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Sudden onset of mortality within a colony of FVB/n mice

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An investigator at Colorado State University received five breeding pairs of FVB/n mice less than 23 days old from a commercial vendor. We housed the mice in a semi-barrier animal room in microisolator cages on a 12-h light/dark cycle and gave them *ad libitum* access to water and rodent chow (Harlan Teklad 8640, Madison, WI). Serologic evaluations of two sentinel ICR mice caged in the same room were negative for serum antibodies reacting with mouse hepatitis virus (MHV), minute virus of mice (MVM), Sendai virus, mouse parvovirus (MPV), *Mycoplasma pulmonis*, Theiler's murine encephalomyelitis virus (TMEV), and epizootic diarrhea of infant mice (EDIM) antigens. One mouse tested negative for all of the aforementioned except for MPV. The five pairs of FVB/n mice were therefore moved to a different MPV-positive semi-barrier room that also housed immunocompromised strains of mice.

Three of the five females subsequently gave birth to 37 FVB/n offspring (17 males and 20 females) over a four-day period. Animal care technicians weaned the pups at 21 days old. Four weeks later, they noticed wounds on the tails and tail bases of 7-week-old female FVB/n mice in two cages. One of us (M.D.R.) diagnosed conspecific aggression as the likely etiology and separated the animals in an attempt to alleviate the intracage aggression. We did not note any other abnormalities in the FVB/n mice or in any of the other mice housed in the same room.

Approximately 5 weeks later (when the mice were 12 weeks old), we found a dead female FVB/n mouse with no premonitory symptoms. M.D.R. performed a complete necropsy; no gross lesions were noted. Over

FIGURE 1 | Photomicrographs of brain sections taken from (a) a 14-week-old female FVB/n mouse found dead with nonspecific gross lesions and no premonitory signs and (b) a clinically normal 14-week-old FVB/n mouse. The sections are of the thalamus. In the brain of the mouse that died suddenly (a), many of the neurons are undergoing degeneration and necrosis, most likely due to acute ischemia. (H&E stain; low-medium (a) and low (b) power magnification.)

the next 4 weeks, animal care technicians found an additional 16 mice (1 male, 15 female) dead in their cages, again without any premonitory symptoms.

We took blood from one of the remaining five female mice and submitted serum for a serology panel that tested for antibodies to ectromelia virus, EDIM, lymphocytic choriomeningitis virus (LCM), *M. pulmonis*, MHV, MNV, Parvo NS-1, MPV, MVM, pneumonia virus of mice (PVM), REO3, Sendai, and TMEV-GDII; all test results were negative. M.D.R. performed necropsies on 10 of the mice that had previously been found dead (9 female, 1 male). All mice were considered in good body condition, with a score of >3 out of 5 (ref. 1). The mice had adequate body fat stores and food within the stomach; the small and large intestines contained normal amounts of ingesta and feces. All mice appeared normally hydrated. We noted occasional superficial excoriations of the dermis on the dorsum of the tail base. Additionally, all

the mice had wet fur below the mandible and on the ventrum of the neck.

We performed histopathologic examinations on all major organs (brain, liver, heart, lungs, stomach, spleen, lymph nodes, salivary glands, small intestine, colon, kidney, adrenals, bladder, and gonads) from four mice that were necropsied. Brain sections of all mice had multifocal areas of neuronal necrosis and neuronal depletion in the cerebral cortex (Fig. 1). We also detected astrocytosis and early gliosis in the brain of one of two affected mice that were labeled with an antibody that recognizes glial fibrillary acidic protein (GFAP), a cell marker for neuroglia.

Are these brain lesions of neuronal necrosis and loss common among FVB/n mice? Does the case history and epidemiology point to a syndrome associated with this strain?

What's your diagnosis?