HISTOPLASMOSE DISSEMINADA EM PACIENTE PÓS-TRANSPLANTE AUTÓLOGO DE CÉLULAS-TRONCO HEMATOPOIÉTICAS

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Introdução: A histoplasmose é uma doença infecciosa com apresentações variáveis, desde uma infecção pulmonar crônica até em formas disseminadas e agudas. Na literatura, a maior parte dos casos relacionados ao Transplante de Células Tronco Hematopoéticas (TCTH) pertencem ao TCTH alogênico. O presente trabalho pretende discorrer sobre a apresentação atípica desta infecção em um paciente com diagnóstico de Linfoma de Hodgkin (LH) Clássico 6 meses após o TCTH autólogo. **Material e métodos:** Relatamos o caso de um paciente assistido em hospital universitário público do interior do Rio Grande do Sul e revisão de literatura em bibliotecas eletrônicas, utilizando os termos "Histoplasmosis in transplant recipients". **Resultados:** Homem, 30 anos, com LH Clássico, subtipo Depleção Linfocitária, Estágio Clínico IV B, desde novembro/21. Realizou 3 linhas de quimioterapia prévias à realização do TCTH, o qual ocorreu em fevereiro/2023 e vinha em uso de Brentuximabe Vedotina a cada 21 dias. Em abril/2023, passou a apresentar sudorese, picos febris vespertinos e perda ponderal. Realizado PET-CT, demonstrando aumento da atividade metabólica de linfonodos cervicais, axilares e retroperitoneais, além de, surgimento de lesões ósseas hipermetabólicas. Internou com quadro de insuficiência respiratória, cuja TC do tórax demonstrou pequenos nódulos distribuídos difusamente em ambos os pulmões, tendo como principal suspeita processo infeccioso, todavia, também devendo-se considerar a possibilidade de se tratar da doença de base. Realizado lavado broncoalveolar, com a presença de hifas hialinas septadas. Coletado material medular para análise patológica e cultura. No mielograma, observaram-se numerosos histiócitos, com restos celulares em meio ao citoplasma e o anatomopatológico mostra comprometimento medular pelo LH. Pesquisa de anticorpo urinário para histoplasmose, com resultado reagente. Realizou terapia com Anfotericina B Complexo Lipídico por 14 dias com excelente evolução clínica. Aguarda atualmente inicio de Pembrolizumabe para tratamento de recaída do LH. **Discussão:** A incidência desta patologia após o TCTH ainda permanece desconhecida, porém se acredita que ela seja rara, ainda mais em paciente submetidos ao transplante autólogo. Durante pesquisa realizada não fora encontrado nenhum relato em paciente com LH Clássico pós TCTH autológo. A apresentação clínica nestes pacientes geralmente inclui sintomas inespecíficos, como febre, fadiga, náuseas, vômitos, perda de peso e anorexia. O padrão ouro para diagnóstico é o isolamento do fungo em meio de cultura. Antígenos para histoplasma podem ser pesquisados na urina ou soro. No que se refere à forma disseminada, o uso do antígeno possui maior sensibilidade, visto haver maior carga de infecção fúngica. Além disso, a depuração do antígeno pode ser usada para monitorar a resposta ao tratamento. O tratamento se pauta no uso de azólicos, os quais possuem ação fungicida e a anfotericina B que causa a morte celular. **Conclusão:** Histoplasmose disseminada é comum em indivíduos imunocomprometidos, porém mais rara em paciente transplantados de medula óssea. A ocorrência em pacientes hematológicos é mais comumente relatada em pacientes submetidos a TCTH alogênicos. Neste caso, relatamos o acometimento de um paciente com histórico de LH, pós TCTH autólogo, com doença atualmente recaída e que teve excelente controle infeccioso com tratamento fungicida.

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GENETICALLY ENGINEERED T CELLS EXPRESSING HIGH AFFINITY TCR ANTI-NY-ESO-1:HLA-A*02 ARE ABLE TO CONTROL SOLID TUMOR GROWTH IN VIVO

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Despite the remarkable success in the use of T cells expressing Chimeric Antigen Receptors (CAR) for hematologic malignances, their application to solid tumors, which represents the majority of neoplasms, remains challenging. However, T lymphocytes expressing artificial T Cell Receptors (TCR) with enhanced affinity, refered as TCR-T cells, have been providing encouraging results against solid neoplasms. Unlike conventional CAR, these receptors are able to recognize intracellular proteins presented by Human Leukocyte Antigen (HLA), expanding the options for therapeutic targets. The NY-ESO-1 is a prominent target in this immunotherapeutic approach due to its restricted expression in healthy cells, its capacity to induce an immune response and its strong expression in tumors of different origins. Therefore, our main goal was the generation of TCR-T cells targeting the NY-ESO-1:HLA-A*02 complex with antitumor capacity. Additionally, it is suggested that the co-expression of both endogenous and artificial TCR may result in TCR hybridization, compromising the efficacy and safety of TCR-T cells. Thus, we also generated NY-ESO-1:HLA-A*02 TCR-T cells modified to concomitant expression of a short hairpin RNA (shRNA) for endogenous TCR silencing (TCR + shRNA- T cells). The lentiviral transduction efficiency (3 donors), evaluated 8–12 days after, was 18.2% (±5.2%) for TCR-T cells and 9.9% (±5.9%) for TCR + shRNA- T cells. The engineered T cells displayed in vitro antitumor activity (1–2 donors) against NY-ESO-1+/HLA-A*02+ human tumor cells (SW982*luc*: synovial sarcoma; A375*luc*: melanoma). The TCR-T cells were able to lyse 67.7% of SW982*luc* or 22.3% (±7.6%) of A375*luc* cells in a co-culture at the 1:1 effector-to-target ratio. Similarly, the TCR + shRNA- T cells lysed 73% of SW982*luc* or 25.6% (±14.2%) of A375*luc* cells. Also, engineered T cells had

no cytotoxic potencial against HCT116*luc* cells (NY-ESO-1−/HLA-A*02+), demonstrating target specificity. Next, we generated an in vivo melanoma model through subcutaneous injection of 1×106 A375*luc* cells in NSG mice and after 6 days the animals (3–5 per group) were intravenously treated with 7×106 engineered T cells or non-transduced T cells (NT T cells) (1 donor). Twenty days after the treatment, the tumor burden of 80% (4/5) of animals treated with TCR-T cells increased up to 1.5 times (average: 4.5 ± 7.7 times) and in 80% (4/5) of the animals that received TCR+ shRNA- T cells this increase was ≤3.4 times (average: 2.4 ± 2.9 times). However, the average tumor burden increased 39.9 times (±35.3) in animals treated with NT T cells and 824.1 times (±1302.1) in untreated mice. From day 20 to 34 post treatment only untreated animals (5/5) had tumors with volume ≥2cm^3 and were euthanized. Collectively, these data demonstrate the successfull generation of T cells expressing high affinity TCR anti-NY-ESO-1:HLA-A*02 with NY-ESO-1 specific and potent antitumor activity. These results lay the groundwork for the development of a new advanced cell therapy product for solid neoplasms and other NY-ESO-1+ malignancies.

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RECURRENT CYTOMEGALOVIRUS REACTIVATIONS: FREQUENCY, VIRAL DYNAMIC AND RISK FACTORS IN ALLOGENEIC STEM CELL TRANSPLANTATION.

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Background: Cytomegalovirus reactivation (CMVi) is a significant concern following allogeneic sStem Cell Transplantation (allo-SCT) and is associated with considerable morbidity and mortality. High immunosuppression increases the risk of CMV reactivation, leading to recurring episodes, and CMV viremia has been associated with high overall and non-relapse mortality rates. **Objective:** This study aims to describe the frequency, the differences in the viral dynamic compared to the first episode, and the risk factors for recurrent CMV (CMVrec). **Methods:** A prospective cohort of 260 allo-SCT transplants, enrolled between 2016 and 2023, underwent CMV screening using quantitative PCR (Qiagen/Abbott) in plasma. The screening began during the first week after SCT and was repeated weekly until D+100. Additional screenings were performed if immunosuppression continued beyond D+100. Recurrent CMV (CMVrec) was defined as a new viremia in a patient with a previous episode who had tested negative for the virus for at least four weeks. **Results:** Among the 260 allo-SCTs, the median age was 41 years (ranging from 2 to 76), and acute myeloid leukemia represented 36%, followed by acute lymphocytic leukemia with 21%. The distribution of Haploidentical (Haplo), Unrelated Donor (URD), and Related Donor (RD) was 110 (42%), 80 (31%), and 70 (27%), respectively. The median follow-up duration was 240 days. CMVi occurred in 189 transplants (73%), with 285 episodes. The frequencies of reactivation in URD, Haplo, and RD cohorts were similar (60%, 76%, and 81%, respectively; p = 0.007). At least one CMVrec occurred in 63 (33%) transplants with CMVi. One, 2, 3, and 4 recurrent episodes were documented in 35 (13%), 20 (8%) 6 (2%), and 2 (1%) transplants, respectively. CMVrec showed lower peak viral load (median 115 vs. 1600 IU/mL; p < 0.001) and shorter duration of viremia (median 8 vs. 37 days; p < 0.001) but similar initial viral load (median 84 vs. 94 IU/mL; p = 0.098) compared to the first episode. CMVrec was more frequent in RD transplants (43.4%) compared to URD (23.9%) and Haplo (32.7%) (p < 0.005). The viral dynamic including first viral load (90 vs. 101 IU/mL; p = NS), peak viral load (1297 vs. 1908 IU/mL; p = NS), duration of viremia (37 vs. 36; p = NS), the median time for the episode (D + 24 vs. D + 26; p = NS) and frequency of treatment were similar (81% vs 86% p = NS) in the first episode from transplants with or without recurrence. **Conclusion:** In our data, the frequency of recurrent CMV was high and the CMVrec episodes had different viral dynamics compared to the first episodes. Characteristics of the first episode were not associated with the frequency of recurrence, except for the type of donor.

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DESCRIPTIVE ANALYSIS OF HEMATOPOIETIC STEM CELL TRANSPLANTS PERFORMED IN A PUBLIC SERVICE BETWEEN 1984 AND 2023

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Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is a treatment modality for some benign and/or malignant diseases that affect blood cells. The first successful HSCT took place in the USA in 1957 and later in Brazil in 1979. Several changes have occurred over the decades from scientific and technological advances. Studies that explore descriptive analysis are important in order to monitor trends and changes over time and generate knowledge for practice and actions in public policies. **Objective:** To describe the characteristics of transplants performed in a public HSCT center. **Material and methods:** This is a descriptive study carried out in a HSCT center that used an institutional database and the Center for International Blood and Marrow Transplant Research (CIBMTR) between July 1984 and June 2023 as a