resultado da biopsia mediastinal liberado em 14/02/2023 (CD20+CD30+ EBV+ PAX5- CD3- CKAE1/AE3- ALC-OCT3/4-): Linfoma da Zona Cinzenta (LZC) com características intermediárias entre linfoma de Hodgkin clássico esclerose nodular e linfoma difuso de grandes células B. Realizou novo PET CT após o segundo ciclo de R-ICE, cujo resultado foi satisfatório com poucas áreas de hipercaptação evidenciando resposta parcial. Paciente encontra-se clinicamente bem, aguardando a realização de novo PET-CT após o quarto ciclo de R-ICE. A continuidade do tratamento será com radioterapia e transplante de medula óssea alogênico. **Discussão:** LZC foi apresentado em 1998 e incorporado na classificação WHO2008 como linfoma B não classificado com características intermediarias entre LDGC e LHC. Tanto o diagnóstico quanto a terapêutica são desafiadores até os dias atuais. Afeta mais comumente adultos jovens, mas pode também ser diagnosticado em crianças. O mediastino anterior é o sítio mais comum e ocasionalmente pode ser sistêmica sem acometimento mediastinal. Pacientes com LZC tem alta taxa de recaída. O tratamento de primeira linha pode ser com R-CHOP ou EPOCH-R. Na doença refratária ou em recaída está indicado o transplante de medula óssea, radioterapia, brentuximabe, imunoterapias e terapias celulares. **Conclusão:** Este relato ilustra a dificuldade diagnóstica e da decisão terapêutica descrita na literatura e reafirma o quanto é necessária a integração entre a equipe clínica e laboratorial para o diagnóstico de certeza.

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CONTRIBUTION OF NEXT-GENERATION SEQUENCING TO THE DIAGNOSIS OF JUVENILE MYELOMONOCYTIC LEUKEMIA: A CASE REPORT

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Juvenile Myelomonocytic Leukemia (JMML) is a rare myeloproliferative neoplasm of childhood characterized by infiltration of abnormal myelomonocytic cells in peripheral blood, bone marrow, and spleen. The majority of JMML patients have somatic and/or germline variants in RAS signaling pathway genes. Although the karyotype is predominantly normal, monosomy of chromosome 7 is observed in about 25% of cases. The diagnosis of JMML can be made by combining clinical, laboratory, and molecular data. In this study, we report the case of a six-year-old male patient with an initial presentation of rectal bleeding accompanied by severe thrombocytopenia. The bone marrow examination showed a mildly hypercellular bone marrow with moderate dysgranulopoiesis and blasts with myeloid characteristics, 1.6% basophils, 3.4% monocytes, and 3.4% promonocytes, suggesting Myelodysplastic Syndrome (MDS) or JMML. Immunophenotyping of peripheral blood revealed signs of granulocytic dysplasia, monocytosis (11.7%), 3.5% promonocytes, and 6.0% immature myeloid cells, which were also suggestive of MDS or JMML. Hemoglobin electrophoresis revealed 13.6% fetal hemoglobin. Bone marrow biopsy showed a cell-to-fat ratio of 98% due to the proliferation of blastoid immature cells. No fibrosis or deposits were observed in the bone marrow. Karyotyping of the bone marrow was normal, and BCR:ABL1 fusion was negative. Next-Generation Sequencing (NGS) panel testing was performed to detect variants in 40 genes (including CBL, KRAS, NRAS, PTPN11, and NF1) and gene fusions involving 29 driver genes. Variants were detected in the PTPN11 gene (c.215C>T, p.Ala72Val, VAF: 42.7%) and NRAS gene (c.35G>A, p.Gly12Asp, VAF: 28.9%), both of which are RAS pathway genes. No gene fusions were detected. Somatic variants in PTPN11 are the most common molecular alterations in JMML, detected in 35% to 40% of patients, and are associated with an aggressive clinical course and adverse prognosis. Approximately 25% to 30% of patients have somatic variants in NRAS or KRAS. The current diagnostic criteria for JMML include blast percentage in peripheral blood or bone marrow less than 20%, splenomegaly, monocyte count $\geq 1.0 \times 10^9$/L, absence of BCR:ABL1 fusion, and the presence of at least one variant in RAS pathway genes. In this context, the findings of the NGS panel were decisive for the diagnosis of JMML. Despite advances in understanding the molecular landscape of JMML, this disease remains challenging, with a wide range of phenotypes and outcomes, ranging from rare forms that resolve spontaneously to aggressive cases with adverse prognosis. Characterization of genomic alterations not only contributes to elucidating the oncogenic mechanisms involved in the pathogenesis of the disease but also provides relevant information for prognosis definition and clinical decision-making.

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DIAGNÓSTICO MOLECULAR DE BETA TALASSEMIA INTERMÉDIA: RELATO DE HETEROZIGOTO COMPOSTO PARA MUTAÇÃO HBB:C.118C>T (CD39) E HBB:C.-138C>T (-88C>T)

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