Characterization and differentiation of equine experimental local and early systemic inflammation by expression responses of inflammation-related genes in peripheral blood leukocytes

Local inflammation may progress into systemic inflammation. To increase our understanding of the basic immunological processes during transition of equine local inflammation into a systemic state, investigation into the equine systemic immune response to local inflammation is warranted. Therefore, the aim of this study was to investigate the innate peripheral blood leukocyte (PBL) immune response to local inflammation in horses, and to compare this response with the PBL immune response during the early phase of acute systemic inflammation. Expression of 22 selected inflammation-related genes was measured in whole blood leukocytes from 6 horses in an experimental cross-over model of lipopolysaccharide- (LPS-) induced acute synovitis (3 μg LPS intraarticularly; locally inflamed [LI] horses) and endotoxemia (1 μg LPS/kg intravenously; systemically inflamed [SI] horses). Multiple clinical and hematological/biochemical examinations were performed, and serial blood samples were analyzed by reverse transcription quantitative real-time PCR. Post-induction expression profiles of all genes were compared between study groups using principal component analysis (PCA) and hierarchical clustering. Moderate synovitis and mild systemic inflammation of approximately 24 h duration was confirmed by clinical and paraclinical observations in LI and SI horses, respectively. In the LI group, samples obtained 3-16 h post-injection showed distinct clustering in the PCA compared with baseline levels, indicating a transcriptional response to local inflammation in PBLs in this time interval. There was no clinical or hematological indication of actual systemic inflammation. There was a clear separation of all LI samples from all SI samples in two distinct clusters, indicating that expression profiles in the two study groups were different, independent of time since LPS injection. Co-regulated genes formed four clusters across study groups which were distinctly differently regulated. Only few of individual genes displayed different expression between the study groups at all times after LPS injection. Local inflammation in horses initiated an innate transcriptional response in PBLs, which differed from the transcriptional response during the early phase of systemic inflammation. This study may provide new insights into the immunobiology of PBLs during the transition of local inflammation into a systemic state.

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