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ACOMETIMENTO NEOPLÁSICO E HEMORRÁGICO DO SISTEMA NERVOSO CENTRAL EM PACIENTE COM LLA PRÓ-B E REFRATARIEDADE PLAQUETÁRIA: UM DESAFIO TERAPÊUTICO

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Introdução: A leucemia linfoblástica aguda (LLA) pró-B em adultos é uma neoplasia hematológica de evolução agressiva, caracterizada por proliferação clonal de linfoblastos e potencial infiltração do sistema nervoso central (SNC). A presença de blastos no líquor no diagnóstico demanda esquemas terapêuticos intensivos com quimioterapia sistêmica e intratecal. Complicações durante o tratamento das leucemias agudas, como hemorragias intracranianas e refratariedade plaquetária, representam desafios importantes para o manejo clínico. **Descrição do caso:** Paciente de 50 anos, previamente diabética, internou com quadro de sintomas inespecíficos, presença de 75 mil leucócitos no sangue periférico e mielograma (11/12/24) com 90% de blastos. A avaliação diagnóstica demonstrou leucemia linfoblástica aguda pró-B, envolvimento do sistema nervoso central (6% de blastos no líquor ao diagnóstico), Ph e KMT2A não detectados no painel molecular, e cariótipo sem crescimento celular. Iniciado protocolo HyperCVAD com profilaxia intratecal. Após o bloco 1A, evoluiu com cefaleia intensa, no contexto de plaquetopenia severa, sendo evidenciado hematoma subdural bilateral por tomografia. A ressonância nuclear magnética de crânio, realizada após avaliação da neurocirurgia, evidenciou, além das coleções subdurais bilaterais heterogêneas com componente hemático recente e efeito de massa discreto, realce paquimeníngeo difuso supratentorial, irregular, com pequenos focos nodulares, e espessamento paquimeníngeo no clivus, sugestivos de disseminação neoplásica. De forma concomitante, teve o diagnóstico de refratariedade plaquetária de origem imune, dificultando o suporte transfusional. Após discussão multidisciplinar, foi tratada com radioterapia hemostática (200 cGy/6 sessões, totalizando 12 Gy, de 17 a 24/01/2025). A paciente evoluiu de forma satisfatória, com SNC negativo. Seguiu o tratamento oncológico com protocolo quimioterápico HyperCVAD, sem maiores intercorrências. Atualmente, encontra-se internada para realização de transplante de células tronco hematopoiéticas haploidêntico, e previsão de irradiação corporal total como parte do regime de condicionamento. **Conclusão:** O caso evidencia uma paciente com diagnóstico de LLA B pró-B de alto risco, associado ao envolvimento inicial do SNC com comprometimento paquimeníngeo e evolução para hematoma subdural. O diagnóstico de refratariedade plaquetária de origem imune dificultou sobremaneira o suporte transfusional, tornando o caso um desafio terapêutico. Após discussão multidisciplinar envolvendo as equipes de hematologia, hemoterapia, radioterapia e neurocirurgia, a paciente foi tratada com radioterapia hemostática. Este procedimento erradicou a doença no SNC, controlou o sangramento, e permitiu uma evolução favorável até o momento.

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ACUTE PROMYELOCYTIC LEUKEMIA IN THE BRAZILIAN PUBLIC HEALTH SYSTEM: A 25-YEAR SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Acute promyelocytic leukemia (APL) is the acute myeloid leukemia subtype with the highest curability when treated with targeted agents such as all-trans retinoic acid (ATRA) and arsenic trioxide (ATO). Despite therapeutic advances, early mortality remains a major challenge, particularly in public institutions with limited access to prompt diagnosis and specialized care. Real-world data from public centers are essential to identify gaps in APL management in Brazil. **Objectives:** To describe the clinical outcomes of an APL cohort over 25 years. **Material and methods:** This retrospective study included adults (≥18 years) with genetic confirmation of APL, consecutively admitted from 2000 to 2025 to a single public referral Cancer Center in Rio de Janeiro. The hospital maintains an on-demand ATRA stock for newly admitted patients. Outcomes were overall survival (OS), non- relapse mortality (NRM), and relapse, analyzed using Kaplan–Meier, cumulative incidence, and Cox models. All analyses were performed in R. The local Ethics Committee approved the study. **Results:** We included 57 patients with a median follow-up of 7.4 years. Fifty-one percent were male. Median age was 37 years; 8 cases were therapy-related. Risk distribution: high (51%), intermediate (35%), low (14%). Thirty-day mortality was 19%, 3.6% in non-high-risk vs. 34,5% in high-risk patients, of which two thirds had hyperleukocytosis above 50.000/mm^3. The distribution of deaths over the 30-day period was 36,4% ≤3, 18,2% 4-8 and 45,5% 9-30 days. The main cause of death within the first week was bleeding and later, infection. NRM at 6 months was 13%, 32%, and 38% for low-, intermediate-, and high-risk groups, respectively; NRM correlated with age (HR = 1.46 per decade; 95% CI 1.13–1.89; p = 0.004) and secondary APL, with 6-month NRM 75% vs. 25% in de novo APL. Five-year relapse was 8%, independent of risk. Five-year OS was 88%, 62%, and 51% for low-, intermediate-, and high-risk groups. In the last decade, >92% initiated ATRA within 24h vs. 64% in earlier years, without significant reduction in 30-day mortality. **Discussion and conclusion:** Survival and relapse rates were comparable to international ATRA-based data, but secondary APL and high-risk presentations were more frequent. While the former is expected in a Cancer Center, the latter likely reflects

referral bias and delayed diagnosis and may be responsible for the high number of patients with hyperleukocytosis. Early mortality remains high, despite despite almost complete coverage of patients receiving ATRA within the first 24 hours of admission in recent years, underscoring the need for improved pre-admission management. NRM during consolidation phases appears to have been influenced by the high incidence of cases related to prior cancer therapy in our cohort and deserves special attention Despite high curability, APL management in the public health system faces structural barriers. Ensuring early diagnosis, rapid referral to experienced centers, as well as intensive supportive care, are critical to reduce mortality and improve outcomes.

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ADVANCES IN CHEMOTHERAPY PROTOCOLS FOR CHILDHOOD LEUKEMIAS: EFFICACY, NEW THERAPIES AND CHALLENGES

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Introduction: Acute Lymphoblastic Leukemia (ALL) represents approximately 75% of childhood leukemia cases, with survival rates now exceeding 90% in high-income countries due to therapeutic advances. This review evaluates recent improvements in chemotherapy protocols, focusing on comparative efficacy between traditional regimens and novel approaches incorporating targeted therapies and immunotherapies. **Objectives:** To analyze survival outcomes, treatment efficacy, and cost-effectiveness of contemporary chemotherapy protocols for pediatric ALL, with emphasis on emerging therapeutic strategies. **Material and methods:** An integrative literature review was performed following the PICCO framework. Searches in PubMed and Cochrane databases employed Boolean operators, limited to studies published within the last five years. Selection criteria included clinical trials and systematic reviews addressing pediatric ALL treatment in hospital settings, while excluding diagnostic or prophylactic studies. After PRISMA-guided screening and duplicate removal, 13 studies met inclusion criteria. **Results:** The analysis revealed significant progress in treatment protocols. The ALL-B12 regimen demonstrated superior survival rates (≥90%) through intensified chemotherapy combining pulsed vincristine/dexamethasone with high-dose methotrexate and PEG-asparaginase, while showing reduced toxicity compared to conventional asparaginase. Immunotherapies exhibited remarkable outcomes, particularly in high-risk and relapsed cases. Blinatumomab improved survival rates while proving more cost-effective than standard chemotherapy. CAR-T cell therapy (tisagenlecleucel) achieved durable remission in refractory cases, and inotuzumab ozogamicin showed high response rates in relapsed B-cell ALL. The combination of venetoclax with chemotherapy enhanced survival in relapsed AML. Despite these advances, higher costs and infrastructure requirements for novel therapies pose challenges for implementation in resource-limited settings, highlighting disparities in global accessibility. **Discussion and conclusion:** Contemporary treatment protocols integrating chemotherapy with immunotherapy and targeted agents have transformed pediatric ALL management, particularly for high-risk cases. While therapeutic innovations show promising efficacy and safety profiles, equitable access remains a critical challenge. Future research should address cost barriers and optimize implementation strategies to ensure global benefit.

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ALBUMIN SERUM LEVEL AND INTENSITY OF PRE-PHASE CYTOREDUCTIVE THERAPY ARE MODULATORS OF EARLY MORTALITY IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute lymphoblastic leukemia (ALL) in adults has a substantial mortality within 30 days of diagnosis, defined as early mortality (EM). EM in ALL demonstrates relevant disparities between low-middle income countries (LMICs) and high-income, with reported rates of 10-25% versus <5%, respectively. This mortality gap persists due to multiple factors, exemplified by intensity of induction protocol, social disparities and others, but the precise contributors to elevated EM in LMICs remain poorly defined. **Objetivos:** Identify independent risk factors for EM in adult ALL patients in a high-complexity cancer treatment center in São Paulo, with focus on pre-therapeutic biomarkers and treatment intensity. **Material and methods:** Retrospective cohort study (2009 −2023) including adult patients (≥ 15 years) with newly diagnosed ALL or ambiguous lineage leukemia. Pre-phase regimens varied between corticosteroid alone and corticosteroid plus cyclophosphamide. Data were analyzed using Kaplan-Meier survival estimates and competing-risk methods for 60-day outcomes. Univariate and multivariable logistic regression identified EM risk factors; variables with $p < 0.2$ in univariate analysis or clinical relevance were included in the multivariable model, selected by lowest Akaike Information Criterion. A two-sided $p < 0.05$ denoted significance. **Results:** Of 203 patients (median age 36 years; 54.2% male; 76% B-cell phenotype; 34% Philadelphia chromosome−positive), 89.8% underwent corticosteroid-only pre-phase (prednisone 49.7%, dexamethasone 16.4%, methylprednisolone 1.6%), and 32.2% received cyclophosphamide + dexamethasone. The overall EM rate was 9.8% (95%CI:6.3-15.0). In univariate analysis, low