PLASMODIUM BERGHEI ADHERENCE AND ENDOTHELIAL PROTEIN C RECEPTOR EXPRESSION IN EXPERIMENTAL MALARIA-ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME

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Introduction: Malaria-associated acute respiratory distress syndrome (ARDS) often results in morbidity and mortality. Nevertheless, little research has been done on ARDS. Recently, murine models have been used to study malaria-associated ARDS; however, the effect mechanism of adhesion of infected erythrocytes to murine lung endothelial cells remains unknown. The aim of this study was to elucidate the effects and mechanism of infected erythrocytes adhesion to murine lung endothelial cells and aspects of the innate immune response that will bring important contribution to the understanding of malaria-associated ARDS.

Methods: DBA/2 mice were infected with 106 infected red blood cells (iRBC) of Plasmodium berghei ANKA (PbA) and classified as ARDS or HP (hyperparasitemia) before death, on the 7th day after infection (dai). Perfused lungs of mice classified as ARDS or HP were collected and the EPCR, ICAM, VCAM and PbA mRNA expression was analyzed by qRT-PCR and lung tissue sections were stained with H&E to analyze the parasite localization or hemozoin concentration by polarized light. DBA/2 mice were also infected with P. berghei ANKA luciferase and analyzed in vivo on the 7th dai to identify the parasite distribution. Primary culture of DBA/2 mice microvascular lung endothelial cells (DBA-PMLEC) were stimulated with IFN- gamma (50ng/ml), TNF (50ng/ml) and mature forms of iRBC were added for 1 hour and then removed to check the capacity of iRBC to adhere to DBA-PMLEC. In addition, transwells membranes were used containing peritoneal macrophages (MΦ) or bone marrow's neutrophils (BMN) and stimulated with iRBC to analyze if soluble factors from these cells affect the capacity of iRBC to adhere in DBA-PMLEC. Dexamethasone was administered to the mice to verify the effect of the anti-inflammatory in the experimental model. Stimulated cells were collected to mRNA analyses (ICAM, VCAM, CD36 and EPCR).

Results: Microscopy analyses have shown the presence of iRBC in close contact with endothelial cells in lung tissue sections. Higher levels of 18s Plasmodium berghei ANKA mRNA expression and hemozoin were observed in perfused in lungs of ARDS mice compared to HP (qRT-PCR). P. berghei ANKA luciferase is distributed in the peripheral blood and tissue of DBA/2 mice but when mice were perfused, the (luciferase/luciferin) signal was more concentrated in lungs. ICAM-1, VCAM, and EPCR expression is altered in TNF-stimulated cells. IRBC-PbA in contact with MΦ or BMN increase iRBC-PbA cytoadhesion in (DBA-PMLEC) and MΦ produce TNF. Dexamethasone-treated mice have lower gene expression of VCAM, EPCR and less TNF in serum (compared to untreated controls) and die with hyperparasitemia symptoms.

Conclusion: Our data suggest that P. berghei ANKA infected erythrocytes adhere to DBA-PMLEC and TNF suggested modulating EPCR expression. Financial support: CAPES, CNPq and FAPESP.

Biography

Luana dos Santos Ortolan is a biologist graduated from University Fundação Santo André, São Paulo, Brazil (2009) and has a Master's Degree in Chemical Biology from Federal University of São Paulo, Brazil (2013). She is currently a PhD candidate in Immunology at the Institute of Biomedical Sciences of the University of São Paulo, Brazil.

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