pertencem ao grupo de indutores da trombopoese via receptor de trombopoetina dos megacariócitos, objetivando aumentar a contagem plaquetária enquanto aguarda-se a recuperação imune. Por fim, a esplenectomia é realizada raramente devido ao risco de infecção, sendo reservada para casos refratários geralmente maiores de 5 anos de idade onde outras terapias foram tentadas e o paciente segue com sangramentos graves; apresenta uma taxa de sucesso de até 80%. **Conclusão:** A trombocitopenia imune crônica continua sendo um desafio terapêutico, porém apenas 12% persistem com uma contagem de plaquetas menor que 20.000 após 5 anos. A combinação de terapias pode ajudar a aumentar a efetividade do manejo, além do uso de imnunossupressores, como dapsona, mercaptopurina, azatioprina e ciclosporina podem ser úteis em casos não responsivos à segunda-linha habitual. Além do mais, deve-se atentar para possibilidade de uma imunodeficiência ser a causa da trombocitopenia.

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RESPOSTA AO TRATAMENTO: ELTROMBOPAG NA PEDIATRIA

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Objetivos: Descrever dois casos clínicos de pacientes Portadores de Trombocitopenia Imune (PTI) crônica que apresentaram boa resposta terapêutica ao uso do Eltrombopag. **Materiais e métodos:** As informações foram obtidas através de revisão de prontuário eletrônico. **Relato de caso:** Caso 1: Paciente 7 anos, diagnostico de PTI há 1 ano e 4 meses, refratário a tratamento com corticoterapia e imunoglobulina. Iniciado Eltrombopag com dose primária de 25 mg dia, sem resposta após 1 mês, progredida dose para 50 mg dia com uma resposta plaquetária após 34 dias de 21000 U/mm^3 para 169000 U/mm^3, sem intercorrências clínicas. Caso 2: Paciente 14 anos, PTI pós COVID, diagnosticado há 1 ano e 11 meses, refratário a terapia com corticoide, imunoglobulina e azatioprina, iniciado Eltrombopag 50 mg dia com resposta plaquetaria após 1 mês de 15000 para 401000 U/mm^3, sem intercorrências clínicas. **Discussão:** A trombocitopenia imune caracteriza-se por um processo imunomediado, onde ocorre a degradação de plaquetas com contagem total menor 100,000U/mm^3. é classificada como crônica quando o tempo de doença ultrapassa 12 meses e pode trazer grande morbidade aos seus pacientes, não só pelos sintomas e prejuízo na qualidade de vida, como pelos efeitos colaterais das terapias a longo prazo. o presente estudo relata 2 casos de trombocitopenia imune crônica em crianças, refratária às terapias tradicionais, que apresentaram boa resposta terapêutica ao uso de Eltrombopag. O Eltrombopag é um agonista oral não peptídico do receptor da trombopoietina que age estimulando a produção de plaquetas. Um estudo randomizado, multicentrico, controlado por placebo, PETIT 2, comprovou a eficácia e segurança do uso do Eltrombopag na faixa etária pediátrica, estabelecendo as doses iniciais de 25 a 50 mg/dia para pacientes de 6 a 17 anos, sendo sua dose maxima diária recomendada de 75 mg. Nos estudos PETIT e PETIT 2, o tratamento com Eltrombopag demonstrou uma resposta plaquetária satisfatória, contagem de plaquetas de pelo menos 50,000U/mm^3, entre 1 e 6 semanas de uso, sem necessidade de terapia de resgate. foram observados também uma redução nos sangramentos e de medicações concomitantes. não foram constatados eventos adversos graves, e os efeitos relativos a medicação encontrados se relacionavam a alteações laboratoriais hepatobiliares, logo tendo seus parâmetros de normalidade restabelecidos após descontinuação do uso.resultados semelhantes também foram encontrados em um estudo observacional de centro único realizado na china. Embora ainda haja poucos estudos sobre o uso do eltrombopag na faixa etária pediátrica, estes têm apresentado resultados semelhantes aos encontrados em adultos, porém sem descrição de eventos trombóticos ou malignidade.

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FLEXIBILITY OF FISH PROBES IN MONITORING IAMP21 ACUTE LYMPHOBLASTIC LEUKEMIA: STUDY OF FOUR BRAZILIAN CHILDREN

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Objectives: Intrachromosomal Amplification of chromosome 21 (iAMP21) is an independent outcome indicator in B-cell Precursor ALL (BCP-ALL). IAMP21 is characterized by multiple RUNX1 copies in blast cells, and comprises 2% of children with BCP-ALL. It was first detected during routine screening for ETV6-RUNX1 fusion by FISH. This disease features protocol-dependent outcomes. For example, in pediatric patients, iAMP21-ALL presents poor outcomes when standard therapy is used. Although, when children receive intensive treatment, they usually show lower relapse risk and improved survival. Thus, the early detection of iAMP21 is crucial to guide therapeutic strategies. In this regard, FISH probes may provide a rapid and effective screening, being a valuable ally for

banding cytogenetics. In this work, we describe the clinical and molecular data of four pediatric patients with BCP-ALL iAMP21, showing the importance of RUNX1-RUNX1T1 and ETV6-RUNX1 FISH probes in screening this high-risk entity. **Material and methods:** This collaborative study included four children with BCP-ALL iAMP21. The peripheral blood and Bone Marrow (BM) samples were referred to the cytogenetics laboratory at the Brazilian National Cancer Institute between 2013 and 2021. We performed G-banding and FISH experiments in interphase nuclei and metaphase spreads. We used commercial Locus-Specific (LSI) ETV6-RUNX1, RUNX1-RUNX1T1, and centromeric 13/21 FISH probes. **Results:** Using the FISH technique with LSI ETV6-RUNX1 and RUNX1-RUNX1T1 probes, we identified the derivative chromosome 21 and the precise number of RUNX1 signals for each patient. It also helped disclose whether the RUNX1 amplifications were intra- and or extrachromosomal. **Discussion:** The intrachromosomal amplification of chromosome 21 is an uncommon high-risk chromosomal aberration in pediatric B-ALL. iAMP21 can be elusive, sometimes escaping detection by banding cytogenetics. Thus, confirmation by molecular techniques is necessary. Besides, recent studies suggest a relapse risk associated with therapy intensity, emphasizing the importance of a rapid and early detection of iAMP21 for appropriate risk stratification and therapeutic intervention. The FISH approach used through our experimental design has proved efficient in the early detection of iAMP21 in all patients. Importantly, it helped determine the diagnosis of iAMP21 48 hours after initial diagnosis. Our approach can also be valuable in monitoring patients for Minimal Residual Disease (MRD). According to the literature, those who continuously present MRD should be eligible for BM transplantation. **Conclusion:** In summary, the flexibility of FISH probes enabled the rapid detection of this high-risk neoplasm. Besides, the precise characterization of iAMP21, including the aberrant chromosomes 21 and extra RUNX1 signals, was important to guide treatment strategies and the monitoring of patients. In addition, we reinforce the importance of investigating the heterogeneity of iAMP21 marker chromosomes, their molecular complexity, and genomic association with disease progression. Novel genetic findings may provide valuable information about this entity, which could open perspectives regarding novel therapeutic approaches for children with BCP-ALL iAMP21.

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CLINICAL AND MOLECULAR REPORT OF A RARE RAM POSITIVE NON-DOWN SYNDROME INFANT CBFA2T3-GLIS2 NEGATIVE, PRESENTING THE DRIVER P210-BCR-ABL1

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Objectives: Pediatric Acute Megakaryoblastic Leukemia (AMKL) comprises 4%–15% of Acute Myeloid Leukemia (AML) cases. Down Syndrome (DS)-AMKL usually displays a favorable outcome, whereas the prognosis of non-DS-AMKL is generally poor. Here we present the clinical and genomic data of a rare non-DS-AMKL infant with p210-BCR-ABL1 fusion, co-occurring with a high-risk WT1 mutation. The baby was RAM positive and CBFA2T3-GLIS2 negative, showing refractoriness to treatment. **Material and methods:** A 1-year-old girl was referred to the Hospital with a history of fever and motor developmental delay for four months. On admission, she presented ecchymosis, swelling, and organomegaly (spleen and liver). The WBC count was $26.5 \times 10^3/\mu$L, hemoglobin level was 7.6 g/dL, platelet count was $25 \times 10^3/\mu$L, and LDH was 2.887. At diagnosis, she showed bilateral myeloid sarcoma. Morphological analysis of the Bone Marrow (BM) showed clustered cytoplasmic blebs. Flow cytometry analysis revealed 83% of blast cells and a profile compatible with AMKL and RAM phenotype. The patient was treated under the high-risk AML-BFM-2004. Imatinib was incorporated into the treatment after BCR-ABL1 detection. However, minimal residual disease remained positive throughout the treatment, making BM transplantation unfeasible. Disease refractoriness was persistent even with the administration of Dasatinib, FLAG-IDA and Venetoclax. The patient died one year after diagnosis due to sepsis during BM aplasia. We performed G-banding, FISH, and Multiplex RT-PCR experiments. The molecular response was assessed by absolute quantification via RT-qPCR assays. Sanger sequencing and NGS were performed on a targeted approach. **Results:** The karyotype was 46,XX,t(9;22)(q21;q34). We observed polyploidy (3–20N). FISH in polyploid Nuclei (8N) showed four BCR-ABL1 fusion signals. In diploid metaphases, we observed two BCR-ABL1 signals. Multiplex RT-PCR detected the p210-*BCR-ABL1*. RT-qPCR monitoring detected persistent high levels of BCR-ABL1 transcripts associated with disease refractoriness. Sanger sequencing showed no GATA1 mutation. NGS revealed a missense WT1 pathogenic mutation, and CBFA2T3-GLIS2 was not present. **Discussion:** RAM phenotype is characterized by overexpression of CD56 and under-expression of CD38, CD45, and HLA-DR. This phenotype is characteristic of children, usually associated with AML-M7 (38%) and intermediate-risk cytogenetics not associated with prognostic subgroups. RAM is related to a poor prognosis with high MRD and induction failure rates compared to non-RAM patients. This phenotype is associated with the CBFA2T3-GLIS2 fusion, which is related to