Latin Comparative Pathology Group

The Latin Subdivision of the CL Davis Foundation

Diagnostic Exercise

Answer Sheet

Case #: 55 Month: April Year: 2015

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Clinical History: A 37-kg, stillborn, chestnut Quarter horse filly from a surrogate mare with no history of prior illness presented to necropsy. The mare went into labor 2 weeks prior to due date.

Necropsy Findings: The foal had a crown-to-rump length of 101.7 cm; cranial features and limbs were well proportioned. Carcass was in good post-mortem state with minimal internal fat reserves. Both lungs were deep red, heavy and wet, and samples of the lung sank in 10% formalin. Liver was diffusely deep red and there were few linear streaks of hemorrhage in the papillary muscle of the heart, and scattered pinpoint hemorrhages in the cerebellum. All other viscera and submitted fetal membranes with placenta were macroscopically normal.

Microscopic images: Based on the following Figures 1 and 2 (hematoxylin and eosin-stained sections of heart, papillary muscle).

Morphologic diagnosis: Heart, papillary muscle: Cardiomyocyte degeneration, necrosis and mineralization, multifocal, moderate, acute, and intrasarcoplasmic PAS-positive globular deposits (Figure 3) consistent with glycogen.

Etiology: Glycogen storage disease, glycogen branching enzyme deficiency (GBED).

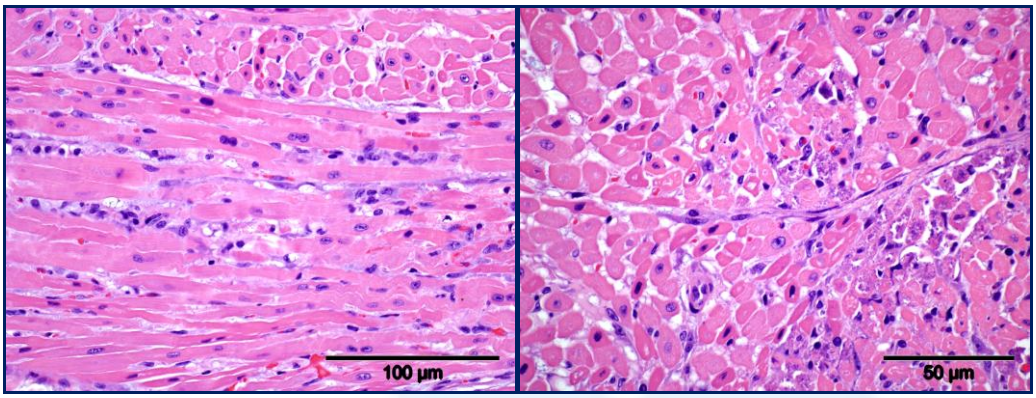

Figure 1 and 2

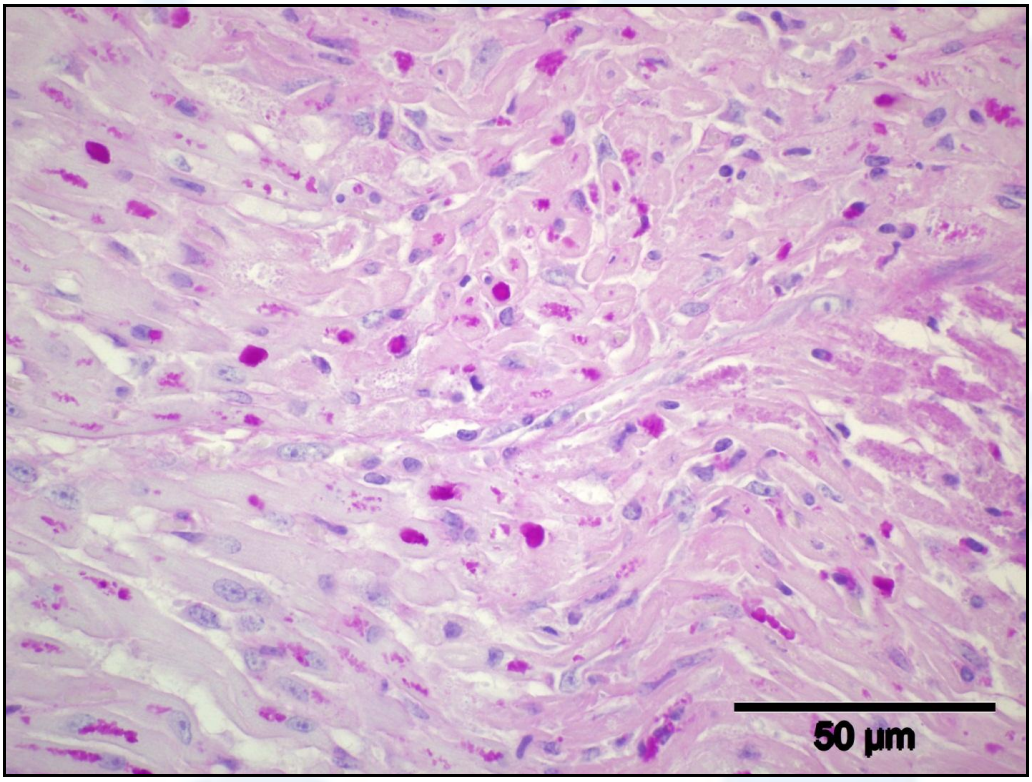

Figure 3: Heart, papillary muscle: PAS stain with diastase highlights intrasarcoplasmic PAS-positive globular deposits consistent with glycogen.

Gross findings: No specific gross lesions. Affected foals are aborted, stillborn, or weak at birth with contracted tendons and rhabdomyolysis; die at a young age due to cardiac failure; or need to be euthanized due to weakness.

Clinical Pathologic: Findings include leukopenia and elevations in serum creatine kinase (CK), aspartate aminotransferase (AST), and/or gamma glutamyltransferase (GGT).

Typical microscopic findings: Round to elongate, often perinuclear, homogenous hyaline to amphophilic globular material (inclusions) in skeletal myofibers, cardiac muscle especially Purkinje fibers, brain, spinal cord and less often in hepatocytes. Inclusions are PAS-positive and resistant to amylase digestion (i.e., diastase-resistant).

Ancillary laboratory testing: Homozygous for glycogen branching enzyme deficiency gene.

Discussion: The diastase-resistant PAS-positive globular deposits predominantly in cardiac and skeletal muscle, but also noted in other tissues including the brain, are characteristic for glycogen branching enzyme deficiency (GBED), also known as glycogenosis type IV. Hyaline inclusions resemble amylopectin or polyglucosan bodies. This condition affects Quarter horse and American Paint horse breeds, is inherited as an autosomal recessive trait, and has been reported as a cause of neonatal mortality. GBED is due to a C to A point mutation at base 102 resulting in a stop codon in exon 1 of the GBE1 gene encoding glycogen branching enzyme. Tissues from GBED foals have no measurable GBE-enzyme activity or immuno-detectable GBE and cannot form normally branched glycogen. Consequently, cardiac and skeletal muscle, liver and the brain cannot store or mobilize glycogen to maintain normal glucose homeostasis, and death is associated with hypoglycemia.

References:

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3. Ward TL, Valberg SJ, Adelson DL, Abbey CA, Binns MM, Mickelson JR, 2004.Glycogen branching enzyme (GBE1) mutation causing equine glycogen storage disease IV. Mammalian Genome. 15:570-577

4. Wagner ML, Valberg SJ, Ames EG, Bauer MM, Wiseman JA, Penedo MC, Kinde H, Abbitt B, Mickelson JR, 2006. Allele frequency and likely impact of the glycogen branching enzyme deficiency gene in Quarter Horse and Paint Horse populations. J Vet Int Med 20:1207-1211

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A final document containing this material with answers and a brief discussion will be posted on the C. L. Davis website by the end of the current month (http://www.cldavis.org/lcpg_english.html).