rara. Os auto-anticorpos, na maioria monoclonais, da classe IgM e cadeia leve K destroem os eritrócitos via ativação do complemento, a 4°C. O TAD poliespecífico é positivo e monoespecífico positivo para C3d, título de crioaglutinina ≥ 64 a 4° C e ausência de doença maligna na clínico e/ou radiológico. Sob baixas temperaturas, 90% manifestam acrocianose e fenômeno de Raynaud. Observa-se doença linfoproliferativa clonal medular: linfoma linfoplasmocitário, linfoma da zona marginal, linfoproliferação clonal não classificada e a linfocitose reativa, gamopatia monoclonal de significado indeterminado e macroglobulinemia. A Imunofixação sérica, quantificação de classe de imunoglobulina, citometria de fluxo e biópsia de medula óssea caracterizam o clone. Se negativos não excluem o diagnóstico. O manejo envolve medidas comportamentais, tratamento da infecção bacteriana, reduzir o conteúdo plasmático do hemotransfundido, a plasmaférese realiza o clerance do auto-anticorpo, uso de imunoterapia ao clone: anticorpo anti-CD20 isolado ou associado a fludarabina ou a bendamustina. O anticorpo monoclonal anti-C1s, inibe a via clássica do complemento. **Conclusão:** A CAD é uma AHAI rara, com panaglutinação eritrocitária a 4°C, com diagnóstico laborioso e alta morbimortalidade na ausência de tratamento adequado.

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PATHWAYS ALTERED DURING VASO-OCCLUSIVE EVENTS ARE AMELIORATED BY TREATMENT WITH HYDROXYUREA IN SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is an inherited multisystem blood disorder that produces sickle-shaped erythrocytes that obstruct blood flow, leading to severe clinical complications, including painful vaso-occlusive events (VOE). VOE are often initiated by adhesive interactions between sickle erythrocytes, leukocytes and endothelial cells. Hydroxyurea (HU), a disease-modifying therapy approved for pediatric and adult patients with SCD, increases fetal hemoglobin (HbF) levels, and has been demonstrated to reduce the frequency of pain crises. Much of the research into HU focuses on HbF induction; however, HU has many other effects, which can be investigated through transcriptomics. **Objective:** Describe transcriptome changes in erythroid precursor cells with VOE, and correlate these with pathways affected by treatment with hydroxyurea. **Methods:** Samples were obtained on an IRB approved protocol. CD71+ cells were collected using magnetic bead extraction from 141 patients with SCD during steady state or during hospitalization for a VOERNA-Seq was performed with a 101-base pair, paired-end protocol on a NovaSeq 6000 instrument. The R package SNM was used to adjust for the effect of multiple covariates. Differential gene expression analysis was performed using limma; genes with a Benjamini-Hochberg p-value < 0.05 were considered to be differentially expressed. The R package fgsea was used for gene set enrichment analysis with the Molecular Signature Database as reference. Whole-blood samples from 23 patients with SCD were collected before HU treatment (age < 21 years) and at the maximum tolerated dose of hydroxyurea (HU MTD). RNA-Seq was carried out with a 150 base pair, paired-end protocol. SNM was used to adjust for the effects of age, sex, and cell-type abundances on gene expression. Differential gene expression and biological pathway enrichment analyses of the pre- HU and HU-MTD samples were performed using limma and fgsea. **Results:** We performed gene expression profiling of CD71+ cells to determine differentially expressed genes between steady state and VOE; 373 genes were upregulated, and 68 genes were downregulated at VOE. Pathways associated with cell proliferation, such as G2M checkpoint, E2F targets and mitotic spindle were upregulated at VOE when compared to steady state. IL6 JAK STAT3 signaling and interferon alpha response pathways were elevated at VOE in comparison with steady state. Samples collected pre-HU versus HU-MTD revealed that 1563 genes were upregulated, and 561 genes were downregulated. Genes known for their anti-inflammatory effects, such as TNFAIP3 and ADORA2A, exhibited increased expression after treatment. HU downregulated genes associated with heme metabolism and interferon alpha response pathways. **Conclusions:** Samples collected during a VOE showed significant changes in the CD71+ transcriptome when compared with steady state. Multiple pathways linked to inflammation were elevated at VOE; these pathways are downregulated after treatment with HU, indicating that treatment with HU offers several benefits not directly linked to HbF induction that may reduce VOE severity.

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MODULAÇÃO DA ATIVIDADE DE SUPERÓXIDO DISMUTASE PELA HIDROXICARBAMIDA EM PORTADORES DE ANEMIA FALCIFORME

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Objetivo: Este estudo teve como objetivo investigar a atividade da enzima antioxidante Superóxido Dismutase (SOD) em portadores de AF em uso e não uso de hidroxicarbamida (HC) e um grupo de indivíduos sem hemoglobinopatias, com a finalidade de avaliar a possível modulação do medicamento sobre uma via enzimática associada à homeostase redox. **Materiais e métodos:** Para tanto, foram investigados 43 indivíduos organizados do seguinte modo: 25 indivíduos portadores de AF que fizeram uso da HC; 12 indivíduos portadores de AF que não fizeram uso da HC e seis indivíduos saudáveis. O ensaio foi realizado utilizando o kit de atividade de SOD (Sigma-Aldrich), que determina a inibição da enzima xantina oxidase pela SOD, utilizando hemolisados preparados de amostras do sangue periférico dos participantes. Os grupos foram comparados por teste *one way* ANOVA, seguido de teste