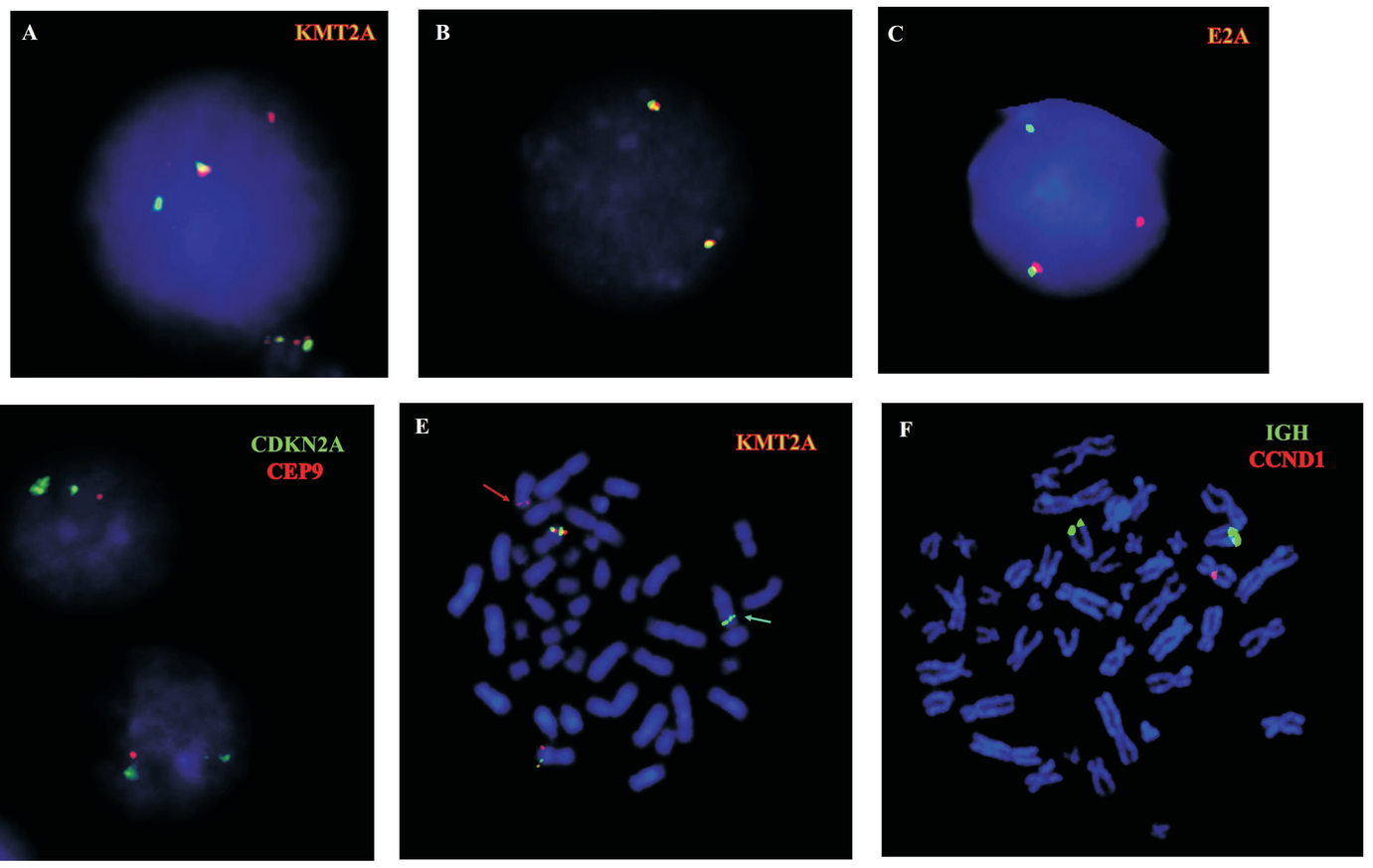

Figure 1. LSI FISH experiments: A: Nuclear interphase analysis with LSI MLL (KMT2A) break-apart probe showing an rearranged split signal; **B:** Nuclear interphase analysis with LSI normal break-apart pattern example **C:** Nuclear interphase analysis with LSI E2A break-apart probe showing an rearranged split signal; **D:** analysis with *CDKN2A*/CEP9 probe showing heterozygous deletion of *CDKN2A* (loss of red signal); (KMT2A); **E:** Nuclear methaphase analysis with LSI MLL (KMT2A) break-apart probe showing two normal *KMT2A* signals, and one extra copy of KMT2A gene with split signals; the proximal *KMT2A* signal on der(14) (green signal – green arrow) and distal *KMT2A* signal on der(9) (red signal – red arrow); **F:** Nuclear methaphase IGH/CCND1 probe showing a heterozygous loss of CCND1 gene (loss of red signal);

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Conclusion

We highlight that banding cytogenetics combined with molecular cytogenetic techniques such as LSI-FISH was crucial to better characterize the rearrangement and adjust properly further risk stratification for the patient.

Projeto Gráfico: Setor de Edição e Informação Técnico-Científica / INCA

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