“A17-15495”

SHANNON KIREJczyk, DVM, MPH
ANATOMIC PATHOLOGY RESIDENT II
UNIVERSITY OF GEORGIA

CO-CONTRIBUTORS:
ELIZABETH UHL, DVM, PHD, DACVP
ELIZABETH HOWERTH, DVM, PHD, DACVP
History

- 5-month-old, intact male, DSH kitten
- One of a litter of 5 kittens, 3 of which had similar clinical signs.
- Evaluated at UGA’s Neurology Service for progressive tetraparesis.
Physical Examination

- Poor muscling

- Hyperextension of the carpus and tarsus

- Neurologic Examination:
  - Gait: knuckling on forelimbs, crouched stance
  - Cerebellar: intention tremors
Differential Diagnosis

- Lysosomal storage disease
  - Mannosidosis
  - Gangliosidosis
  - Mucopolysaccharidosis
- Toxoplasmosis
- Neoplasia
  - Lymphoma
Clinical Pathology

CSF (CISTERNA)  PERIPHERAL BLOOD SMEAR

Image credit: Drs. Bridgette Wells & Jaime Tarigo

Permission granted only for viewing on SEVPAC website.
Previously reported in kittens with alpha mannosidosis and gangliosidosis.

Due to poor prognosis, kitten was euthanized and submitted for necropsy.
Histopathology
Purkinje cell
A mononuclear cell contains intracytoplasmic punctate vacuoles.
Cerebral Leptomeninges

Permission granted only for viewing on SEVPAC website.
Ancillary Tests

- No significant staining of material within cytoplasmic vacuoles
  - PAS reaction stain
  - Sudan Black
  - Luxol fast blue-cresyl violet

- Concanavalin A (Con A)
  - Lectin immunomarker
  - Specific for alpha-D-mannose and alpha-D-glucose residues
Morphologic Diagnosis

- Brain and spinal cord:
  - Neuronal vacuolation, diffuse, chronic, severe, with lysosomal accumulation of granular to flocculent, electron lucent material and spongiosis
Discussion
Mannosidoses

- Defects in alpha or beta mannosidase enzymes, which results in lysosomal accumulations of mannose-containing oligosaccharides.

- Alpha reported in cats and cattle (heritable).
  - *Sida carpinifolia* toxicity in goats (acquired)

- In humans, alpha can be distinguished from beta using Con A.
  - Also positive for succinyl wheat germ agglutinin (sWGA).

- Clinical signs vary
  - Neurologic signs most common
**GM$_1$ Gangliosidosis**

- Deficiency in beta-galactosidase.
- Occasional staining with Con A (humans).
- Less likely based on the absence of membranous whorls.

**Niemann-Pick**

- Types A & B = Deficiency in sphingomyelinase.
- Type C = Defect in NPC-1 membrane transporter.
- Less likely based on the absence of concentric membranous bodies and parallel palisaded lamellar (“zebra”) bodies.

---

Permission granted only for viewing on SEVPAC website.
Mucopolysaccharidosis

- Altered glycogosaminoglycan degradation.
  - Lysosomal accumulation of heparan, dermatan and/or chondroitin sulfate.
- Types I, IV, and VII reported in cats.
- Similar EM appearance to alpha mannosidosis.
- Less likely in this case due to:
  - Involvement of endothelial cells.
  - Lack of hepatosplenomegaly and cardiac valvular defects.
Case Summary and Conclusions

- Alpha mannosidosis is most likely in this case.
  - Electron microscopic appearance
  - Involvement of the endothelium
  - Immunofluorescence for Con A

- Ultrastructure may not be sufficient to identify a specific LSD, but can be used to refine the differential diagnosis.

- Molecular studies currently underway to identify specific genetic defect in this case.
Acknowledgments

Clinical pathology colleagues for CSF, Blood smear and Con A preparation and images
- Bridgette Wells, VMD, MLAS
- Jaime Tarigo, DVM, PhD, DACVP

Elizabeth Uhl, DVM, PhD, DACVP
Elizabeth Howerth, DVM, PhD, DACVP
Mary Ard
- Electron microscopy

UGA Histology Lab
UGA Residents
References


