World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:13, No:03, 2019

Morphological and Molecular Evaluation of Dengue Virus Serotype 3 Infection in BALB/c Mice Lungs

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Abstract : The establishment of animal models for studies of DENV infections has been challenging, since circulating epidemic viruses do not naturally infect nonhuman species. Such studies are of great relevance to the various areas of dengue research, including immunopathogenesis, drug development and vaccines. In this scenario, the main objective of this study is to verify possible morphological changes, as well as the presence of antigens and viral RNA in lung samples from BALB/c mice experimentally infected with an epidemic and non-neuroadapted DENV-3 strain. Male BALB/c mice, 2 months old, were inoculated with DENV-3 by intravenous route. After 72 hours of infection, the animals were euthanized and the lungs were collected. Part of the samples was processed by standard technique for analysis by light and transmission electronic microscopies and another part was processed for real-time PCR analysis. Morphological analyzes of lungs from uninfected mice showed preserved tissue areas. In mice infected with DENV-3, the analyzes revealed interalveolar septum thickening with presence of inflammatory infiltrate, foci of alveolar atelectasis and hyperventilation, bleeding foci in the interalveolar septum and bronchioles, peripheral capillary congestion, accumulation of fluid in the blood capillary, signs of interstitial cell necrosis presence of platelets and mononuclear inflammatory cells circulating in the capillaries and/or adhered to the endothelium. In addition, activation of endothelial cells, platelets, mononuclear inflammatory cell and neutrophil-type polymorphonuclear inflammatory cell evidenced by the emission of cytoplasmic membrane prolongation was observed. DEN-like particles were seen in the cytoplasm of endothelial cells. The viral genome was recovered from 3 in 12 lung samples. These results demonstrate that the BALB / c mouse represents a suitable model for the study of the histopathological changes induced by DENV infection in the lung, with tissue alterations similar to those observed in human cases of DEN.

Keywords : BALB/c mice, dengue, histopathology, lung, ultrastructure
Conference Title : ICV 2019 : International Conference on Virology
Conference Location : Miami, United States
Conference Dates : March 11-12, 2019