

comprometimento das funções renal e hepática além de reação leucocitotrófica 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 sobrevivência. 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 sobrevivência.

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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*, *Cervus elaphus*, *Gallus gallus*, *Lagopus muta*, *Petromysus marinus*, *Felis catus*, *Rattus norvegicus*, *Alopias 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 (*Petromysus 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 protein expression 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