associated with increased HbF concentration and milder clinical phenotypes in children with SCA. Moreover, we found HbF-boosting haplotypes formed by these SNPs to be associated with reduced rate of clinical outcomes in children with SCA: BCL11A haplotype with the minor alleles of rs1427407, rs766432, and rs4671393 ("TCA") was associated with higher HbF, total hemoglobin, and lower reticulocyte count compared to reference haplotype "GAG"; the HBS1L-MYBhaplotype with the minor alleles of rs9399137, rs4895441, and rs9494145 ("CGC") was associated with higher HbF and total hemoglobin compared to reference haplotype "TAT". We further found that these HbF-boosting haplotypes may interact to regulate HbF levels. However, no previous study has examined their interaction and association with risks of vaso-occlusive and hemolytic complications of SCA. Objective: We examined whether the interaction of HbF-boosting haplotypes of BCL11A and HBS1L-MYB modifies their individual effect on the rate of transfusion, acute chest syndrome (ACS), pain crisis, infection and acute splenic sequestration (ASS). Methods: We analyzed a retrospective cohort of 220 unrelated children with SCA recruited from the Center of Hematology and Hemotherapy of Minas Gerais State. Haplotype frequencies were estimated using Haplo.stats. Reference and minor haplotypes combined wild-type and minor SNP alleles for BCL11A (GAG or TCA) and HBS1L-MYB (TAT or CGC), respectively. We grouped children who carry ("TCA+"or "CGC+") or not carry ("TCA-"or "CGC-") the "TCA"and "CGC"minor haplotypes, respectively. Incidence of clinical outcomes was reported by relative rates to 10 patient-years, with 95% confidence intervals. Incidence Rate Ratio of clinical outcomes was compared between haplotype combinations using OpenEpi online software. Cumulative incidence of ASS was estimated using Kaplan –Meier and logrank test to compare the incidence between haplotypes using SPSS. Results: Non-carriers of both HbF-boosting haplotypes (TCA-/CGC-) had a significantly higher need for transfusion than children carrying only the HbF-boosting haplotype of BCL11A (TCA+) or those carrying both HbF-boosting haplotypes (TCA+/CGC+). Regarding ACS and infection, non-carriers of both HbF-boosting haplotypes (TCA-/CGC-) had a significantly higher risk of events than children carrying only the BCL11A (TCA+) or HBS1L-MYB (CGC+) haplotypes. Carriers of both HbF-boosting haplotypes (TCA+/CGC+) did not show significant lower rate of ACS and infection. Cumulative incidence of ASS was marginally significant lower (P = 0.051) in children carrying only the HbF-boosting haplotype of BCL11A (TCA +/CGC-) than the HBS1L-MYB (TCA-/CGC+) or non-carriers of both haplotypes (TCA-/CGC-). Discussion: Our findings showed that the presence of the HbF-boosting haplotypes don't make a difference in rate of ACS, ASS and infection. On the other hand, our data support that the presence of, at least, one of the HbF-boosting haplotypes are related to lower rates of transfusion. Conclusion: Therefore, our novel findings contribute to understand multilocus interactions underlying molecular basis of major clinical events of SCA.

https://doi.org/10.1016/j.htct.2024.09.1082

RESPOSTA À TERAPIA IMUNOSSUPRESSORA EM CRIANÇAS COM ANEMIA APLÁSTICA E HEMOGLOBINÚRIA PAROXÍSTICA NOTURNA

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Objetivos: Avaliar a presença de clone de Hemoglobinúria Paroxística Noturna (HPN) em crianças com Anemia Aplástica grave (AAG) e sua correlação como fator preditor de resposta à terapia imunossupressora (TI). **Materiais e métodos:** Estudo retrospectivo, baseado em coleta de dados de prontuários de pacientes pediátricos com AAG, tratados no Hospital Infantil Darcy Vargas de 2003 a 2021 e que receberam terapia imunossupressora com timoglobulina de cavalo ou de coelho associada a ciclosporina. Todos os pacientes incluídos realizaram citometria de fluxo para HPN ao diagnóstico ou em algum momento durante o seguimento. Considerado clone HPN positivo se > 0,15% em neutrófilos ou monócitos, e a resposta terapêutica foi avaliada aos 6 e 12 meses do início da TI. Para verificar a correlação da presença de clone HPN como fator preditor de resposta à TI realizado teste exato de Fisher. **Resultados:** Participaram do estudo 35 pacientes, de 2 a 17 anos, com média de 10 anos (±3,81), sendo 80% do sexo masculino. Todos os pacientes tinham DEB teste negativo e citogenética de medula óssea normal. Clone HPN foi encontrado em 53,1% dos pacientes. Dos 35 pacientes que participaram do estudo, ocorreram três óbitos precoces, assim, 32 pacientes tiveram resposta à imunossupressão avaliada 6 meses após início do tratamento e em 30 pacientes foi avaliada a resposta aos 12 meses, pois um paciente perdeu seguimento e outro realizou transplante de medula óssea. O tempo de seguimento variou de 7 meses a 13 anos, com média de 6,1 anos (±3,53). O clone permaneceu estável em 58,8% dos casos, aumentou em 17,7% e diminuiu ou desapareceu em 23,5%, nenhum paciente com ausência de clone HPN ao diagnóstico positivou durante o acompanhamento. Dos 32 pacientes avaliados aos 6 meses, 13 (40,6%) tiveram resposta parcial à TI e nenhum resposta completa. Aos 12 meses, 15 (50%) pacientes responderam, sendo, 11 com resposta parcial e 4 com resposta completa. Aos 6 meses houve resposta à TI em 10 (58.8%) dos 17 pacientes com clone HPN e apenas em 3 (20%) dos 15 pacientes sem clone HPN (p = 0,036) e aos 12 meses, houve resposta em 11 (68.8%) dos 16 pacientes com clone HPN e em 4 (28,6%) dos 14 sem clone (p = 0,065). **Discussão:** A HPN clássica é rara na pediatria, porém sua associação com AA é semelhante a encontrada em adultos. Existem poucos estudos em crianças que avaliaram a presença de clone HPN na AAG e sua relação com resposta à TI. Outro ponto importante é a definição do tamanho do clone HPN, pois a falta de padronização nos estudos em definir o tamanho do clone a ser considerado, pode se tornar um viés na correlação com a resposta terapêutica. Nesse estudo, encontramos clone HPN em 53,1% dos pacientes com AAG, semelhante ao encontrado na literatura exclusivamente pediátrica, com variação de 39-73%. Em adultos diversos estudos correlacionam a presença do clone a melhor resposta à TI, entretanto na pediatria esta boa correlação permanece discutível, uma vez que os poucos estudos diferem entre si, sendo o nosso estudo mais um a verificar que a presença de clone HPN pode ser um preditor de

boa resposta à TI em pacientes pediátricos. **Conclusão:** Muito há ainda para se entender sobre a associação de AA e HPN, porém a pesquisa de clone HPN em todos os pacientes pediátricos com AA deve ser realizada ao diagnóstico, podendo predizer maior chance de resposta à imunossupressão.

https://doi.org/10.1016/j.htct.2024.09.1083

IMPACT ON LEUKEMIC TRANSFORMATION OF HYPERDIPLOID KARYOTYPE IN PEDIATRIC MYELODYSPLASTIC SYNDROME

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Introduction: Myelodysplastic syndrome (MDS) comprises a heterogeneous group of clonal hematopoietic stem cell diseases. MDS is characterized by bone marrow dysplasias, peripheral blood cytopenias, and has an increased risk of progression to acute myeloid leukemia (AML). MDS mainly affects elderly patients over 65 years of age and it is rare in childhood. Clonal cytogenetic alterations are found in 30-70% of cases. The most frequent chromosomal abnormalities in pediatric MDS are alterations on chromosome 7 [-7/del(7q)]. Given the importance of karyotype in the prognosis of patients with MDS, it has been incorporated into prognostic risk systems. The most recent is the Revised International Prognostic Scoring System (IPSS-R). Karyotype is classified into five prognostic risk groups according to the IPSS-R: very good, good, intermediate, poor, and very poor. Hyperdiploidy is considered a rare karyotype in pediatric MDS. Therefore, its prognostic impact has not yet been elucidated. **Objective:** To report hyperdiploid karyotypes in children with MDS and their impact on the progression from MDS to AML. **Material and methods:** This study included five pediatric patients with MDS in a cohort of 200 patients. Chromosomal and clinical studies were performed between 2000-2023. Cytogenetic analyses were performed on bone marrow cells by G-banding and fluorescence *in situ* hybridization (FISH) according to the International System for Human Cytogenomic Nomenclature (2020). **Results:** The frequency of hyperdiploid karyotype was 2.5% of all cytogenetically analyzed cases (5/200). This chromosomal pattern was divided into two groups: patients with only chromosomal gains (3/5) and patients with structural alteration (2/5). The structural alterations associated with hyperdiploidy were: dup(1q) (one patient), der(6)del(6)(q21) and der(12)del(12)(p11) (one patient). Most of these patients had advanced subtypes with severe pancytopenia and hypocellular BM. All of these patients were indicated for allogeneic hematopoietic stem cell transplantation (HSCT), but four progressed to AML and three died before HSCT. Only two patients underwent HSCT; the patient with the initial subtype responded well to HSCT and is still alive. The patient with hyperdiploidy and structural alteration had cytogenetic and clinical relapse after HSCT and died. **Discussion:** Hyperdiploidy can be divided into two main subtypes: high hyperdiploidy (51-65 chromosomes) associated with favorable prognosis, and low hyperdiploidy (47-50 chromosomes) related to unfavorable prognosis in acute leukemias of childhood. In MDS, the hyperdiploid karyotype is rare. In this study, we describe 5 cases of hyperdiploid karyotype. According to the IPSS-R, hyperdiploid karyotypes are classified into the group of poor and very poor prognosis (three or more chromosomal alterations). In our study, hyperdiploidy was observed in the initial subtype and advanced subtypes. However, HSCT was successful only in the patient presenting the initial subtype. **Conclusion:** Hyperdiploid karyotype is a rare cytogenetic event in pediatric MDS. This karyotypic pattern was mainly associated with advanced subgroups and progression to AML. Our results suggest that hyperdiploidy in pediatric MDS is a predictive marker of leukemic progression and can be used to indicate these patients for HSCT, the only potentially curative treatment for patients with MDS. **Supported by:** : Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro – FAPERJ (E-26/201.2018/2022).

https://doi.org/10.1016/j.htct.2024.09.1084

OSTEOPETROSE MALIGNA DA INFÂNCIA: RELATO DE CASO

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Introdução: Osteopetrose é um grupo de displasias ósseas raras e hereditárias, caracterizadas pelo aumento da massa óssea. Há diferentes subtipos e pode se manifestar de forma leve a fatal. A osteopetrose maligna da infância possui alta morbimortalidade, com formas graves surgindo logo após o nascimento. **Objetivos:** Descrever características clínicas, radiológicas e laboratoriais de uma paciente com Osteopetrose Maligna e realizar uma revisão bibliográfica não sistemática com base em artigos publicados em banco de dados de periódicos nacionais e internacionais nos últimos dez anos. **Relato do caso:** Lactente de 1 ano e 10 meses, previamente hígida, foi diagnosticada com anemia grave e plaquetopenia leve em exames pré-operatórios para correção de craniossinostose, sendo encaminhada para investigação pela Hematologia Pediátrica. Além da craniossinostose, apresentava esplenomegalia e sangue periférico leucoeritroblástico. O aspirado e a biópsia de medula óssea foram tecnicamente difíceis de serem realizados e imediatamente levantaram a suspeita de osteopetrose, a imunofenotipagem afastou leucemias. O inventário radiológico revelou aumento difuso da densidade óssea, com imagens características de osteopetrose, como vértebras em sanduíche. A tomografia de crânio mostrou hipertensão intracraniana compensada, com sinais de compressão de canal auditivo, órbita e nervo óptico; ainda sem manifestações clínicas, exceto pelo papiledema. Além de anemia, leucocitose e plaquetopenia, hipocalcemia e hiperfosfatemia também foram encontradas. A paciente foi encaminhada para avaliação pelo centro transplantador em cinco meses após o diagnóstico, para ser submetida ao transplante