PATHOLOGIC STUDIES OF HAMSTERS EXPERIMENTALLY INFECTED BY ENTEROVIRUS 71

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Abstract

Enterovirus 71 (EV71) is an RNA virus in the *Picornaviridae* family. EV71 was first isolated in an outbreak of neurological disease in California in 1969. Fatal cases have occurred in recent outbreaks of hand, foot and mouth disease in Malaysia in 1997, Taiwan in 1998 and China in 2008. In human autopsies of EV71 encephalomyelitis, virus was found to be neuronotrophic. To study the viral pathogenesis further, a mouse model was developed. Similar to human EV71 encephalomyelitis, the mouse model demonstrated strong neuronotropism in the CNS and provided evidence for viral transmission into the murine CNS via the peripheral nervous system. Preliminary findings suggested that 4-week-old hamsters could be infected using a mouse adapted viral strain and used as an animal model for EV71 infection. The development of a permissive four-week-old hamster model is better than the current 2-week-old mouse model as vaccine and drug testing can be done over a longer window period.

To study the pathological changes in a 4-week-old hamster model infected with murine adapted EV71, four-week-old hamsters were inoculated by an infective dose of murine adapted enterovirus 71 strains by intraperitoneal and intramuscular routes. The animals were sacrificed as soon as they fell sick. Their organs were harvested, formalin fixed and embedded in paraffin blocks. Tissue sections were stained using Haematoxylin and Eosin (H&E), immunohistochemistry (IHC) and in situ hybridization(ISH) following standard protocols. All the hamsters inoculated by the intraperitoneal and intramuscular routes showed paralysis of the hind limbs. The adult hamsters consistently showed involvement of skeletal muscles via both intraperitoneal (i.p.) and intramuscular (i.m.) inoculation routes. The histological examination showed myositis with skeletal muscle tissue exhibiting necrotic fibers and variable inflammation, and viral antigens and RNAs were present in these muscle groups. However EV71 viral antigens or RNA via IHC or ISH, were not demonstrated in the central nervous system or other tissues.

We have shown that skeletal muscle cells are the main cell types targeted by EV71 in the 4-week-old hamster. Compared to murine model and human cases, this hamster model lack CNS infection and thus our hamster model was more suitable as an animal model for EV71 myositis than encephalomyelitis. It could still be useful as an infectious model of EV71 infection if myositis is used as an endpoint to assess vaccine or therapeutic effectiveness.