REPORT

New evidence of the contribution of apoptosis to dengue hemorrhagic fever pathophysiology

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ABSTRACT

Dengue is considered the most important arthropod-borne viral disease in humans and is caused by any of the four dengue virus (DENV-1-4) serotypes. DENV may cause the potentially fatal disease named dengue hemorrhagic fever/ dengue shock syndrome (DHF/DSS). Although apoptosis has been implicated in DHF/DSS pathogenesis, the *in vivo* mechanisms have not been largely explored yet. In this study, formalin fixed and paraffin embedded tissues of eight fatal DHF/DSS cases from two Cuban dengue epidemics were examined, in 1997 by DENV-2 and 2001 by DENV-3. We detected DENV antigens by an immunohistochemistry assay and apoptotic cells by the TUNEL, (Terminal deoxynucleotydil Transferase-mediated dUTP nick-end labelling) technique in sections from different organs. Apoptosis was demonstrated in six out of the eight studied fatal cases. Apoptotic cells were observed in brain, intestine, liver and lung. This is the first report in literature demonstrating apoptosis in white blood cells, brain cells, and endothelial cells from the intestinal and pulmonary microvasculature from DENV infected individuals. Interestingly, it is likely that apoptotic microvascular endothelial cells were associated to plasma leakage manifested by the studied subjects. These results suggest that apoptosis may contribute to DHF/DSS pathophysiology. More studies are necessary to clarify the apoptotic cell death implications in DHF/DSS pathogenesis.

Keywords: Apoptosis, dengue, Cuba, plasma leakage, immunohistochemistry, shock

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