Case 14-2607

A neurologic Emu

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Signalment & Clinical History

• 8 mo old, 14.6 kg, male emu

• Herd history:
  • 230 bird production flock intended for meat processing
  • Previous history of undiagnosed neurologic disease, typically affecting juvenile birds
  • Currently 4 affected birds in the flock
Clinical History

• Slowly progressive neurologic signs including head tremors, walking backwards and ataxia

• **Neurologic examination**: Marked ataxia and intention tremors
  • Localization: cerebellar/vestibular

• **CBC/Chem**: Unremarkable

• **MRI**: Possible subluxation of AA joint

• Submitted for postmortem examination
Gross Findings

- Intracoelomic hemorrhage
- Pale liver with multifocal subcapsular hemorrhages
- Grossly normal CNS
Luxol Fast Blue (400x)

Periodic Acid Schiff (400x)
Morphologic Diagnosis:

• Brain: Marked diffuse neuronal cytoplasmic vacuolization and cell swelling

Additional findings:

• Cytoplasmic vacuolization and swelling in all ganglia
• Histiocytosis with cytoplasmic vacuolization in the liver, gastrointestinal tract, and the spleen
• Diffuse vacuolization of renal tubular epithelium
Additional Tests

• Samples of normal and affected Emus were sent for gene analysis
• Affected emus had a homozygous 2 base pair deletion in the N-Acetyl-α-glucosaminidase (NAGLU) gene
• Diagnosis: Mucopolysaccharidosis IIIb (Sanfilippo syndrome type B)

Testing performed by Urs Giger and Keijiro Mizukami at University of Pennsylvania School of Veterinary Medicine, funded by NIH Grant for animal models of human genetic diseases (NIH OD 010939)
Mucopolysaccharidosis

• Lysosomal storage disease
• Mucopolysaccharidosis- a deficiency in 1 of 11 enzymes involved in the breakdown of glycosaminoglycans (GAGs)
  – Heparan sulfate
  – Keratan sulfate
  – Dermatan sulfate
  – Chondroitin sulfate
• 7 types of deficiencies have been characterized in animals species
Mucopolysaccharidosis

- Mucopolysaccharidosis type III, also known as Sanfilippo syndrome, results from the absence of 1 of 4 lysosomal enzymes involved in the degradation of heparan sulfate
  - heparan sulfate sulfamidase (SGSH; MPS type IIIA)
  - α-N-acetylg glucosaminidase (NAGLU; MPS type IIIB)
  - acetyl-CoA:α-glucosaminide-α-acetyltransferase (GNAT; MPS type IIIC)
  - N-acetylglucosamine-6-sulfatase (GNS; MPS type IIID)

(Valstar, 2008)
Mucopolysaccharidosis IIIB

• Deficiency of NAGLU is specific for MPS IIIB

• Results in accumulation of undegraded heparan sulfate within lysosomes, with some excretion through the urine testing

(Palmieri, 2015)

• In neurons and retina, there is also secondary accumulation of gangliosides
  - Variable staining with PAS and LFB
  - Variable appearance on EM
  - Variable results with biochemical
MPS in Emus

- In Emus, MPS IIIB causes progressive neurologic dysfunction in juvenile birds
  - May present as acute death
  - Acute hemorrhage is frequently observed
- Neuronal swelling and vacuolation present in cerebrum, cerebellum, brainstem, spinal cord, retina, autonomic ganglion of intestine, adrenal gland and ear
- Cytoplasm vacuoles also in pancreas, liver, intestine, adrenal glands, and kidney
- Foamy macrophages infiltrated the liver, intestine, aortic tunica media and spleen
Confirmatory Testing

• Biochemical: high levels of heparan sulfate in liver
• Lysosomal enzyme activities: Serum and liver NAGLU <8% of healthy controls; all other enzymes normal to increased
• Gene analysis: 2 bp deletion of NAGLU gene
• EM: 3 patterns
  • Nonmembrane bound electron dense bodies (GAG)
  • Multilaminar membrane bodies (Ganglioside)
  • Combined
Questions?

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