Pulmonary glycocalyx degradation in malaria-associated respiratory syndrome: role of matrix metalloproteinases and their inhibitors

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Introduction: Inflammation, microthrombi and the cytoadherence of parasitized erythrocytes in the microcirculation can lead to the development of malaria-associated acute respiratory distress syndrome (MA-ARDS), a severe form of malaria. The pulmonary endothelial glycocalyx, mainly composed of syndecan-1, prevents cellular adhesion to the endothelium. During the inflammatory response against *Plasmodium*, increased production of reactive oxygen and nitrogen species activates matrix metalloproteinases (MMPs), leading to glycocalyx degradation and exposure of adhesion molecules such as ICAM-1, CD36, and EPCR, which facilitates cytoadherence to endothelial cells. **Objectives and Methods:** To quantify serum syndecan-1 levels throughout infection by ELISA and to analyze the pulmonary endothelial glycocalyx by immunohistochemistry; to investigate the expression of MMPs and their inhibitors (TIMPs) by qRT-PCR in lung tissue. **Results and Conclusions:** Initial results indicate that serum syndecan-1 concentration was higher in DBA/2 mice infected with *P. berghei* ANKA that developed MA-ARDS compared with non-infected (NI) animals on day 7 post-infection. Increased expression of neutrophil collagenase (MMP-8) was observed in infected animals compared with non-infected controls, whereas MMP-3 expression was reduced over the course of infection. In addition, infected mice that developed MA-ARDS at 7 dpi showed overexpression of TIMP-1. In previous studies, we observed that mice that develop MA-ARDS exhibit elevated levels of ROS and MPO, correlated with NET release. TIMP-1 can stimulate NETosis in neutrophils via CD63, while myeloperoxidase (MPO) prevents TIMP-1 from inactivating MMPs but allows it to remain functional in activating CD63. These are preliminary results from a master's project, which will be further confirmed and expanded. **Funding:** CNPq, CAPES, and FAPESP.

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