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Suspected viral hepatitis of nude mice in Australia

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Early in 1975 a disease syndrome characterised by depression and emaciation was seen in homozygous nude mice maintained at the Queensland Department of Primary Industries Tick Fever Research Centre (TFRC), Wacol, Brisbane. Later in the same year, a small group of nude mice were submitted from the Repatriation General Hospital (RGH), Greenslopes, Brisbane, with an identical syndrome.

Because they congenitally lack all or part of the thymus (Pantelouris, 1968) and are thus immunodeficient, nude mice are usually bred and maintained under germ-free conditions. The nude mice from both TFRC and RGH originated from the Walter and Eliza Hall Institute, Melbourne, and were housed conventionally in rooms containing other mouse stocks. At TFRC nude progeny were produced by mating homozygous nude males (*nu/nu*) with heterozygous females (*nu/+*) and cross-fostering the resulting young to achieve all-nude litters. Litters were weaned at 5 to 6 weeks of age.

An adult male nude mouse introduced to TFRC from Melbourne 5 weeks previously became depressed, emaciated, adopted a hunched posture and died after about 10 days of illness. These signs were then seen in TFRC nude mice of 4-12 weeks of age. Later it was noted that about 10% of animals in nude litters at TFRC were affected by this syndrome. Neither heterozygotes nor other mice from either colony were affected.

At autopsy, multiple pale irregular foci were present beneath the capsule and throughout the body of the liver. Depressions of the capsule due to these lesions made the liver surface very irregular.

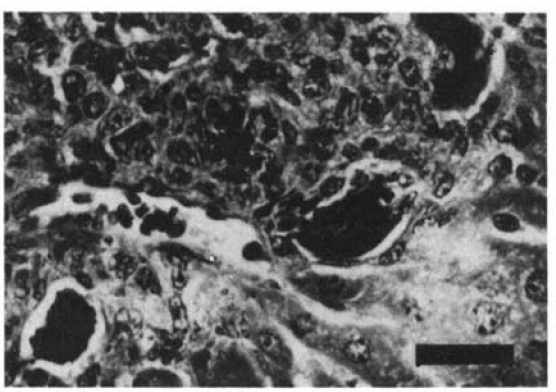

Fig. 1. Nude mouse liver lesion with degenerateand viable giant cells. Haematoxylin and eosin stain. Line represents 25 μm.

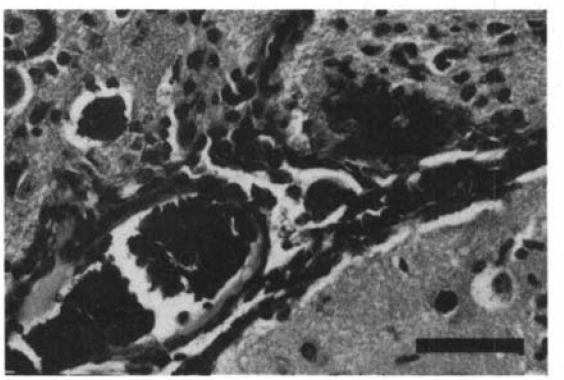

Fig. 2. Giant cells in nude mouse brain. Haematoxylin and eosin. Line represents 25 μm.

Histologically, liver lesions were foci of hepatocyte necrosis containing proliferating reticuloendothelial cells, with haemorrhage and polymorphonuclear leucocytes in some larger lesions. These lesions became confluent in advanced cases. The most striking microscopic finding was the presence of multinucleated giant cells. Some giant cells were degenerate with intensely eosinophilic cytoplasm and pycnotic nuclei (Fig. 1). Giant cells were also observed in the spleen, lymph nodes and brain of affected mice. In the brain, giant cells and mild gliosis were seen mainly, adjacent to blood vessels in the cerebrum (Fig. 2). Attempts to isolate virus from affected nude mice failed.

The morphological findings in our cases were consistent with those reported caused by murine hepatitis virus infection in nude mice in England (Sebesteny & Hill, 1974). Certain strains of murine hepatitis virus are known to be neurotropic and to induce giant cell formation in various tissues (Niven, 1967). To our knowledge, this condition has not been previously reported in Australia. Murine hepatitis virus commonly infects conventional mice but rarely causes disease (Niven, 1967). The affected nude mice in our cases may have derived such an infection from the conventional mice housed in the same rooms, their athymic condition predisposing them to clinical disease.

References

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