EXPERIMENTAL MURINE MODEL FOR THE PATHOGENESIS STUDY OF DENGUE VIRUSES

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A great difficulty to study dengue virus (DENV) infection in humans and for a virus vaccine developing is the absence of a suitable animal model which presents a disease with similar aspects of the Dengue haemorrhagic fever and Dengue shock syndrome. In the majority of models the animals are immunocompromised and/or inoculated by routes like the intracerebral, with neuroadapted DENV. Tissues of adult BALB/c mice infected with non-neuroadapted DENV-1 and DENV-2 serotypes from patient sera were analyzed. The tissue fragments were processed following the standard techniques of fotonic and transmission electron microscopy. In primary infection with DENV-1 and DENV-2 morphological alterations were observed inside hepatic, lung, kidney and cerebellum tissues. DENV-1 particles and specific DENV antigen was observed in C6/36 cells inoculated with the supernatant of spleen and lung macerates and with the animal sera. Ultrastructural studies of alveolar macrophages of animals infected with DENV-2 showed DENV-like particles inside the rough endoplasmic reticulum and Golgi complex, suggesting viral replication. DENV particles were ultrastructurally identified, and immunolocalized inside C6/36 cells, inoculated with the supernatant (liver, lung kidney and cerebellum) of tissue macerates. The corporal temperature in the majority of mice increased after the second day post-infection. Elevated enzyme levels of alanine aminotransferase and aspartate aminotransferase were observed. In secondary infections morphological alterations were observed in liver, lung and heart. The tissue injuries were more severe than those seen in animals with signs of primary infection. DENV-1 particles, specific DENV-1 antigen and DENV-1 RNA were present in C6/36 cells inoculated with the animal sera. These studies confirm the susceptibility of BALB/c mice to infection and reinfection by DENV-1 and DENV-2 and those they can be used as a model for testing of drugs and vaccine candidates against DENV.

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