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Research Report

Some observations on the tropism of Japanese encephalitis virus in rat brain

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ABSTRACT

The clinical picture of viral encephalitis is determined by the affinity and persistence of the virus to different brain regions. Therefore, the present study was aimed to investigate the neuropathological changes following Japanese encephalitis virus (JEV) infection in rat at different time points. Twelve days old Wistar rats were infected by intracerebral inoculation of JEV. Presence of JEV antigen was detected in thalamus, striatum, cortex and mid brain on 3, 6, 10 and 20 days post inoculation (dpi). Histopathological changes were also studied in different brain regions at different time points. The highest expression of JEV antigen was found on 6 dpi in all the brain regions studied. JEV antigen was maximum in thalamus on 6 dpi and mid brain on 10 dpi. JEV antigen, however, was almost undetectable on 20 dpi in all the regions. The classical pathological changes such as cellular infiltration, perivascular cuffing, meningeal disruption, neuronal damage, neuronal shrinkage, and plaque formation were observed up to 10 dpi. The present study reveals high affinity of JEV to thalamus, brainstem and striatum. Rat model of JEV infection may serve as a useful model for studying mechanism of cell injury and recovery in JE.

1. Introduction

Japanese encephalitis virus (JEV) is a flavivirus having single-stranded RNA genome, an etiological agent of acute zoonotic infection commonly affecting children and is one of the major causes of epidemic encephalitis in Asia identified as Japanese Encephalitis (JE). Japanese encephalitis is occurring in a broad band extending from India to Japan and from China to Papua New Guinea (UNICEF, 1994). Approximately 50,000 cases of JE occur annually in Asia with a mortality of 20% to 40% (Tiroumourougane et al., 2002; Grossman et al., 1973). The virus is transmitted to humans by mosquito vector, principally by *Culex tritaeniorhynchus* that proliferates in close proximity with other vertebrate hosts like pigs, water birds and chicks. JEV localizes in specific brain tissues and cause neuronal damage. Since 1870s, Japanese encephalitis has emerged as a most important form of viral encephalitis. Several studies have been carried out to understand the pathophysiology of JE. Some human autopsy studies have characterized the classical pathological changes in brain (Zimmerman, 1945; Miyake

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1964; Shankar et al., 1983). However, the sequential studies on changing pattern of these features in JE are lacking. For studying the mechanism of pathogenesis and response to therapeutics, the mice model is commonly used (Hase et al., 1990a; Hase et al., 1990b; Hasegawa et al., 1992; Hase, 1993; Chen et al., 1996; Wang et al., 1998; Mishra and Basu, 2008). However, mice model is limited by short survival after JEV infection and high mortality. This limitation prevents the evaluation of long term structural and functional changes following JEV infection. Greater susceptibility and longer survival in younger rats compared to the older ones following intracerebral inoculation of JEV has been reported (Ogata et al.,

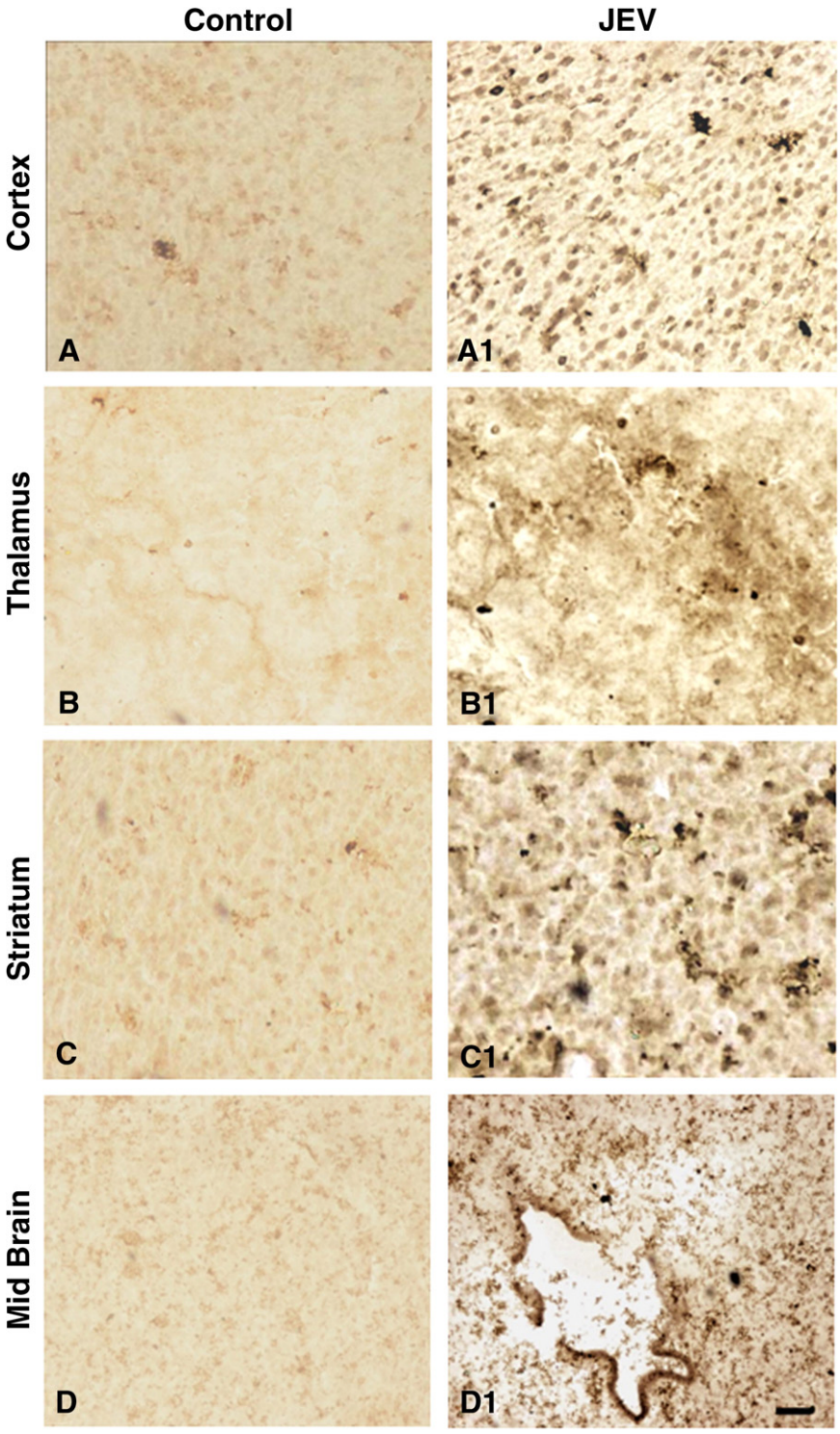

Fig. 1 – Representative photomicrograph showing immunostaining to JEV antigen in cortex (A1), thalamus (B1), striatum (C1) and mid brain (D1) in 12 days old rats inoculated with 3×10^6 pfu/ml of JEV solution. No immunoreactivity in cortex (A), thalamus (B), striatum (C) and mid brain (D) of control rats. Scale bar=300 μm.