DRM por citometria na LMA e quais seriam os tempos ideais de avaliação durante o tratamento quimioterápico não eram padronizados até então e precisam ser avaliados em estudos futuros.

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PATTERNS AND PROGNOSTIC IMPACT OF CNS INFILTRATION IN ADULTS WITH NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA

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Acute lymphoid leukemia (ALL) is a subtype of acute leukemia which portends a high risk of central nervous system (CNS) infiltration, which decreases overall survival (OS). Conventional cytology (CC) has been the standard for CNS disease assessment, although flow cytometry (FC) has gained space across several centers. In this study, we intend to: i) access the impact of CNS involvement (defined by CC or FC) on OS, event-free survival (EFS) and relapse of ALL patients treated in a public health center; ii) find variables associated with CNS infiltration. **Methods:** This retrospective study encompassed 105 cases of newly diagnosed ALL at Instituto do Cancer de São Paulo. Data were collected from Leukemia clinic database, approved by Local Ethics Committee. Variables related to cerebrospinal fluid (CSF) were collected from the first lumbar puncture (LP). Traumatic LP was defined as more than 10 red blood cells/μL. CNS status was assessed through the COG's classification and divided into positive/negative. Intensive intrathecal chemotherapy was given in CNS2 or 3 cases, while cranial irradiation was scheduled for CNS3 patients. **Results:** A total of 105 cases were diagnosed from 2014 to 2020. Median age at diagnosis was 37 years (range, 15-79) with a male majority (58%). Most cases had a B-cell phenotype (76%), followed by T (19%) and ambiguous (5%). Philadelphia chromosome was found in 39%. Eighty-nine percent received corticosteroid at the time of LP with a median time of 7 days. Traumatic LP was reported in 50%. CSF was positive for disease in 15% (16/104) and 26% (19/72),by CC and FC, respectively. Among those with a positive CC, 56% (9/16) had a traumatic LP,but they were not statistically correlated ($p = 0.8$). Prior chemotherapy was associated to higher traumatic LP rates (56 vs 31%, $p = 0.019$). CNS1, CNS2 and CNS3 were found in 84%, 14% and 2% of cases, respectively. At the time of PL,44% of patients presented blasts in peripheral blood. By comparing CC and FC, we found one case with CC^{pos}/FC^{neg} whereas 9/19 with FC^{pos} did not have CC^{pos}. Sensitivity and specificity of CC for CNS disease were 53% and 98%. Higher white-blood cell (WBC) counts were found in subjects with positive CC or FC (Mann-Whitney test, $p = 0.007$ for CC). Also, the blast percentage was relevant for CNS positivity ($p = 0.027$). Genetic subgroup, age, CD34 expression and phenotype were not correlated with CNS invasion. Most patients received adapted versions of BFM (n = 43), GRAAPH (n = 24) and GRAALL-Elderly (n = 18) regimens. Median OS for the whole cohort was 16.4 months, with a 3y OS of 42.5% (95% CI 33.5-54). For BFM subset, OS and EFS were 53.5% and 37.3%. We did not find correlation between CNS disease with OS or EFS in univariate analysis. Three-year relapse rate was 38.5% (95% CI 29-49) whereas non-relapse mortality (NRM) was 33%. In multivariate analysis, a positive CC increased relapse rate (HR = 2.3 [95% CI 1.1-4.9, p 0.029]), aswell as initial WBC. Among relapses, only one was isolated in CNS and 13 had also concomitant bone marrow involvement. **Conclusion:** Several studies have demonstrated correlation between CNS infiltration and shorter OS in ALL, even though it relies on how these patients are managed and how CNS is assessed upfront. Our data showed that those with a positive CSF cytology had a higher risk of relapse, whereas FC was not able to discriminate this risk. Survival rates are increasing over the last years by the adoption of a stratified risk strategy. CSF contamination did not increase CNS involvement or relapse rates.

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PERFIL DA EXPRESSÃO DE TERRA E PROTEÍNAS TELOMÉRICAS NA LEUCEMIA MIELÓIDE AGUDA E AUMENTO DA TAXA DE APOPTOSE EM LINHAGENS CELULARES DE LEUCEMIA MIELÓIDE AGUDA COM A DIMINUIÇÃO DE TERRA

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TERRA (do inglês *telomeric repeat-containing RNA*) é um RNA longo não-codificante transcrito a partir das regiões subteloméricas e teloméricas. Os transcritos de TERRA possuem sequências repetidas em tandem ricas em Guanina oriundas das sequências teloméricas TTAGGG e formam híbridos de DNA:RNA nas regiões teloméricas denominados *R-loops*. A alta expressão de TERRA e a formação de R-loops promove dano ao DNA telomérico e, consequente, encurtamento telomérico. TERRA participa de um mecanismo de *feedback* que depende do ciclo celular e do comprimento telomérico. Em telômeros longos, os R-loops são degradados pelas enzimas RNaseH1 e RNaseH2 antes da replicação telomérica, o que permite o alongamento telomérico a partir da telomerase. Em tolemeros criticamente curtos, essas enzimas não são recrutadas, ocorre acúmulo de R-loops, estresse replicativo e ativação de vias de reparo dirigido por homologia. Essas vias promovem alongamento telomérico por via alternativas a telomerase. As leucemias mielóides agudas (LMAs) são caracterizadas pela expansão de células mielóides imaturas e insuficiência da medula óssea. Atualmente, as LMAs são classificadas em 6 grandes grupos: 1) LMAs com alterações