

Cardiopulmonary involvement in Puumala hantavirus infection

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Abstract

Puumala hantavirus (PUUV) causes hemorrhagic fever with renal syndrome in Europe. After inhalation of virus shed by bank voles, the virus systemically targets the vascular endothelium leading to vascular dysfunction and leakage. Many patients with PUUV infection experience cardiopulmonary manifestations but the underlying mechanisms have not been determined.

The aims of the studies presented were to describe cardiopulmonary manifestations, investigate pathogenetic mechanisms including presence of virus in the lungs and the local immune response in PUUV infection.

The results showed cardiopulmonary involvement of varying severity in almost all studied patients. High-resolution computed tomography frequently revealed vascular leakage into the lungs or pleural cavities. Pulmonary function tests generally showed reduced gas diffusing capacity, evidenced in patients as dyspnea, poor oxygenation and frequent need of oxygen treatment. Among patients who were not fully recovered at 3 months follow-up, remaining decreased gas diffusing capacity was highly common.

Echocardiography revealed mainly right heart dysfunction which was related to manifestations within the lungs, in terms of increased estimated pulmonary vascular resistance, mild to moderate pulmonary hypertension, and reduced right ventricular systolic function in patients with more pronounced lung involvement, as indicated by need of oxygen treatment.

Analyses on bronchoalveolar lavage (BAL) and bronchial biopsies revealed a highly activated cytotoxic T cell (CTL) response in the lungs. The CTL response was not balanced by the expansion of regulatory T cells and high numbers of CTLs were associated with more severe disease. PUUV RNA was detected in almost all patients' BAL samples and the viral load was inversely correlated to the number of CTLs.

Three patients presenting with severe and fatal cardiopulmonary distress were also described. Autopsies revealed PUUV protein in vascular endothelium in all investigated organs, including the heart and lungs, along with a massive CTL response mainly in the lungs.

In conclusion, cardiopulmonary involvement of varying severity was present in almost all patients with PUUV infection. Cytotoxic immune responses could contribute to disease development but also help in clearing the infection. Long lasting fatigue after hantavirus infection may be explained by remaining manifestations within the lungs.

Keywords

Hemorrhagic fever with renal syndrome, hantavirus, echocardiography, respiratory function tests, computed tomography, bronchoalveolar lavage, biopsy, cytotoxic T cells, disease severity

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