comprometimento das funções renal e hepática além de reação leucoeritroblástica ou pancitopenia, quadro apresentado por nossos pacientes embora nossos casos destoem da literatura quanto ao genótipo, onde apenas 15% são HbSS. Suspeitar do diagnóstico é fundamental para o desfecho dos casos. Na suspeita, a instituição rápida de terapia transfusional, para reduzir HbS, é determinante para a sobrevida. Uma revisão sistemática descreveu mortalidade de 29, 61 e 91% para quem recebeu troca, reposição ou nenhuma transfusão, respectivamente. **Conclusão:** A falta de suspeita diagnóstica dificulta o reconhecimento da síndrome, determinando taxas altas de mortalidade. Familiaridade com o quadro clínico e início imediato de terapia transfusional têm se mostrado os únicos indicadores de sobrevida.

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EVOLUTIONARY HISTORY OF THE APEX1 GENE: FROM VERTEBRATES TO SICKLE CELL ANEMIA

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Objective: In sickle cell anemia, it is known that the *APEX1* gene, which encodes the APE1 protein, plays several roles, including DNA strand repair and redox functions, and it is highly expressed during the inflammatory process. The present study sought to investigate how conserved the *APEX1* gene is in vertebrates. **Methods:** For this, the coding sequences of the APEX1 gene were obtained by searching genomic databases at the NCBI, with 14 sequences (*Pan troglodytes, Macaca mulatta, Homo sapiens*, *Bos taurus, Cervos elaphaus, Gallus gallus*, *Lagopus muta*, *Petromyson marinus, Felis catus, Rattus norvengicus, Alosa alosa, Dermochelys coriacea, Caretta caretta, Trachemys scriptaelegans)* being chosen, using up to 300 amino acids as a selection criterion. After the sequences of the species were aligned using MAFFT v7.407 software, the quality of the sequences was verified and the aligned regions without divergence information were removed using Gblocks. Following this, phylogenetic trees were constructed using the MEGA-X software using the Maximum Likelihood method with 1,000 bootstraps. The generated phylogenies were edited using the FigTree version 1.44 program. **Results and discussion:** A similarity in gene conservation has been observed in Primate species (*Pan troglodytes*, *Macaca mulatta*, and *Homo sapiens*). There was a grouping in the same clade of the species, *Bos taurus* and *Cervus elaphus*; the same happened with the order Galliforme (*Gallus gallus* and *Lagopus muta*) and among the studied reptile species. The vertebrate that presented the least evolutionarily conserved gene was the marine lamprey (*Petromyson marinus)*. According to the findings, *APEX1* is linked to the oxidative stress pathway in diseases such as sickle cell anemia, preventing further oxidative damage and regulating transcription factors involved in the redox process. Interesting to note is the existence of sicklings of erythrocytes in deer; however, the genetic basis of the phenomenon is still unknown. It is, however, evident that sickling and the *APEX1* gene may be related in an adaptive manner. There was a genetic distance of seventy for the *APEX1* gene in *Felis catus*, which suggests that the presence of sickle erythrocytes is not related to the type of hemoglobin since feline hemoglobin contains six additional sulfhydryl groups compared to human hemoglobin. As for reptiles, grouped into a single clade, it is known that they may have sickled erythrocytes, however, unlike Primates, these are nucleated. Unlike the other groups, the capillary diameter in reptiles is greater, which in turn could favor a decrease in vaso-occlusive processes. The inflammatory process in vertebrates is accompanied by a series of cellular and molecular mechanisms that can trigger different costs, which are optimized by the forces of natural selection. **Conclusion:** The sickling of erythrocytes, which can culminate in inflammatory events, is common in some groups of the animal kingdom. It increases the expression of the *APEX1* gene, which has been shown to be evolutionarily more conserved in animals with similar erythrocyte sickling mechanisms, suggesting that it has evolved convergently to protect against oxidative stress.

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PATIENTS WITH SICKLE CELL DISEASE TREATED WITH HIDROXIUREA HAVE HIGHER EXPRESSION OF PD-L1 IN MONOCYTES.

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Background: Inflammation plays a key role in pathophysiology of sickle cell disease (SCD). Monocytes are important mediator cells in the inflammation pathway. There is a remarkable lack of knowledge about how monocytes behave in patients with SCD and whether they are modulated by different treatments. **Objective:** To assess possible changes in monocyte maturation and proteinexpression among sickle cell disease patients in different treatment modalities and compare them to healthy subjects. **Methods:** 25 patients with SCD followed at the outpatient service of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo and 3 healthy controls were included. We included patients with sickle cell anemia (HbSS), over 18 years of age, without acute complications. Pregnancy was an exclusion criteria. Patients were divided in three groups: treatment with Hydroxyurea (HU) (n = 10) using the same dose for at least three months; chronic exchange transfusion (n = 9) (TP); and no specific treatment (NST) (n = 6). We performed peripheral blood mononuclear cells (PBMC) separation. Monocytes were analyzed by flow cytometry (Dx Flex, Beckman Coulter), using CD14 and CD16 as markers of subpopulations of monocytes as classical (CD14+/CD16-), intermediate (CD14+/CD16+) and

non-classical (CD14-/CD16+). We also assessed the expression of CD 86 (a co-stimulation chemokine receptor), CD 163 (receptor for the conjugate hemoglobin-haptoglobin) and PD-L1 (an inhibitor receptor). Comparison between groups were made using ANOVA and Tukey test. **Results:** Gender and age distribution yielded no significant difference. The mean of total leukocytes and monocytes were, respectively: 8,816 ± 2,133/mm^3 and 900 ± 563/mm^3 (HU), 11,487 ± 3,813/mm^3 and 1,343 ± 754/mm^3 (TP), 9,081 ± 1879/mm^3 and 1,373 ± 432/mm^3 (NST), 7,080 ± 642/mm^3 and 700 ± 0/mm^3 (control). Among the total nucleated cells, the percentage of classical monocytes was lower in HU compared with controls (3.8 ± 2.1%vs.7.7 ± 1.3%, p 0.008), lower in TP vs NST (2.4 ± 1.8%vs. 5.6 ± 2.8%,p 0.04) and in TP vs Controls (2.4 ± 1.8% vs. 7.7 ± 1.3%,p 0.001). No significant differences were shown in the intermediate monocytes. However, nonclassical monocytes were higher in HU compared with TP (0.44 ± 0.3% vs. 0.22 ± 0.2%, p 0.013) and in controls vs TP (0.35 ± 0.07% vs 0.22 ± 0.2%, p 0.017). In classical monocytes, expression of PD-L1 was higher in HU compared with NST (86.1 ± 17.4% vs. 43.9 ± 31.0%) and HU vs Controls (86.1 ± 17.4% vs. 34.9 ± 8.9%, p 0.019). Expression of PD-L1 in intermediate monocytes and in non classical monocytes were also higher in HU compared with controls (88.9 ± 16.3% vs. 58.6 ± 8.6%, p0.02 and 79.6 ± 30.2%vs.37.1 ± 4.6%, p 0.02). **Conclusion:** Different treatments for sickle cell disease have affected the monocyte subsets distribution and PD-L1 expression in the population studied. HU and Transfusion Program induced a reduction in the Classical Monocyte subset, more pronounced in the latter. The higher expression of PD-L1 in patients submitted to exchange transfusion and in use of HU indicate inhibition of inflammation, which is more pronounced in the HU group. Both treatments have immunomodulatory effects on SCD, however, to date, no inflammatory markers that assess response to treatment are available. Our findings might contribute to uncovering the role of PD-L1 in the chronic inflammation of SCD and to identify a potential biomarker.

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SÍNDROME DE UPSHAW-SCHULMAN DIAGNOSTICADA EM PUÉRPERA: RELATO DE CASO

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Relato de caso: Paciente 29 anos, parda, sem comorbidades conhecidas, G1 P0 A0, admitida no setor de emergência em período expulsivo de trabalho de parto com 33 semanas de gestação. Período gestacional e parto transvaginal prematuro sem intercorrências com RN encaminhado para UTI apenas para ganho ponderal. Exames laboratoriais no pós-parto imediato com anemia normocítica (Hb 6,5 g/dL; VCM 95 fL), reticulocitose (7%), trombocitopenia grave (22.000/mm^3), LDH aumentada (1.724 UI/L), bilirrubina indireta 2,3 mg/dL, haptoglobina <7, creatinina 0,5 e INR 1,1. Série branca sem alterações. À hematoscopia: numerosos esquizócitos. Transaminases e USG abdominal sem alterações. Proteinúria de 24h: 2,9 g. Paciente seguiu sem queixas e estável hemodinamicamente. Descartados os principais diagnósticos que cursam com microangiopatia trombótica (MAT) na gestação, a suspeita de Púrpura Trombocitopênica Trombótica (PTT) foi aventada (PLASMIC score: 6 pontos; French score: 2 pontos). Foi, então, realizada pesquisa de atividade da enzima ADAMTS13 no oitavo dia após o parto, com resultado 0,02 UI/mL, e com a pesquisa do inibidor negativa. Apesar do hemograma e dos marcadores de hemólise apresentarem melhora evolutiva espontânea, diante da potencial gravidade do diagnóstico, a terapia com transfusão de plasma fresco foi realizada em sessão única, mantendo a evolução clínica e laboratorial favorável nos dias subsequentes. Paciente recebeu alta após 15 dias da internação, para seguimento ambulatorial. Realizou nova pesquisa de ADAMTS13 após 1 mês do parto, com atividade de 0,04 UI/Ml, além de Hb 10,8 g/dL, plaquetas 115 mil/mm^3, haptoglobina<3, LDH 287 UI/L e reticulócitos 4,7%, confirmando atividade de doença. Diante disso, mesmo seguindo a paciente assintomática, foi instituída terapia com infusão de plasma ambulatorial até alcançar remissão hematológica e a paciente seguirá em acompanhamento pela PTT congênita. **Discussão:** O diagnóstico diferencial de MATs no terceiro trimestre da gestação e puerpério é extenso e deve aliar dados clínicos e laboratoriais para a identificação da correta etiologia, resultando no tratamento eficaz. Afastados eclâmpsia, síndrome HELLP, CIVD por descolamento prematuro de placenta e síndrome hemolítica urêmica atípica, ficamos com o diagnóstico de PTT como o mais provável. A forma adquirida, com presença de inibidor anti-ADAMTS13, ocorre em mais de 90% dos casos do adulto. No entanto, a possibilidade de tratar-se da forma congênita da doença, conhecida como síndrome de Upshaw-Schulman, mesmo que nunca antes clinicamente manifesta, deve ser lembrada. Isso porque, nos casos em que a deficiência enzimática é leve ou moderada, há necessidade de elevação dos multímeros de von Willebrand circulantes, como ocorre ao término da gestação, momento mais comum do aparecimento de sintomas, para que surja o desequilíbrio levando às manifestações clínico-laboratoriais da doença. A diferenciação entre as formas da doença é fundamental, pois o manejo é completamente distinto. O caso relatado ilustra a forma de apresentação mais comum dessa raríssima doença, demonstra a importância do acesso à dosagem da atividade da enzima ADAMTS13 ao diagnóstico e no acompanhamento, bem como, a pesquisa de seu inibidor para o diagnóstico diferencial e serve de alerta aos clínicos e hematologistas para que atentem a essa possibilidade diagnóstica.

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ANÁLISE DA PERCEPÇÃO DE DOR EM PACIENTES COM DOENÇA FALCIFORME DA FUNDAÇÃO HEMOMINAS DE BELO HORIZONTE – MINAS GERAIS

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