Arachidonic Acid-Derived Eicosanoids in Visceral Leishmaniasis: Imbalance Between HETEs and Prostaglandins

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Visceral leishmaniasis (VL) is characterized by hepatosplenomegaly and a high parasite burden in these organs. Eicosanoids have been implicated in the regulation of inflammation, a hallmark of the disease. This study aimed to evaluate eicosanoid production during chronic VL in *Mesocricetus auratus* (Golden Syrian hamster). To achieve this, hamsters were infected via intraperitoneal injection with *Leishmania infantum* and analyzed five months post-infection. Parasite load in the spleen and liver was assessed by qPCR, while arachidonic acid (AA) -derived eicosanoids were quantified in tissue extracts using LC-MS/MS. These findings were correlated with clinical, laboratory, and histopathological parameters. Chronic VL in hamsters resembled human disease, presenting with splenomegaly, increased creatinine levels, and elevated liver transaminases. Histopathological analysis revealed granuloma formation, white pulp hypoplasia, and portal infiltrates in the spleen and liver. AA mobilization was elevated in these organs but remained unchanged in plasma. Among AA-derived eicosanoids, hydroxyeicosatetraenoic acids (HETEs) were significantly increased in the spleen but not in the liver or plasma. In contrast, prostaglandins PGE_2, 2-keto-PGE_2, and PGD_2 were reduced in the spleen. Notably, splenomegaly, elevated HETEs, and decreased PGE_2 levels correlated with parasite load, suggesting that *L. infantum* modulates these mediators in vivo. Our results indicate that *L. infantum* alters the local balance between HETEs and prostaglandins, fostering an inflammatory environment that may contribute to parasite persistence. The predominance of HETEs over prostaglandins seems to play a central role in VL progression. Further research is needed to clarify the mechanisms by which HETEs influence the pathogenesis of the disease.

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