as a potential target therapy. CD33^{low} blasts are associated to a more mature AML and its high expression is related to adverse landscapes, highlighting the importance of CD33 evaluation. Standard care for AML enrolls MRD monitoring and failure to achieve an MRD-negative, CR or detected MRD during or after therapy is associated with relapse or poor outcomes. Still, MRD analysis must embrace a set of standards in order to prevent post-analytic errors. Here we present a case report of AML with absent CD33 maintained from diagnosis to MRD follow-ups, mimicking MRD positivity. This data emphasizes the importance of caution in MFC analysis and correlation of diagnostic and follow-ups results interpretation, as well as constant training of the team.

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ACUTE UNDIFFERENTIATED LEUKEMIA WITH BCR-ABL TRANSLOCATION: CASE REPORT AND LITERATURE REVIEW

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The 2016 WHO classification defines acute undifferentiated leukemia (AUL) as a rare type of acute leukemia (AL) without defining markers for either lymphoid or myeloid lineage commitment. Literature suggests AUL does not harbour the genetic mutations commonly seen in lymphoblastic leukemia or acute myeloid leukemia (AML) including FLT3, WT1, rearrangements of KMT2A or BCR-ABL1 and it highly expresses genes associated with poor prognosis in AML (BAALC, ERG, and MN1); therefore, AUL is often associated with dismal outcome (Arber et al. 2016). This case report depicts an unusual genetic presentation of an AUL with BCR-ABL fusion gene. A 54-year-old female patient presented to our hospital in July 2021 with fatigue and adynamia one month before. She was also found with deep vein thrombosis in the left leg and segmental pulmonary thromboembolism. Laboratory exams showed Hb 9,7 g/dL, WBC 75.77×10^9/L (77% blasts), platelets 175×10^9/L. Coagulogram and fibrinogen were normal. Bone marrow (BM) aspiration was hypercellular, showing 86% of agranular blasts. Flow cytometry (FC) from BM blasts exhibited expression of CD34, CD45, HLA-DR, CD33, CD38, and partial expression of CD10 and CD123. The blasts were negative for MPO, CD79a, CD19, CD7, CD3, CD13, C117, CD16, CD11b, CD64, CD15, CD14, CD300e, CD61, NG2, CD71, CD4, CD36, CD22, CD42b. Conventional cytogenetics revealed a Ph+ disease (46,XX,t(9;22)(q34q11.2)[7]/46, idem, add(4)(q35)[7]/46,XX [6]). Real-time quantitative PCR showed positive BCR-ABL with p190 transcripts. FLT3 and NPM1 were found negative. Diagnosis of AUL Ph+ was made. AML chemotherapy was started with 3+7 standard doses regimen plus imatinib 600 mg/day. On day 14th BM evaluation found 89% of blasts with the same immunophenotype as in the diagnosis. The patient presented neutropenic colitis with the need to delay rescue therapy. We searched articles in the Pubmed database using the following strategy: "Bcr-Abl Tyrosine Kinase"AND "undifferentiated leukemia", "Philadelphia chromosome"AND "undifferentiated leukemia"between 1976 and 2021. We found two case reports that described patients with AUL and positive BCR-ABL gene. In 1983, Smadja, N et al. reported a patient with AL considered at diagnosis to be undifferentiated. Neither the diagnosis cytogenetic nor FC data was provided by the authors, and the AL classification was based only on morphological characteristics. After 17 months, the patient developed Ph+ chronic myelogenous leukemia with a complex translocation (2; 9; 22). Hattori, M et al., in 1995, described a patient that following treatment to non-Hodgkin lymphoma developed myelodysplastic syndrome (MDS) which progressed to AUL, both found with the presence of chimeric BCR-ABL transcripts. The FC showed blasts that expressed CD7 and HLA-DR, and were negative for lineage markers: CD14,CD33,CD2,CD3,CD4,CD5,CD8,CDl0,CD19,CD20 and CD41. Qasrawi, A. et al., in 2019 and 2020 performed two studies analyzing data from 24 and 1444 cases of AUL, respectively. The most common pathogenic mutations were PHF6, SRSF2, RUNX1, ASXL1, and BCOR. No BCR-ABL mutation was described. We believe that with the advent of target therapies, the prognosis of AUL can improve. The patient described has the BCR-ABL gene as a potential target to a tyrosine kinase inhibitor. Considering this is not a usual finding, we hope this report can further help treatment decisions.

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ARHGAP6 EXPRESSION IS ASSOCIATED WITH MOLECULAR RISK AND IMPACTS CLINICAL OUTCOMES IN ACUTE MYELOID LEUKEMIA

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Objectives: Despite the advances in the large-scale generation of genomic data from acute myeloid leukemia (AML) patients, much effort is still needed to convert these data into biological functions, which may pave avenues for the discovery of new prognostic markers and therapeutic targets. In a previous study, four cytoskeleton-related genes (ARHGAP6, EZR, MAP3K11 and PAK1) were identified as a prognostic factor in AML. In the present study, we detail the prognostic impact, as well as its functional genomic associations, of the ARHGAP6 gene in AML patients. **Material and methods:** Clinical and genomic data were obtained from the TCGA AML cohort (n = 173). The clinical impact (overall survival [OS] and disease-free survival [DFS]) for ARHGAP6 expression was investigated by the proportional hazards Cox regression model. Functional genomic analyzes were performed by gene set

enrichment analysis (GSEA) and Gene Ontology (GO) from differentially expressed (DEG) genes obtained from the Galaxy tool. All p values were two sided with a significance level of 5%. **Results:** ARGHAP6 expression was higher in the intermediate and high molecular risk groups in AML patients (all $p < 0.01$). High ARGHAP6 expression was identified as an independent risk factor for OS (HR = 1.92; p = 0.001) and DFS (HR = 1.96; p = 0.01) when analyzed with confounders, age, gender, white blood cell count, and molecular risk. In the GSEA, a total of 30 cellular and molecular events were found to be positively enriched in high ARHGAP6-expressing AML patients, which we highlighted the signaling pathways: IL6/JAK2/STAT3 (NES: 1.62; $p < 0.001$), NOTCH (NES: 1.60; $p < 0.001$), KRAS (NES: 1.59; $p < 0.001$), IL2/STAT5 (NES: 1.51; $p < 0.001$), TGF BETA (NES: 1.39; p = 0.03) and BETA CATENIN SIGNALING (NES: 1.36; p = 0.04). In GO analyses, high ARHGAP6 expression was associated with important processes for cancer development and progression such as cell signaling mediated by surface receptors, signal transduction, linkage to growth factors, and regulation of cell population proliferation (all $p < 0.001$). **Discussion:** ARHGAP6 is a RhoGAP that acts converting RhoGTPases in its inactive GDP-bound state, which may regulate the interactions of signaling molecules with the actin cytoskeleton. It promotes continuous elongation of cytoplasmic processes during cell motility and simultaneous retraction of the cell body changing the cell morphology. The role of ARHGAP6 is still poorly established in cancer, but it is known to modulate pathways of RhoGTPases. In this sense, our study is a pioneer in the identification of this gene in processes related to neoplastic hematopoiesis, which will guide future investigations. **Conclusion:** ARHGAP6 gene expression was identified as an independent marker of poor prognosis in AML patients. The GSEA suggested that high ARHGAP6 expression is associated with activation of relevant processes to the malignant phenotype of AML. **Funding:** FAPESP, CNPq and CAPES.

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BLINATUMOMAB E INFUSÃO DE LEUCÓCITOS DO DOADOR (DLI) APÓS TRANSPLANTE DE CÉLULAS-TRONCO HEMATOPOIÉTICAS (TCTH) COM DOADORES ALTERNATIVOS NO TRATAMENTO DE LEUCEMIA LINFÓIDE AGUDA DE LINHAGEM B (LLA-B)

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Introdução: A LLA-B com múltiplas recidivas, cariótipo de alto risco ou doença residual mensurável (DRM) antes do condicionamento têm alto risco de recidiva após o TCTH. O Blinatumomab, imunoterapia que liga linfócitos T CD3 aos blastos CD19 positivos, pode ser utilizado para tratar doença recidivada após TCTH, mas a resposta é transitória com maior parte das crianças apresentando recidiva se não for realizado um segundo TCTH, de alta morbimortalidade, ou imunoterapia com células CAR-T, esse indisponível no país. As recidivas ocorrem geralmente nos primeiros meses após o TCTH, e há déficit no número e função dos linfócitos T. O uso de infusão de leucócitos do doador (DLI) não é convencional em doenças linfoides mas é estratégia que proporciona a administração de células efetoras maduras do doador que se ligam ao blinatumomab e exercem o efeito anti-leucêmico. **Objetivo:** Avaliar a toxicidade e a reposta ao blinatumomab e DLI administrados após o TCTH para tratamento e profilaxia de recidiva de LLA-B após TCTH. **Método:** Pacientes em recidiva hematológica ou considerados de alto risco para recidiva após TCTH (≥ 2 recidivas pré TMO, DRM positiva antes TMO, quimerismo misto após TMO) são submetidos a infusão de blinatumomab a partir da pega e resolução de toxicidades da fase aguda do condicionamento. Realizam 4 ciclos de blinatumomab na dose para tratamento de DRM (15 mcg/m^2/dia por 28 dias) com intervalos de 15 dias. No segundo dia da imunoterapia administra-se a DLI, que é suspensa a qualquer sinal de DECH ou toxicidade aguda relacionada a infusão do blinatumomab. A dose de DLI varia entre 1 e 5 x 10^6 CD3/kg/receptor. Pacientes recidivados sem DECH a dose de células CD3 aumenta progressivamente. **Resultado:** Sete crianças com LLA-B recidivada após TCTH (4) ou alto risco de recidiva (3) receberam o tratamento. A idade variou entre 1.74 e 15.85 anos, mediana de 10.81 anos. Quatro pacientes receberam enxertos haploidênticos e 3 doadores não aparentados (tabela 1). O número de ciclos de blinatumomab variou entre 1 e 4. Os efeitos colaterais esperados foram semelhantes ao uso pré-TCTH: neurotoxicidade (2 - convulsões) e síndrome de liberação de citocinas (4 - sem necessidade de suporte intensivo). O número de infusões de DLI variou entre 0 (paciente recebeu duplo-cordão como enxerto) e 5 infusões, as doses entre 1 x 10^6 a 4,7 x 10^8 células CD3/kg/receptor. Dois pacientes utilizaram inibidores tirosino kinase concomitante por doença Ph+. Nenhum paciente apresentou DECH aguda e 4 apresentaram DECH crônica leve a moderada. Duas crianças faleceram com doença CD19 negativa; sendo uma com microangiopatia trombótica. A mediana de seguimento é 5.2 meses, 5 crianças estão vivas em remissão, sendo 4 delas submetidas a TCTH haploidêntico. **Conclusão:** Blinatumomab com DLI é uma estratégia com potente efeito antileucemico e segura, é necessário expertise na infusão ambulatorial de blinatumomab e no manejo de efeitos adversos.

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CITARABINA 3G/M2 NA INTENSIFICAÇÃO DE ADULTOS COM LEUCEMIA MIELOIDE AGUDA

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