Thomas M. Donnelly, DVM, Column Editor

Sudden death in lactating inbred mice

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At the University of Aarhus animal facility, we observed sporadic cases of sudden death of inbred, mutant and transgenic lactating female mice. The cases were dispersed among all murine genotypes in the facility. Most cases occurred in lactating females with large litters: the average litter size of affected females was 7.5 pups. Generally, female mice with pups that were approximately 14 d old were found dead in their cages. The dead female mice had slightly enlarged abdomens (**Fig. 1**) and no milk production (pups were found hungry and cold).

Some female mice were found moribund, depressed and prostate on the cage floor. On clinical examination, the mammary glands of the dying mice had long nipples but no milk (**Fig. 2**). In a few mice, we also noticed fecal staining of the perineum that was suggestive of acute diarrhea (**Fig. 3**).

Necropsy of affected mice showed bloating of the proximal gastrointestinal tract. The stomach was dilated and filled with either watery contents or partly digested food. The proximal small intestine was distended with thin yellow-brown fluid that often contained black specks. The fluid gradually became thicker as it progressed distally along the length of the small intestine until it became semi-solid or solid. The distal small intestine and large intestine were lacking intestinal contents except for a few fecal pellets. The cecum was empty and reduced in size. Occasionally, we saw scant light brown liquid in the tip of the cecum, whereas the body of the cecum was either empty or slightly filled with a similar tan fluid. On gross pathologic examination of the abdominal and thoracic cavities, we noted congestion and absence of subcutaneous and intra-abdominal fat. No gross pathological changes were seen in lungs, liver, spleen, urinary tract, brain or uterus.

We immediately collected samples of small and large intestine and intestinal contents after opening the carcass. The intestinal fluid samples were placed on glass slides, dried, fixed, Gram-stained and examined microscopically for bacteria. We saw numerous large Gram-positive rods, some containing spores, in the samples from the small intestine. Samples of intestinal fluid were submitted for bacterial culture.

We took representative samples of heart, lungs, spleen, liver, kidneys, stomach, duodenum and colon for histological examination. Tissues were fixed in 10% neutral buffered formalin, routinely processed, embedded in paraffin, sliced into 4-µm sections and stained with hematoxylin and eosin or with Ziehl-Nielsen or modified Brown-and-Hopps stains. Microscopically, lesions were seen in the small intestine. There was a fibrinous exudate in the intestinal lumen, a moderate neutrophilic infiltration of the mucosa and multifocal hemorrhages and diffuse edema in the lamina propria. We made a diagnosis of necrotizing enteritis. Large Gram-positive bacilli with spores were seen in sections of small intestinal necrotic debris stained by modified Brown-and-Hopps method. Sections of heart, lungs, spleen, liver, kidneys, stomach and duodenum appeared normal.

Based on the clinical signs, intestinal fluid cytology, necropsy and histopathological findings, what do you think was the etiological cause of death in the lactating female mice? Is this a common condition? How might you prevent its occurrence in other lactating mice?

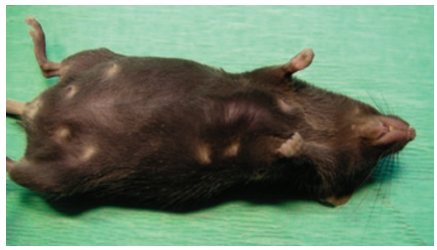

FIGURE 1 | A dead female C57BL/6J mouse that had been lactating and that had 14-d-old pups. The abdomen is abnormally bloated for a fresh mouse carcass.

FIGURE 2 | The mammary glands of a C57BL/6J mouse. The mouse was lactating, as indicated by the long nipples, but was not producing milk.

FIGURE 3 | A lactating female C57BL/6J mouse with fecal staining of the perineum, suggestive of acute diarrhea.

What's your diagnosis?

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