Objetivo: Relatar uma forma incomum de Leucemia aguda *de novo* pós transplante alôgenico aparentado idêntico. **Material e métodos:** Estudo de caráter descritivo. Dados obtidos através de análise de prontuário. **Relato do caso:** Paciente sexo feminino, 31 anos, diagnosticada com Leucemia Mielóide Aguda risco intermediário. Mielograma: 85% blastos com imunofenótipo positivo para CD13, CD33, CD34, CD71, CD117, CD123, HLA-DR, MPO e cariótipo 46; XX. Ausência de mutações para FLT3 e NPM1. Realizou tratamento quimioterápico com protocolo 3+7 seguida de consolidação com citarabina em altas doses. Ao final do tratamento, doença residual mínima negativa. Submetida a transplante de medula óssea alogênico aparentado HLA idêntico (irmão). No pós transplante quimera completa e cariótipo 46; XY. Apresentou recidiva precoce da doença 15 meses após transplante, com perda de quimeirismo (cariótipo 46; XX). Induzida com protocolo IDA-FLAG, apresentando remissão e retorno de quimeirismo completo, cariótipo 46; XY. Iniciou manutenção com azacitidina e manteve por 21 meses. No 24° mês evolui com segunda recaída. Mielograma: 73,9% de blastos, com imunofenótipo positivo para CD13; CD33; CD34; HLA-DR, CD117; CD38; CD45RA, C9 parcial, CD99, MPO, TdT e cariótipo: 47, XXY [5]; 47, XXY add (14) (q? 32) [7], 46 XY[4]. Paciente com alteração de fenótipo em relação a doença inicial - ganho de marcadores CD9, CD99 e perda do marcador CD123. Em cariótipo, presença de cromossomo Y em todas as metáfases analisadas sendo atribuído quadro a leucemia originada das células do doador. Submetida a novo regime quimioterápico, protocolo MEC, porém apresentou refratariedade ao tratamento. Evoluiu a óbito 3 meses após recaída, devido complicações infecciosas. **Discussão:** A leucemia de células do doador é uma entidade rara e possivelmente subdiagnosticada. Na literatura, a maioria dos casos é de linhagem mielóide e o diagnóstico ocorre em média 15 meses após o transplante. Os mecanismos propostos para o surgimento da doença envolvem a primeira mutação genética ocorrendo nas células do doador, com as células susceptíveis adquirindo novas mutações favorecidas pelo ambiente medular do receptor em que a neoplasia original se desenvolveu, associado ao estado de imunossupressão pós transplante, desencadeando o processo de leucemogênese. Há também a possibilidade do clone maligno ter vindo diretamente do doador, contudo não há evidencias que os doadores possuem risco aumentado de desenvolvimento de leucemia. O prognóstico em geral de recaídas após TCTH alogênico é pobre, e não há consenso sobre o melhor tratamento a ser instituído. Como opção terapêutica há regimes de poliquimioterapia e terapia alvo-dirigida, associado a redução de imunossupressão, infusão de linfócitos do doador e até um segundo transplante. A maioria dos pacientes apresenta baixas taxas de remissão e evolui a óbito poucos meses após o diagnóstico, pois foram previamente expostos a diversos agentes e ainda apresentam efeitos do transplante anterior, como foi o caso da paciente relatada. **Conclusão:** Pacientes submetidos a transplante de medula óssea alogênico podem apresentar leucemia que ocorre nas células no doador como um evento de novo, sendo muitas vezes confundida com recaída. A despeito de tratamento quimioterápico intensivo e mesmo com a possibilidade de um novo transplante, o prognóstico ainda se mantém reservado e até o momento do estudo não se encontra na literatura consenso sobre o melhor manejo desses pacientes.

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HCT-CI AS A PREDICTOR OF ICU ADMISSION: BRAZILIAN SINGLE-CENTER COHORT STUDY

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Introduction: MM is the leading indication for Autologous Stem Cell Transplantation (ASCT) globally. Although it is a safe procedure, it might be accompanied by significant morbidity leading to ICU admissions. The Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) is widely used to gauge the risk of treatment-related mortality for patients receiving allografts. **Objective:** To characterize the outcomes of a large cohort of patients submitted to the first ASCT for MM and to evaluate the HCT-CI as a tool to estimate morbidity for patients with MM undergoing ASCT in a Brazilian single-center retrospective cohort. **Methods:** We retrospectively reviewed the charts of patients undergoing the first ASCT for MM from January 2017 to December 2022. The HCT-CI was calculated for each patient, and the outcome of interest (admission to the ICU) was assessed. The HCT-CI test performance, dichotomized as non-high-risk versus high-risk parameters, was estimated for sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value, and negative predictive value. **Results:** The cohort's median age was 61.6 years, with a similar distribution between genders, 96% obtained at least a partial response before the transplant. The HCT-CI was classified as low-risk in 54.2% of participants, intermediate risk in 35.6%, and high risk in 10.2%. 85% underwent conditioning with 200 mg/m^2 melphalan, and 14.1% with 140 mg/m^2. The 3-year Overall Survival (OS) was 80.6% (95% CI 75.4–86.2). The rates of neutrophil and platelet engraftment by D+25 were 98% and 86%, respectively. The transplant-related mortality (TRM) rate was 3.6% (95% CI 2–6) up to D+60. The cumulative incidence of ICU admission in 30 days was 15% (95% CI 11–19). The reasons for ICU admission were cardiac arrhythmia (35.2%), acute respiratory failure (7.4%), septic shock (55.6%), and trauma (1%). The average ICU length of stay was 10.8 days, with 74% being discharged alive. The HCT-CI had a sensitivity of 12.96% (95% CI 5.37–24.9) and specificity of 90.36% (95% CI 86.28–93.55) in predicting ICU admission. The positive likelihood ratio was 1.34 (95% CI 0.62–2.96), and the negative likelihood ratio was

0.96 (95% CI 0.86–1.08). The positive predictive value was 20.59% (95% CI 8.7–37.9), and the negative predictive value was 84.33% (95% CI 79.72–88.26), with a calculated accuracy of 77.84% (95% CI 73–82.18). **Discussion:** Reliable methods to assess patient vulnerability to HSCT are crucial for an informed therapeutic decision. The HCT-CI is often used to assess the risk of morbidity and mortality after transplantation. In our study, the HCT-CI showed low sensitivity and high specificity. Its positive predictive value was only 20%, with 16% of the cohort being misclassified as at risk for the event without experiencing it. Both positive and negative likelihood ratios, which represent the test's ability to correctly influence our thinking about the presence or absence of disease, showed uncertain results and a minimal effect on basic pre-test probability estimates. **Conclusion:** The HCT-CI is not a reliable method to predict HSCT-related morbidity. The need to improve a specific risk score for myeloma is highlighted by these findings. Not assessing the HCT-CI as an ordinal variable, potentially missing optimal cut-point identification via ROC analysis, could be a study limitation.

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CHARACTERIZATION OF A NOVEL ANTI-CD19 CAR CONSTRUCT CO-EXPRESSING THE COSTIMULATORY MOLECULE GITRL

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Adoptive therapy using Chimeric Antigen Receptor T-cell (CAR-T) technology has emerged as a groundbreaking immunotherapeutic approach for treating various hematological malignancies. Among the diverse CAR-T targets, CD19, a B-cell surface marker, has demonstrated remarkable success in treating B-cell malignancies. However, despite impressive clinical outcomes, challenges such as efficacy and insufficient in vivo persistence still exist. To address these limitations, preclinical investigations are exploring the integration of additional co-stimulatory molecules into CAR constructs to enhance effector functions and persistence. GITRL (Glucocorticoid-Induced TNF Receptor Ligand) belongs to the TNF family and is a type II transmembrane protein. The interaction between Glucocorticoid-Induced Tumor Necrosis factor Receptor (GITR) and its Ligand (GITRL) reverses regulatory T cell suppression, leading to enhanced immunity against tumors. Therefore, the goal of this research was to develop and validate a novel CAR targeting CD19, incorporating GITRL as a co-stimulatory domain in the CAR construct. Initially, peripheral blood mononuclear cells (PBMCs) from a healthy donor were activated with CD3/CD28 beads and transduced with the lentiviral particles using an MOI (multiplicity of infection) of 5. Subsequently, the frequency of CAR-T cells expressing the anti-CD19 CAR or anti-CD19 CAR-GITRL was determined by flow cytometry, resulting in 52.4% and 64.9% CAR+ cells, respectively. The CAR-T cells were then assessed for their ability to recognize and selectively eliminate CD19-expressing cancer cells using in vitro cytotoxicity assays. Both anti-CD19 CAR-T cells and anti-CD19 CAR-GITRL-T cells exhibited potent killing of CD19-positive target cells, with lysis percentages of 92.65%±0.01% and 84.31%±0.01%, respectively. In contrast, non-transduced T cells showed minimal or no activity in eliminating the target cells. Importantly, the cytotoxic activity of the CAR-T cells remained strong even upon re-challenge, leading to the elimination of 78.75%± 0.08% and 63.23%±0.17% of CD19-positive cells, respectively. These findings suggest that CAR-T cells did not demonstrate exhaustion, contributing to the durability of the therapeutic effect. To evaluate the in vivo antineoplastic potential of the generated CAR-T cells, we established a disseminated lymphoma model by intravenously injecting Raji cells expressing luciferase into immunodeficient mice. After six days of tumor cell infusion, animals were treated with cellular suspensions containing a suboptimal dose of 2.5×106 anti-CD19 CAR-T or anti-CD19 CAR-GITRL-T cells in 200 μL of PBS (n = 5). A control group received only PBS (n = 6). After 22 days of treatment, all animals in the control group had to be euthanized due to hind limb paralysis caused by lymphoma cell infiltration or due to the loss of at least 20% of initial body weight. Conversely, bioluminescent signal analyses of the groups treated with anti-CD19 CAR-T cells and anti-CD19 CAR-GITRL-T cells demonstrated a reduction in tumor burden by 83.8% and 93%, respectively. This significant reduction highlighted the in vivo antineoplastic potential of the administered cells. The therapeutic effect translated into extended survival of the treated groups, which were monitored for 36 days post-treatment ($p < 0.0001$, Log-rank test). However, there were no significant differences observed between the treated groups. In conclusion, this study underscores the potential of incorporating GITRL as a co-stimulatory molecule in CD19-targeted CAR-T therapy. Further investigations are warranted to elucidate the mechanisms underlying these positive outcomes and to optimize the utilization of CAR-T cells as a potent tool against neoplastic diseases.

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TRANSPLANTE DE MEDULA ÓSSEA: ANÁLISE COMPARATIVA ENTRE AS MODALIDADES ALOGÊNICA E AUTOGÊNICA

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Introdução: O transplante de medula óssea, também chamado de transplante de células tronco hematopoiéticas, é uma modalidade de tratamento potencialmente curativo para doenças malignas e não malignas hematológicas e para alguns distúrbios não hematológicos. O transplante consiste em fornecer ao paciente células tronco/progenitoras que