College of Veterinary Medicine
Department of Pathology

Case #: A17-15495

Presenter: Shannon G.M. Kirejczyk, DVM, MPH (Shannon.mccook25@uga.edu)

Contributors: Elizabeth Uhl, DVM, PhD, DACVP and Elizabeth Howerth, DVM, PhD, DACVP

Signalment: 7 month old, female spayed, domestic shorthair cat

History: The cat was presented to the Veterinary Teaching Hospital at the University of Georgia for evaluation of progressive neurological signs, which had begun at 3 months of age. Three out of the five kittens from this litter were similarly affected, although this cat had the worst neurological signs. Clinical signs began as paraparesis, and although he initially responded to therapy with oral prednisone, there was eventual forelimb involvement and occasional tremors. Marked joint laxity was present and there was decreased muscle mass, diffusely. Spinal reflexes were decreased to absent in all limbs. Cranial nerves were within normal limits. There was no pain on palpation of the spine or the limbs. Due to worsening of the clinical signs, the cat was euthanized for humane and diagnostic purposes.

Gross Pathology: A full postmortem examination was performed. Gross findings included a diffuse, prominent reticular pattern in the liver. There were few cestodes present within the small intestines. The skeletal muscle, abdominal and thoracic viscera, brain and spinal cord were grossly normal.

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Histopathology: Throughout the brain, spinal cord, and myenteric plexi, neurons contain numerous, 1–6 μm diameter, cytoplasmic vacuoles, which distend the cell body, displacing the nucleus and Nissl substance. The choroid plexus epithelium, cerebellar Purkinje cells, and macrophages within the leptomeninges (gitter cells) exhibit diffuse microvesiculation. The neuroparenchyma contains numerous, round, empty vacuoles (spongiosis). Microvesiculated macrophages with variably Periodic acid-Schiff (PAS) reaction-positive material, as well as vacuolated Schwann cells expand the endo- and perineurium of the sciatic nerves. Endothelial cells, pancreatic islet cells, gastric mucosa, hepatocytes, and renal tubular epithelial cells exhibit similar vacuolation to that described above.

Morphologic Diagnoses: Multiple tissues (brain, spinal cord, myenteric plexi): Cytoplasmic vacuolation, diffuse, severe, chronic, with spongiosis

Comment: The clinical history and histopathology are consistent with a lysosomal storage disease. Ultrastructural study of cerebellar Purkinje cells revealed abundant, 1 – 2.5 μm diameter, intracytoplasmic, membrane-bound vacuoles containing variable amounts of lucent or fine fibrillogranular material, which is consistent with a disorder of glycoprotein degradation (oligosaccharidosis/glycoproteinoses) or a mucopolysaccharidosis (MPS). Both of these metabolic disorders can result in vacuolation of eccrine gland epithelium, endothelial cells, fibroblasts, lymphocytes, macrophages, pericytes, Schwann cells, and smooth muscle cells (1). However, endothelium may be spared in MPS, and the endothelial cell involvement in this case makes a disorder of glycoprotein degradation more likely. The genetic basis for most inborn errors of metabolism in humans are known, but there is still much to learn about the conditions in veterinary species. Alpha mannosidosis has been reported in Persian and domestic shorthair cats, and involves a mutation in the gene encoding alpha-mannosidase, which causes intracellular oligosaccharides to accumulate (2). MPS types I, VI, and VII have been reported in cats in the United States, and involve a variety of metabolic abnormalities that result in the accumulation of glycosaminoglycans (1). Further testing to determine the specific genetic abnormality in this case is currently being pursued.

References:

1. Pytel P, S Koo and D Waggoner. (2015). Inborn Errors of Metabolism. In AN Husain, JT Stocker, and LP Dehner (Ed.), *Stocker and Dehner's Pediatric Pathology*. Available at:
2. Schultheiss PC, SA Gardner, JM Owens, DA Wenger, and MA Thrall. Mucopolysaccharidosis VII in a Cat. Veterinary Pathology 2000;37(5):502-505.