Case 15-001232
Myopathy in a Pembroke Welsh Corgi

DR. JESSICA BAILEY
DR. STEPHANIE SHRADER, DR. RICHARD WEISS
DEPARTMENT OF PATHOBIOLOGY
AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE
Signalment and History

- 5-year-old, intact male, Pembroke Welsh Corgi
  - research colony at Auburn’s Scott-Ritchey Research Center

- 24-hour history of progressive seizures
  - Similar seizure activity noted in specific family of dogs

- History of mild ptyalism, dysphagia, muscle weakness

- Euthanized
Necropsy Findings

- BCS 3/9
- Marked muscle wasting
  - Most significant, temporal muscles
- Marked hypertrophy of outermost 2-cm of the diaphragm (up to 2-cm)
- Pale streaking in skeletal muscles
- Heart grossly normal
Biceps femoris
Biceps femoris
Biceps femoris, trichrome
Cardiac muscle
Diaphragm
Morphological Diagnosis:

Skeletal muscle, biceps femoris:

Moderate, chronic, diffuse, myocyte atrophy, necrosis, regeneration, fibrosis and mineralization
Etiological Diagnosis:

Hereditary muscular dystrophy
Duchenne-like Muscular Dystrophy

- X-linked recessive inherited disease affecting dogs and people
  - Individuals unable to produce adequate amounts of dystrophin

- Dystrophin:
  - Cytoskeletal protein, localized in sarcolemma
  - Forms dystrophin-glycoprotein complex (DGC)
    - Dystroglycan, sarcoglycan and syntrophin/dystrobrevin complexes
    - Acts as membrane stabilizer during muscle contraction
  - Complex associations link cytoskeletal protein actin to basal lamina of muscle fibers

[Diagram of muscle structure and location of dystrophin]

http://www.biogenscience.com/2014/03/future-therapy-for-duchene-muscular.html
Duchenne-like Muscular Dystrophy

Pathophysiology:
- Loss of dystrophin → membrane becomes leaky as result of mechanical or hypoosmotic stress
- Ca²⁺ permeability increased, various Ca²⁺ depended proteases (i.e. calpain) activated
- Defect in DGC → muscle fiber necrosis → inflammation → regeneration → progressive replacement with fibrosis/fatty tissue
Duchenne-like Muscular Dystrophy

- **Murine models:**
  - Mdx mice
  - Mdx52 mice

- **Feline model:**
  - Hypertrophy feline muscular dystrophy (HFMD)

- **Canine models:**
  - Golden Retriever muscular dystrophy (GRMD)
  - Canine X-linked muscular dystrophy (CXMD)
  - Cavalier King Charles spaniels with muscular dystrophy (CKCS-MD)
Duchenne-like Muscular Dystrophy

Pembroke Welsh corgi model
- Mutation - long interspersed repetitive element-1 (LINE-1) insertion in intron 13
- Introduces a new exon containing in-frame stop codon

Clinical signs
- Generalized muscle atrophy, stiff shuffling gait, difficulty standing, exercise intolerance, hyperflexion of hock joint, dysphagia, ptyalism

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http://www.nature.com/abrinvest/journal/v91/n2/fig_tab/abrinvest20101481f1.html
Duchenne-like Muscular Dystrophy

- Dogs significantly smaller than litter mates by 6 weeks
- Clinical heart disease
- Classic histological lesions:
  - Skeletal muscle - variable fiber size, central nucleation, mineralization, fibrosis, neutrophil and macrophage infiltration
  - Cardiac muscle - focal vacuolar degeneration
- Carrier dogs display mild myopathy

https://woodwardswhiskey.wordpress.com/tag/muscular-dystrophy/
Reference


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