NEUROPATHOGENICITY OF MUTANT STRAINS OF MOUSE HEPATITIS VIRUS, 1A AND 2C, FROM DBT CELLS PERSISTENTLY INFECTED WITH JHM STRAIN

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Two plaque mutants 1a and 2c of the mouse hepatitis virus JHM strain (MHV-JHM) from persistently infected DBT cells[2] were examined for neuropathogenicity in mice. The mutant strains had peplomer proteins different from those of the original MHV-JHM[3] and they were plaque purified.

After intracerebral inoculation with MHV-JHM all infected mice died in one week after infection. With 10^4 PFU of the 1a virus, however, only 30% of mice died and all mice survived with the same dose of the 2c virus. Brain titers of the 1a virus were similar to those of MHV-JHM in inoculated mice. In 2c-inoculated mice the titers reached a peak at 24 h later and was about ten times lower than those of mice inoculated with the 1a virus.

In mice inoculated with MHV-JHM viral antigen was distributed within neurons as well as glial cells of the whole brain, suggesting panencephalomyelitis histopathologically. In the early stage of infection in mice 1a infected viral specific antigens were shown in meningocytes, glial cells, ependymal cells, and neurons(Fig. 1), and the antigen positive cells were smaller in number than those of MHV-JHM infected mice. Marked degeneration and necrosis of neurons and collapse of the matrix were seen. In 2c infected mice neuronal degeneration and inflammation were less severe.

At 3 weeks postinoculation or later surviving mice showed distinct demyelination without any inflammatory reaction(Fig. 2). In the white matter of the brain and spinal cord oligodendrocytes carrying viral antigen were scattered.

Another mutant virus MHV-JHM-CC[2] isolated from persistently infected DBT cells caused moderate inflammation and demyelination while its pathogenic ability was not stable enough.[1] The present two plaque mutants 1a and 2c isolated from the same origin were different in pathogenicity from MHV-JHM-CC. After inoculation with 1a virus mice showed degeneration of axons and oligodendroglia cells and demyelination with inflammatory reaction. Lesions produced in most 2c virus infected mice, however, were limited to demyelination without severe neuronal degeneration and inflammation.

The difference of pathogenicity of both mutant strains may be ascribed to the difference of viral structure, which is closely related to the cell tropism of the viruses. Infection of ICR mice with the two mutant virus

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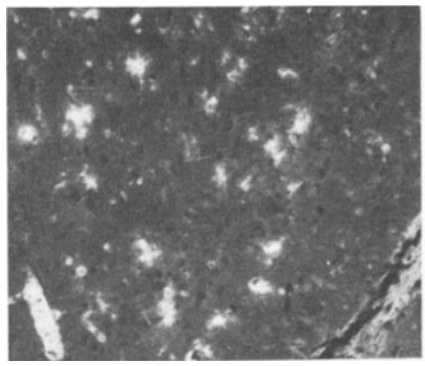

Fig. 1. Viral antigens in neurons and glial cells of the diencephalon of a mouse inoculated with 1a virus. 96 h postinoculation. Immunofluorescence.

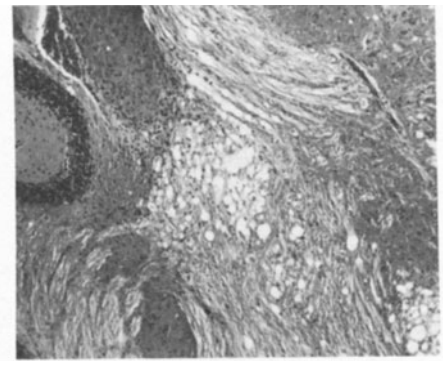

Fig. 2. Distinct demyelination in the cerebellum of a mouse inoculated with 2c virus. 3 weeks postinoculation. HE stain. x 220.

strains, 1a and 2c, may provide a useful model for analysing the course of demyelinating encephalomyelitis.

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