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Serum cytokine profiles differentiating hemorrhagic fever with renal syndrome and hantavirus pulmonary syndrome

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Abstract

© 2017 Khaiboullina, Levis, Morzunov, Martynova, Anokhin, Gusev, St Jeor, Lombardi and Rizvanov. Hantavirus infection is an acute zoonosis that clinically manifests in two primary forms, hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS). HFRS is endemic in Europe and Russia, where the mild form of the disease is prevalent in the Tatarstan region. HPS is endemic in Argentina, as well as other countries of North and South American. HFRS and HPS are usually acquired via the upper respiratory tract by inhalation of virus-contaminated aerosol. Although the pathogenesis of HFRS and HPS remains largely unknown, postmortem tissue studies have identified endothelial cells as the primary target of infection. Importantly, cell damage due to virus replication, or subsequent tissue repair, has not been documented. Since no single factor has been identified that explains the complexity of HFRS or HPS pathogenesis, it has been suggested that a cytokine storm may play a crucial role in the manifestation of both diseases. In order to identify potential serological markers that distinguish HFRS and HPS, serum samples collected during early and late phases of the disease were analyzed for 48 analytes using multiplex magnetic bead-based assays. Overall, serum cytokine profiles associated with HPS revealed a more pro-inflammatory milieu as compared to HFRS. Furthermore, HPS was strictly characterized by the upregulation of cytokine levels, in contrast to HFRS where cases were distinguished by a dichotomy in serum cytokine levels. The severe form of hantavirus zoonosis, HPS, was characterized by the upregulation of a higher number of cytokines than HFRS (40 vs 21). In general, our analysis indicates that, although HPS and HFRS share many characteristic features, there are distinct cytokine profiles for these diseases. These profiles suggest a strong activation of an innate immune and inflammatory responses are associated with HPS, relative to HFRS, as well as a robust activation of Th1-type immune responses. Finally, the results of our analysis suggest that serum cytokines profiles of HPS and HFRS cases are consistent with the presence of extracellular matrix degradation, increased mononuclear leukocyte proliferation, and transendothelial migration.

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Keywords

Blood serum, Cytokine profile, Hantavirus pulmonary syndrome, Hemorrhagic fever with renal syndrome, Nephropathia epidemica

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