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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.

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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

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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

quando somadas as duas induções. **Discussão:** O resultado do tratamento da LMA pediátrica melhorou significativamente nas últimas décadas. As taxas de Sobrevida Global (SG) atuais são superiores a 70%, devido à implementação de estratégias como classificação de risco mais precisa, refinamentos nos cuidados de suporte e acesso ao transplante. No entanto, em locais com recursos limitados e países em desenvolvimento, como o Brasil, a SG varia de 20% a 55%, conforme a região do país, e as mortes relacionadas ao tratamento de indução são excepcionalmente altas (entre 25%–30% de óbitos nos primeiros dois meses de tratamento, contra discrepantes menos de 5% nos países de primeiro mundo). Os regimes com quimioterapia de dose padrão estão associados a complicações com risco de vida, devido à profunda mielossupressão e disfunção orgânica. Há atualmente dados suficientes na literatura, que suportam o risco de utilizar protocolos com baixas doses de indução na LMA. Como demonstrado pelos bons resultados do grupo chinês (reproduzidos em outros países e contextos, inclusive na America Latina), é possível observar taxas índices de remissão completa e sobrevida similares aos protocolos internacionais que fazem uso de poliquimioterapia em altas doses. Os resultados dos primeiros 67 pacientes que receberam o protocolo MAG no Brasil demonstram isso, com mortalidade inferior a 9% durante os dois primeiros meses de tratamento, sem prejuízo na indução da remissão. **Conclusão:** Houve redução importante da mortalidade indutória com o protocolo MAG, com taxas índices de remissão completa similares aos protocolos internacionais estandardizados. Os resultados deste estudo contribuem para a adesão à proposta do novo protocolo da Sociedade Brasileira de Oncologia Pediátrica (SOBOPE) para LMA pediátrica, aprovado em maio de 2022 (CAAE 51679421.6.1001.0098) e já em aplicação em 45 instituições brasileiras.

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NOVEL CHROMOSOMAL ALTERATION DER(2)T (2;15)(Q37;Q21) IN A PEDIATRIC PATIENT WITH MYELODYSPLASTIC SYNDROME: MOLECULAR CYTOGENETIC STUDIES

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Objective: Pediatric Myelodysplastic Syndrome (p-MDS) comprises a heterogeneous group of clonal hematopoietic stem cell diseases with an increased risk of evolution to Acute Myeloid Leukemia (AML). Cytogenetic is one of the most important prognostic factors for MDS and it is present into score prognostic systems as the Revised International Prognostic Scoring System (IPSS-R). Chromosomal translocations are rare cytogenetic abnormalities in *de novo* MDS. Therefore, their reporting is essential for the identification of new cytogenetic prognostic risk groups and possible alterations associated with the MDS pathogenesis.The aim of this study was describe a yet unreported der(2)t(2;15)(q37;q21) in a *de novo* p-MDS associated with evolution to AML. **Material and methods:** Cytogenetic analysis was performed in Bone Marrow (BM) cells by G-banding. Fluorescence In Situ Hybridization (FISH) was performed to investigate the possible rearrangement involving chromosomes 2 and 15, using a Whole Chromosome Painting (WCP) probe for chromosome 2 and LSI PML/RARA for chromosome 15 (PML gene). **Results:** A 12-year-old girl was admitted to the Pediatrics Institute of Federal University of Rio de Janeiro in January 2022. Peripheral blood count showed Hemoglobin (Hb) level of 6.5 g/dL, 794.000 platelets/mm^3, and 2.600 white blood cell (WBC)/mm^3. The myelogram showed dysplasias and 16% of myeloid blasts being classified with MDS-EB-t. The conventional cytogenetic analysis showed the karyotype: 46,XX,add(2)(q37?)[25]. Using molecular cytogenetic methods, we characterized the chromosomal alteration as an unbalanced translocation involving chromosomes 2 and 15. This translocation was observed in 71.6% (190/265) of the interphase nuclei and metaphases. The final karyotype was: 46,XX,der(2)t(2;15)(q37;q21)[25]. Five months later, the patient showed in the myelogram 50.7% of blast cells compatible with AML. The patient was indicated for allogeneic Hematopoietic Stem Cell Transplantation (HSCT) and initiated chemotherapy. **Discussion:** In p-MDS, chromosomal translocations as sole chromosomal abnormality are rare and their real prognostic impact is unknown. The patients with this type of cytogenetic alteration are classified as intermediate-risk group according to the IPSS-R. Our report describes the clinical outcome in a *novo* p-MDS showing a der (2)t(2;15)(q37;q21). A broad scientific review showed that the der(2)t(2;15)(q37;q21) was not yet reported in p-MDS. It is interesting to note that this chromosomal translocation was associated with a poor clinical outcome, with progression from MDS to AML. The cytogenetic and clinical features were important tools for the indication to allogeneic HSCT. **Conclusion:** This study and literature review highlight the importance of cytogenetics and clinical follow-up of *de novo* p-MDS patients for the identification for HSCT. This is the first study that describe the der(2)t(2;15)(q37;q21) in a p-MDS associated with AML evolution.

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DIABETES INSIPIDUS COMO APRESENTAÇÃO INICIAL DE HISTIOCITOSE DE CÉLULAS DE LANGERHANS (HCL) – RELATO DE CASO

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