WARM AUTOIMMUNE HEMOLYTIC ANEMIA ASSOCIATED WITH EPSTEIN BARR VIRUS INFECTION

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Introduction: Autoimmune hemolytic anemia (AIHA) is a disease mediated by autoantibodies, with or without complement involvement. The clinical presentation varies from mild forms with compensated hemolysis to severe forms with life-threatening risk. Warm AIHA occurs in 60-70% of cases, while cold forms occur in 20-25%. Epstein Barr Virus (EBV) has a well-established connection with cold AIHA, but it is not clear how EBV induces warm antibodies agglutination. Objective: To report a rare case of warm AIHA associated with EBV. Methodology: Descriptive study of a single case conducted through data collection recorded in the hospital's operational system. **Results:** A 54-year-old female patient was admitted to the Emergency room with weakness, lethargy, dyspnea, abdominal pain, painful ulcerative lesions of the oral mucosa, splenomegaly, cervical and retroperitoneal lymphadenopathy, that started one month before admission. Initial laboratory tests revealed hemoglobin 5.4 g/dL, hematocrit 15.5%, mean corpuscular volume 94fL, mean corpuscular hemoglobin 32.7pg, red cell distribution width 20.9%, leukocytes 11,400/mm^3 (neutrophils 4275; lymphocytes 5905); platelets 158,000/mm^3, C-reactive protein 22.7 mg/dL, creatinine 2.47 mg/dL (baseline 0.78), with no liver abnormalities. Further investigations revealed positive direct antiglobulin test 4 + with high titles of IgG, slightly elevated lactate dehydrogenase, consumed haptoglobin and increased reticulocytes. Rheumatological causes were ruled out, cryoglobulins were negative, but positive IgM for EBV was identified. A diagnosis of severe AIHA associated with EBV was established. Initially treated with methylprednisolone 1 g/day for 3 days, and prednisone 1 mg/kg/day for the following 7 days. Due to hematimetric decline and the risk of clinical deterioration, the patient received 1 g/kg/day Immunoglobulin with good clinical and laboratory evolution. The patient was discharged and followed up as an outpatient, with complete weaning of corticosteroid therapy, complete improvement of the blood count and negative tests for hemolysis. **Discussion:** Secondary warm AIHA, as presented in this case, is strongly associated with chronic conditions such as rheumatological disorders, immunodeficiencies, chronic lymphocytic leukemia, non-Hodgkin lymphoma, and solid tumors; medications, antibiotics, chemotherapeutic agents and infections, mainly viral. The reported case demonstrated warm autoantibodies probably due to EBV infection, which is rarely described. Other causes of AIHA were excluded after extensive etiological investigation, leading us to conclude that the probable etiology of warm AIHA in this case was due to EBV infection, which is poorly described in the literature. **Conclusion:** We presented a rare case of severe AIHA, mediated by warm antibodies in association with EBV infection. There was a worsening of laboratory results during conventional management with corticosteroid therapy, but with good evolution after treatment with Immunoglobulin, a new pulse therapy and clinical management of EBV infection. To the best of our knowledge, this is the third case of warm AIHA associated to EBV described. Due to the low frequency of this association, the physiopathological mechanisms of warm antibodies agglutination caused by EBV are still not clarified in the literature.

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ANEMIA HEMOLÍTICA INDUZIDA POR ALECTINIB – UM RELATO DE CASO

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Introdução/Objetivos: Anemia hemolítica induzida por drogas é uma causa rara de anemia associada a um amplo espectro de medicamentos, dos quais se destacam antimicrobianos. Neste relato descrevemos um caso de anemia hemolítica associada ao uso de Alectinib - inibidor de quinase de linfoma anaplásico (ALK) de segunda geração. **Materiais e métodos:** trata-se de um relato de caso acerca de rara etiologia de anemia hemolítica. Para este fim, os termos contidos na Declaração de Helsinque foram respeitados. **Resultados:** K.A.S.C, sexo feminino, 30 anos de idade, portadora de adenocarcinoma de pulmão com metástase cerebral e de Doença de Graves. Faz uso de Alectinib (600 mg 12/12horas) há 2 anos e 3 meses e Tapazol 5 mg/dia. Encaminhada ao hematologista devido anemia com aumento dos níveis séricos de desidrogenase lática. Ao exame físico: regular estado geral, corada, afebril, sem visceromegalias, traube livre. Exames laboratoriais (03/07/2023): Hb: 10,5; VCM 89; RDW: 14%; Leucócitos: 6.930; Plaquetas: 296.000; Haptoglobina 136 (36-195); Reticulócitos: 3,5%; Ferritina: 101; ácido fólico > 24; saturação de transferrina: 18% (15-50%); Ferro sérico: 77; Teste da antiglobulina direto: negativo; DHL: 389 (135 – 214); Bilirrubinas totais: 0,74, Bilirrubina indireta: 0,54; Creatinina 0,8; Esfregaço de sangue periférico: observados acantócitos e esferócitos. Considerando importância do inibidor de ALK no presente contexto, definido por conduta expectante no momento. **Discussão:** Alectinib, inibidor de ALK de segunda geração, induz hemólise com alterações morfológicas em eritrócitos, como acantócitos e esferócitos, em todos os casos com exposição prolongada à droga. Até a presente data, não há descrição do mecanismo exato de hemólise induzida pelo alectinib. A presença de anormalidades morfológicas nas hemácias sugere envolvimento do citoesqueleto como potencial mecanismo deflagrador da hemólise. Na maioria dos eventos a hemólise é subclínica, ocorrendo nos primeiros 90 dias de uso do inibidor de ALK. Existem raros casos desta associação relatados na literatura. **Conclusão:** Há um subdiagnóstico desta alteração devido à falta de conhecimento por parte dos médicos sobre

tal efeito adverso. Portanto, monitorização hematológica deve ser realizada de rotina em pacientes que estejam em uso de Alectinib.

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CARDIOVASCULAR BIOMARKERS IN SICKLE CELL DISEASE – CLINICAL AND ECHOCARDIOGRAPHIC CORRELATIONS IN A CROSS-SECTIONAL STUDY WITH 126 PATIENTS

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Introduction: Cardiac biomarkers can be useful in understanding the systemic and heart manifestations of sickle cell disease (SCD). Biomarkers reflect various aspects of heart disease (remodeling, injury and myocardial strain), with discriminatory potential for non-cardiac complications. **Patients and methods:** SCD patients (SS/Sβ^0) in steady state, were studied, correlating clinical manifestations and echo parameters (myocardial work - MW and speckle tracking), pre-MSCD severity score (integrating clinical and echo data), and cardiac biomarkers (high-sensitivity troponins – hs-cTn I and T, NT-pro-BNP, ST2s, and galectin-3 - GAL3). Quantitative characteristics were analyzed by Spearman tests, and qualitative characteristics by Mann-Whitney test. Hemolytic Index (HI) was calculated through Principal Component Analysis. Generalized linear Poisson models were generated for hs-cTn, and γ-distribution models were employed for other markers, with final models selected through the Stepwise Backward method. **Results:** We studied 126 patients (mean age 37.2 ± 11.6 years), 42.1% male, and 80.2% SS. 47% were on hydroxyurea treatment and 30.2% on a chronic transfusion. NT-pro-BNP was elevated in 44% (> 160 ng/mL in 37%), correlated with female gender ($p < 0.001$), severity score ($p = 0.001$), uric acid ($p = 0.017$), HI ($p < 0.001$), Global Work Index (GWI) ($p = 0.003$), left atrial (LA) stiffness ($p = 0.003$), and ventricular mass (VM) ($p = 0.02$). ST2s were elevated in 11% and correlated with male gender ($p > 0.001$), HI ($p > 0.001$), cardiac index ($p = 0.015$), and LA strain reservoir function ($p = 0.034$). GAL3 was elevated in 42.8%, correlated with E/e'ratio ($p = 0.006$), uric acid ($p = 0.005$), and absence of chronic pain ($p = 0.046$). hs-cTn correlated with age (c-TnI $p = 0.004$; c-TnT $p > 0.001$), HI ($p > 0.001$), diastolic dysfunction ($p > 0.001$), left VM ($p < 0.001$), increased GWI ($p < 0.001$), and reduced MW efficiency ($p < 0.001$). hs-cTn I also correlated with increased LA reservoir function ($p < 0.001$) with reduced conduit function ($p < 0.001$). hs-cTn T correlated with uric acid ($p = 0.001$), and in univariate analysis was also correlated with severity score. The values of both hs-cTn correlated with increased GWI ($p < 0.001$) and reduced MW efficiency ($p < 0.001$). **Discussion:** The biomarkers demonstrated various clinical and pathophysiological aspects of SCD. NT-pro-BNP is a routine marker with correlations similar to literature, except for higher values in females, also observed in non-SCD population. ST2 and GAL3 had limited correlations with echo findings, likely due to their production in extracardiac tissues affected by inflammation/vaso-occlusion. Both were linked to the HI, and the decrease in GAL3 in chronic pain can be attributed to chronic opioid use causing reduced synthesis of it. The elevation of hs-cTn was expected due to the analytical characteristics of high-sensitivity assays, but low in terms of the extent of heart involvement. hs-cTnT was more associated with general severity, like in the general population, where it is associated with overall mortality, while hs-cTnI is more connected to heart disease. MW in SCD is optimized to the maximum with a very low Global Work Wasted, and hs-cTn elevation is associated with reduced MW efficiency, indicating mecano-energetic uncoupling and subtle systolic dysfunction. **Conclusion:** Our study demonstrates that cardiac biomarkers can be used for clinical and pathophysiological evaluation, with NT-pro-BNP confirming its role in clinical stratification. ST2s and GAL3 may reveal new pathophysiological pathways in hemolysis and the interaction of opioids and chronic pain. Troponins are promising as prospective tool and may unveil ischemic damage resulting from myocardial mecano-energetic dissociation.

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JORNADA DO PACIENTE COM TALASSEMIA BETA NO BRASIL: PERCEPÇÕES DO TRATAMENTO

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Introdução/Objetivos: A talassemia é um tipo de anemia hereditária que faz parte de um grupo de doenças do sangue chamadas hemoglobinopatias. A jornada do paciente envolve diversas etapas e mapear sua experiência é fundamental para encontrar formas de atuar e discutir melhorias no tratamento e garantir que todos os pacientes sejam atendidos, de forma correta, nos centros de tratamento. Este estudo tem como objetivo analisar as perspectivas e mapear os desafios encontrados durante a jornada do paciente com Talassemia. **Material e métodos:** Estudo observacional e descritivo baseado na