Dynamics of Human Leukocyte Antigen-D Related expression in bacteremic sepsis

av

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Akademisk avhandling

Avhandling för medicine doktorsexamen i medicinsk vetenskap inriktning medicin,
som kommer att försvaras offentligt fredagen den 19 maj 2017 kl. 13.00,
HSC3, Campus USÖ, Örebro Universitet

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Abstract


Monocytic human leukocyte antigen – D related (mHLA-DR) expression determined by flow cytometry has been suggested as a biomarker of sepsis-induced immunosuppression.

In order to facilitate use of HLA-DR in clinical practice, a quantitative real-time PCR technique measuring HLA-DR at the transcription level was developed and evaluated. Levels of HLA-DR mRNA correlated to mHLA-DR expression and were robustly measured, with high reproducibility, during the course of infection. Dynamics of mHLA-DR expression was studied during the first weeks of bloodstream infection (BSI) and was found to be dependent on the bacterial etiology of BSI. Moreover, mHLA-DR was shown to be inversely related to markers of inflammation. In patients with unfavourable outcome, sustained high C-reactive protein level and high neutrophil count were demonstrated along with low mHLA-DR expression and low lymphocyte count. This supports the theory of sustained inflammation in sepsis-induced immunosuppression. The association between mHLA-DR and bacterial etiology may be linked to the clinical trajectory via differences in ability to cause intractable infection. *Staphylococcus aureus* was the dominating etiology among cases with unfavourable outcome. With focus on patients with *S. aureus* BSI, those with complicated *S. aureus* BSI were found to have lower HLA-DR mRNA expression during the first week than those with uncomplicated *S. aureus* BSI. If these results can be confirmed in a larger cohort, HLA-DR measurement could possibly become an additional tool for early identification of patients who require further investigation to clear infectious foci and achieve source control.

In conclusion, PCR-based measurement of HLA-DR is a promising method for measurements of the immune state in BSI, but needs further evaluation in the intensive care unit setting to define the predictive and prognostic value for deleterious immunosuppression. The etiology of infection should be taken into consideration in future studies of translational immunology in sepsis.

*Keywords*: monocyte HLA-DR, sepsis, immunosuppression, bloodstream infection, HLA-DRA, CIITA, qRT-PCR

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