CMHD Pathology Report

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ReportID: Report Date: October 08, 2013
Pathologist: Dr. H. Adissu

CMHD LabID: N13-696

Relevant History:
Phenotype:

decreased CD4-positive
decreased CD8-positive

AnimalID: M00454129 (Male)

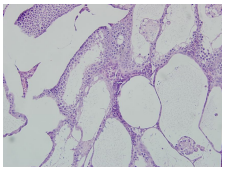
Histopathology Findings:

testis (MA:0000411)

Histopath Description:
There is extensive vacuolar degeneration and atrophy of the seminiferous tubules affecting upto 50% of the testis.

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** mild; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:
Testicular degeneration and atrophy



Testis, degeneration and atrophy, 20x, HE

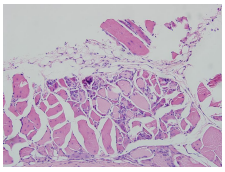
muscle (MA:0000015)

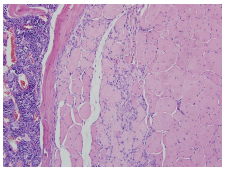
Histopath Description:
Affecting nearly 20% of the various skeletal muscles in the sternum, epaxial muscle and the limbs are multifocal degenerate and necrotic myocytes admixed with numerous slender myotubules with striated basophilic cytoplasm and central rows of nuclei (regeneration). Occasional myofibers are replaced by basophilic granular material (mineralization).

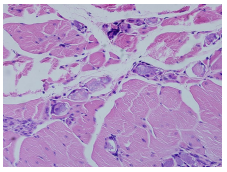
Morphological Diagnosis:
Severity: mild; **MPATH Diagnosis:** degenerative change MPATH:14; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:
Mild multifocal myodegeneration and myonecrosis with regeneration and mineralization

Histopathology Comments:
The presence of swollen myofibers instead of angular shrunken features suggests non-neurogenic pathogenesis. Ongoing degeneration and regeneration suggests repeated insult likely associated with repeated needle injury. Age-associated degenerative muscular lesions are documented in mice (Pathology of the Aging Mouse. Mohr DL et al. (eds). Vol. 1. ILSI Press. Washington, DC, 1996.)


Skeletal muscle, muscle degeneration and regeneration, 20x, HE


Skeletal muscle, muscle degeneration and regeneration, 20x, HE

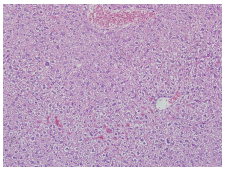

Skeletal muscle, multifocal mineralization, 40x, HE

liver (MA:0000358)

Histopath Description:
Mild lipidosis

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42;

Definitive Diagnosis:
Mild Hepatic lipidosis


Liver, mild lipisosis, 20x, HE

Organ/Tissue Analyzed:
Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, testis, epididymis, seminal vesicle, and prostate.

AnimalID: M00454130 (Male)

Histopathology Findings:

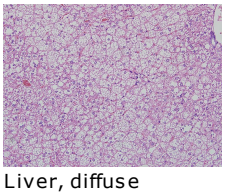
liver (MA:0000358)

Histopath Description:
The overall hepatic lobular architecture is normal. Diffusely, hepatocytes contain intracytoplasmic clear vacuoles (lipid). The lipid vacuoles within the midzonal and periacinar regions are small (2-3 um in diameter) and surround a central nucleus (interpreted as microvesicular lipid). The lipid vacuoles within the portal areas are large (8-12 um in diameter) and displace the nucleus to the margin (macrovesicular lipid).

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** extreme; **MPATH Diagnosis:** lipid deposition MPATH:42;

Definitive Diagnosis:
Hepatic lipidosis

Histopathology Comments:
Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet.


Liver, diffuse lipidosis, 20x, HE

brain (MA:0000168)

Histopath Description:
There is mild dilation of the lateral ventricles

Morphological Diagnosis:
Distribution: bilateral; **Severity:** mild; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:

Dilation of the brain ventricles

Histopathology Comments:
Mild dilation of the lateral ventricles is a background condition in mice of C57BL/6N background (Brayton et al., 2004).

retina (MA:0000276)

Histopath Description:
There are multifocal indulation of the retinal layers

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:
Retinal folding (dysplasia)

Organ/Tissue Analyzed:
Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, testis, epididymis, seminal vesicle, and prostate.

AnimalID: M00460062 (Female)

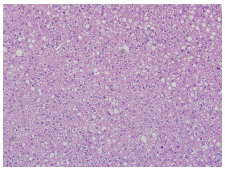
Histopathology Findings:

liver (MA:0000358)

Histopath Description:
Mild lipidosis

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42;

Definitive Diagnosis:
Mild Hepatic lipidosis



Liver, mild lipisosis, 20x, HE

ovary (MA:0000384)

Histopath Description:
There ovarian stroma is markedly expanded.

Morphological Diagnosis:
MPATH Process Term: hyperplasia MPATH:134

Definitive Diagnosis:
Ovarian stromal hyperplasia

Organ/Tissue Analyzed:
Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, uterus, oviduct, and ovary, and mammary gland.

AnimalID: M00460063 (Female)

Histopathology Findings:

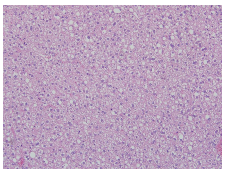
liver (MA:0000358)

Histopath Description:
Moderate lipidosis

Morphological Diagnosis:

Distribution: multifocal; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42;

Definitive Diagnosis:
Moderate Hepatic lipidosis


Liver, moderate lipisosis, 20x, HE

brain (MA:0000168)

Histopath Description:
There is mild dilation of the lateral ventricles

Morphological Diagnosis:
Distribution: bilateral; **Severity:** mild; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:
Dilation of the brain ventricles

Histopathology Comments:
Mild dilation of the lateral ventricles is a background condition in mice of C57BL/6N background (Brayton et al., 2004).

spleen (MA:0000141)

Histopath Description:
Mild erythropoiesis

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** mild; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:
Mild erythropoiesis

Organ/Tissue Analyzed:
Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, uterus, oviduct, and ovary, and mammary gland.

Report Summary and Recommendation:
Main lesions in this line are reduced hepatic lipidosis in three mice, generalized muscle degeneration and regeneration in one mouse, testicular degeneration and atrophy in one mouse, and ovarian stromal hyperplasia in one mouse.

Generalized and systemic skeletal muscle degeneration and regeneration is unique and is only seen in mouse models of myopathy. The lesion is present only in one mouse; hence genetic cause should be cautiously considered. Analysis of larger number of mice is warranted to determine genetic cause of low penetrance. In aging rats, impaired expression of the Catalytic Subunit of Glutamate Cysteine Ligase has been observed in soleus muscle under stress (chen et al., 2010). The decrease in GCL activities is partially responsible for the decline in glutathione levels in aging muscles with disuse. The impairment in GSH homeostasis may render aging muscle more susceptible to the ongoing oxidative damage from stress (Chen et al., 2010).

The minimal hepatic lipidosis,testicular and ovarian lesions were unpredictable by clinical phenotyping.

We did not find morphological correlates to the decreased CD4-positive and decreased CD8-positive cells. Histopathology is not sensitive enough to detect changes in lymphocytes subpopulations in hemolymphatic tissues.

Lines summary

Liver: Minimal lipidosis (2/4)
Skeletal muscle (generalized): Degeneration and regeneration (1/4)
Testis: Degeneration and atrophy (1/2)
Ovary: Ovarian stromal hyperplasia (1/2)

References:

Chen et al. (2010). Aging Impairs the Expression of the Catalytic Subunit of Glutamate Cysteine Ligase in Soleus Muscle Under Stress. J Gerontol A Biol Sci Med Sci. 65A(2): 129-137.