extramedullary involvement, a particular blast morphology, and a worse outcome as compared to fusion-negative AML pediatric patients, including a high frequency of disease refractoriness and relapse. NGS studies did not show CBFA2T3-GLIS2 in our patient. Thus, our results indicate that RAM+ associated with the driver p210-BCR-ABL1, even with specific targeted therapy, may lead to treatment resistance regardless of CBFA2T3-GLIS2+. **Conclusion:** Here we highlight for the first time the presence of p210-BCR-ABL1 associated with RAM phenotype in the absence of CBFA2T3-GLIS2 and disease refractoriness in a non-DS-AMKL infant.

https://doi.org/10.1016/j.htct.2022.09.582

MOLECULAR CYTOGENETIC AND NEXT-GENERATION SEQUENCING STUDIES OF AN ADOLESCENT WITH ACUTE MYELOID LEUKEMIA AND INV(16) ASSOCIATED WITH A KIT PATHOGENIC MUTATION

MM Rocha [a], RRC Matos [a,b], AF Figueiredo [c], AH Melgaço [a], PR Horn [a], TJ Marques-Salles [d], R Binato [a,b], MLM Silva [a,b], E Abdelhay [a,b], GM Ferreira [a]

[a] *Instituto Nacional do Câncer José de Alencar Gomes da Silva (INCA), Rio de Janeiro, RJ, Brazil*
[b] *Post-Graduation Program in Oncology, Instituto Nacional do Câncer (INCA), Rio de Janeiro, Brazil*
[c] *Laboratório de Genética, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*
[d] *Pediatric Oncohematology Center, Hospital Oswaldo Cruz, Post Graduation Program, Faculty of Medical Sciences, Biologic Sciences Institute, Universidade de Pernambuco, Recife, PE, Brazil*

Objectives: Inv(16)(p13q22)/CBFb-MYH11 in Acute Myeloid Leukemia (AML) is hard to characterize and comprises about 5%–7% of all cases and 5%–9% in children. Inv(16) is associated with a good prognosis both in adults and children. However, approximately 30%–40% of affected patients experience relapse. In this context, additional type I and II mutations have been related to inv(16). KIT mutations associated with inv(16) have been related to a worse prognosis. Here we describe the clinical and molecular data of a pediatric patient with AML, presenting inv(16) associated with a KIT pathogenic mutation. **Material and methods:** A 12-year-old boy with bleeding was referred to Pedro Ernesto University Hospital (HUPE), Rio de Janeiro, Brazil. The patient presented with suspected hyperleukocyte acute leukemia. Laboratory tests revealed a WBC count of 80×10^3, a platelet count of 9×10^3, and a hemoglobin level of 5.1 g/dL. Flow cytometry results demonstrated an immunophenotypic profile characteristic of LMA-M4. We conducted G-banding, FISH, and NGS studies. **Results:** Cytogenetic analysis was non-informative. Based on the clinical and immunophenotypic data, we conducted an experimental design using PML-RARA and CBFB-MYH11 FISH probes. The patient was negative for the PML-RARA fusion, but CBFb-MYH11 was confirmed. The NGS Assay revealed a pathogenic missense mutation in KIT. The results were negative for FLT3/ITD mutations. **Discussion:** AML patients presenting inv(16)/CBFb-MYH11 usually have a good prognosis with better remission and overall survival rates compared to those with normal karyotypes. However, due to the high rates of disease relapse, the prognostic value of alterations associated with inv(16)/CBFb-MYH11 has been widely discussed in the literature. Our patient presented with excessive bleeding and heavy hemorrhage, which initially raised the suspicion of acute promyelocytic leukemia. Due to the heterogeneity of the CBFb-MYH11 fusion, featuring distinct clinical and genetic profiles depending on its molecular size molecular and the association of these profiles with specific genomic alterations, a precise genomic characterization is necessary. KIT mutations, such as the one observed in our patient, are present as alterations associated with inv(16) in approximately 9%–53% of AML cases. Previous studies have demonstrated the potential prognostic impact of KIT mutations in the affected patients. In this context, missense mutations may lead KIT to an overactive state. This type of mutation has been shown to play a pivotal role in mediating clinical response and disease refractoriness in patients treated with targeted therapeutics. Therefore, the information provided through the NGS can be crucial for treatment adaptation. **Conclusion:** In this work, we contribute with the literature showing the clinical, molecular, and genomic data of an adolescent with AML and inv(16) associated with a KIT pathogenic mutation. Besides, we highlight the importance of NGS studies in characterizing the genomic profile of patients affected by this neoplasm. Although, the prognostic implications of these findings remain to be investigated, especially in the context of new generation tyrosine kinase inhibitors targeting KIT in future clinical trials for inv(16)/CBFb-MYH11 pediatric patients.

https://doi.org/10.1016/j.htct.2022.09.583

NEXT-GENERATION GENOMIC MONITORING REVEAL A NOVEL RUNX1 PATHOGENIC MUTATION ASSOCIATED WITH TRISOMY 4 AS A SOLE ABNORMALITY IN A YOUNG ADULT WITH ACUTE MYELOID LEUKEMIA

RRC Matos [a,b], MM Rocha [a], AF Figueiredo [c], MG Land [d], AH Melgaço [a], JM Souza [e], TF Padilha [a], E Abdelhay [a,b], GM Ferreira [f], MLM Silva [a,b]

[a] *Instituto Nacional do Câncer José de Alencar Gomes da Silva (INCA), Rio de Janeiro, RJ, Brazil*
[b] *Postgraduate Program in Oncology, Instituto Nacional do Câncer (INCA), Rio de Janeiro, RJ, Brazil*
[c] *Laboratório de Genética, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*
[d] *Internal Medicine Post-Graduation Program of Faculty of Medicine, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*
[e] *Hospital Universitário Pedro Ernesto (HUPE), Rio de Janeiro, RJ, Brazil*
[f] *Pediatric Oncohematology Center, Hospital Oswaldo Cruz, Graduate Program, Faculty of*

Medical Sciences, Instituto de Ciências Biológicas, Universidade de Pernambuco, Recife, PE, Brazil

Objectives: Acute Myeloid Leukemia (AML) with a single trisomy show particular clinical, morphological, genomic, and immunophenotypic features. Trisomy 4 was first described in 1986 as the sole chromosomal abnormality in AML. However, due to its rarity (< 1%), there are not enough data concerning its clinical impact. Here we report clinical, cyto-molecular, and genomic data of a young adult with AML and a rare trisomy 4 associated with a novel RUNX1 pathogenic mutation. **Material and methods:** A 19-year-old man was referred to Hospital dos Servidores do Estado, Rio de Janeiro, Brazil. He presented a history of 30 days of anemia, fever, weight loss, thrombocytopenia, and mucocutaneous bleeding. Physical examination revealed hepatomegaly (15 cm) and splenomegaly (14 cm). Laboratory data included hemoglobin level of 6.9 g/dL, WBC of 350×10^9/L, and platelet count of 8×10^9/L. The LDH was 1650 U/L. Flow cytometry analysis revealed 83.4% of blasts showing myeloid morphology that expressed CD34, CD117, CD13, CD7, CD38, and HLA-DR, compatible with FAB AML-M0 with minimal differentiation/undifferentiated. The patient was treated under a high-risk AML protocol. On day 14 of treatment, he developed visceral septicemia and died due to septic shock. We performed G-banding and FISH experiments. NGS was performed on a targeted approach. **Results:** G-Banding revealed the karyotype 47,XY,+4. FISH with a centromeric probe for chromosome 4 confirmed trisomy 4. Molecular biology tests were positive for FLT3/ITD and negative for NPM1 mutations. NGS results revealed a novel RUNX1 missense pathogenic mutation. **Discussion:** Trisomy 4 is a rare chromosomal abnormality in AML, accounting for 1 < % of cases. Although its prognostic relevance has been a frequent topic of discussion in the literature, its relation to prognosis remains to be elucidated. Chilton and coworkers (2016) described 35 patients with trisomy 4 as an isolated abnormality and observed only two patients (6%) in the 16–25 age group. Patients with trisomy 4 have a poor prognosis when associated with mutations in KIT, mapped at position 4q12, which may influence the role of trisomy 4 in leukemogenesis. The patient in the present study belongs to the same age group as the patients in the abovementioned study. However, to our knowledge, it is the first case with trisomy 4 as a sole abnormality presenting FAB AML-M0. Our patient had a poor prognosis, including hyperleukocytosis. In addition, we characterized a missense RUNX1 mutation not yet described in the literature. RUNX1 is a transcription factor part of a complex that provides stability to the RUNX1 protein, which plays a pivotal role in generating hematopoietic stem cells and their differentiation. Loss of RUNX1 function has been shown to impair cell differentiation, often resulting in leukemogenesis. Besides, RUNX1 mutations are known to cause thrombocytopenia and familial platelet disorder. **Conclusion:** Here we present a rare AML-M0 case with trisomy 4 as a sole abnormality and highlight its association with a novel RUNX1 mutation. Although, the prognostic implications remain to be elucidated. In particular, when to consider stem cell transplantation as curative therapy of choice in RUNX1 mutated individuals to maximize benefit and minimize risk.

https://doi.org/10.1016/j.htct.2022.09.584

PRIMEIROS RESULTADOS DO PROTOCOLO DE INDUÇÃO COM BAIXAS DOSES PARA CRIANÇAS COM LEUCEMIA MIELÓIDE AGUDA NO BRASIL E DO PROTOCOLO BRASILEIRO PARA TRATAMENTO DE LEUCEMIA MIELÓIDE AGUDA INFANTO JUVENIL

ALM Rodrigues [a], A Vieira [b], AM Silva [c], AF Oliveira [d], CGC Junior [e], CR Carvalho [f], J Costa [g], MLM Lee [h], M Lins [f], P Godinho [i], A Seber [j], R Ribeiro [k]

[a] *Hospital Erastinho, Complexo Hospitalar Erasto Gaertner e Hospital de Clínicas da Universidade Federal do Paraná (UFPR), Curitiba, PR, Brasil*
[b] *Hospital Oncológico Octávio Lobo, Belém, PA, Brasil*
[c] *Hospital Aristides Maltez, Salvador, BA, Brasil*
[d] *Fundação Pio XII – Hospital de Amor, Barretos, SP, Brasil*
[e] *Hospital São Camilo, São Paulo, SP, Brasil*
[f] *Instituto de Medicina Integral Professor Fernando Figueira (IMIP), Recife, PE, Brasil*
[g] *Hospital Martagão Gesteira, Salvador, BA, Brasil*
[h] *Hospital Beneficência Portuguesa de São Paulo, São Paulo, SP, Brasil*
[i] *Fundação Pio XII – Hospital de Amor da Amazônia, Porto Velho, RO, Brasil*
[j] *Hospital Samaritano São Paulo, Grupo de Apoio ao Adolescente e Criança com Câncer (GRAAC), São Paulo, SP, Brasil*
[k] *St. Jude Children's Research Hospital, Estados Unidos*

Objetivo: Descrever os resultados do tratamento de indução com baixas doses (MAG – Mitoxantrone: 5 mg/m^2/dia do D1 a D3, Citarabina: 10 mg/m^2 do D1 a D10, GCSF: 5 mcg/kg/dia do D1 a D10) das primeiras crianças e adolescentes com Leucemia Mielóide Aguda (LMA) no Brasil. **Material e métodos:** Estudo retrospectivo, multicêntrico, não controlado, aberto, de braço único, fase 2, para avaliação da atividade antitumoral (taxa de resposta/remissão) e segurança do esquema MAG, proposto como primeira indução no Protocolo Brasileiro para Tratamento de LMA Pediátrica, seguido de outro MAG ou ADE (segunda indução) e de três intensificações, adaptadas conforme grupos de risco (baixo, intermediário e alto), definidos segundo a avaliação genética e a resposta aos dois primeiros ciclos de indução. Critérios de inclusão: pacientes menores de 21 anos com LMA de novo ou LMA secundária. Critérios de exclusão: pacientes com leucemia promielocítica e pacientes com LMA e Síndrome de Down. **Resultados:** Dados coletados de maio de 2022 a julho de 2022. Foram registrados 70 pacientes, dos quais 3 foram excluídos por possuírem Sd. de Down. Dos 67 restantes, 27 do sexo feminino e 40 do sexo masculino. A mediana de idade ao diagnóstico foi 7 anos e 9 meses. Dos 65 pacientes avaliáveis (2 foram a óbito no início do tratamento), 41 (63%) apresentaram menos de 5% de blastos em medula óssea após a primeira indução e 83% após a segunda indução (50 de 60 pacientes avaliáveis). Houve dois óbitos durante a primeira indução com MAG (2,98%) e 4 óbitos durante a segunda indução, totalizando 8,95% de óbitos