CMHD Pathology Report

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ReportID: Report Date: February 07, 2013
Pathologist: H. Adissu

CMHD LabID: N12-1506

Relevant History:
Phenotype:
Weight Curves (males decreased Weight). DEXA (weight).
Hom Via at P14. RL.

AnimalID: M00743476 (Male)

Histopathology Findings:

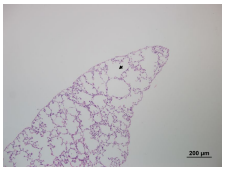
lung (MA:0000415)

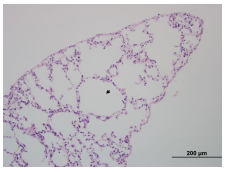
Histopath Description:
Multifocally alveoli are enlarged up to 2-3X normal

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** emphysema MPATH:31

Definitive Diagnosis:
Dilation of air alveoli

Histopathology Comments:
Definitive diagnosis of emphysema is problematic in non-perfused lung tissues.


Lung, dilated alveoli

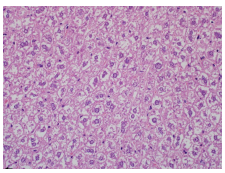

Lung, dilated alveoli

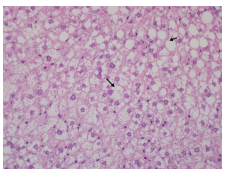
liver (MA:0000358)

Histopath Description:
Lipid deposition not observed

Definitive Diagnosis:
No lipid deposition in hepatocytes

Histopathology Comments:
Compare with liver from a wildtype mouse on high fat diet (image included)


Liver, absent lipidosis


Liver from WT high fat diet, lipidosis

kidney (MA:0000368)

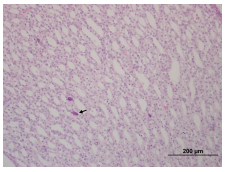
Histopath Description:
Occasional papillary tubules contain granular basophilic material that variably occludes lumina

(mineral).

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

Definitive Diagnosis:
Renal papillary intratubular mineral deposits

Histopathology Comments:
This minimal level of intraluminal mineral deposites is occasionally seen in wild type mice.


Kidney, papillary tubular mineralization

spleen (MA:0000141)

Histopath Description:
marked erythroid hyperplasia. Lymphoid follicles are enlarged with many of them having germinal centres.

Morphological Diagnosis:
Severity: moderate; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595

Definitive Diagnosis:
extramedullary erythroid hyperplasia; lymphoid hyperplasia

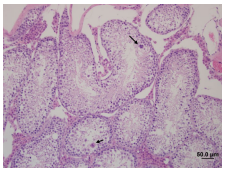
testis (MA:0000411)

Histopath Description:
Occasional large (50-100 um diamater), multinucleated cells are present within the seminiferous tubules. Some of these cells have pyknotic or fragmented nuclei.

Morphological Diagnosis:
Distribution: Multifocal; **Severity:** mild; **MPATH Diagnosis:** degenerative change MPATH:14

Definitive Diagnosis:
Multinucleate cells within the seminiferous tubules

Histopathology Comments:
The number of multinucleated giant cells within the testis appears to be increased in this mouse compared to the levels routinely seen. The significance of this change is uncertain in presence of robust spermatogenesis and abundant sperm stored within the epididymis. Multinucleated germ cells are often seen in the seminiferous tubules of fertile males from a number of species of rodents (Bryan, 1977). They can be present as spontaneous age associated lesions (Gordon et al., 1996), or are caused by various insults including ligation of the efferent duct (Singh and Abe, 1987), chemicals (Chinoya et al., 2005) and radiation toxicity associated with tritium (Bhatia, 1985). Ultrastructural studies suggest that the giant cells are formed as a result of the fusion of spermatids due to alterations in the intercellular bridges (Singh and Abe, 1987) or from degenerate spermatocytes or spermatids (Gordon et al., 1996).


Testis, multinucleated giant cells

brain (MA:0000168)

Histopath Description:
mild hydrocephalus of the lateral venticles

Morphological Diagnosis:
Distribution: bilateral; **Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

Definitive Diagnosis:
Mild hydrocephalus

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: M00739496 (Male)

Histopathology Findings:

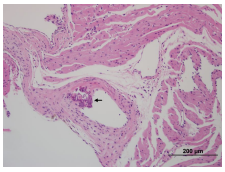
coronary artery (MA:0002453)

Histopath Description:
Focal osseous metaplasia

Morphological Diagnosis:
Duration: chronic; **Distribution:** focal; **Severity:** mild;

Definitive Diagnosis:
Osseous metaplasia

Histopathology Comments:
Osseous metaplasia of valves and blood vessels are occasionally seen as incidental lesion


Coronary artery, mineralization and osseous metaplasia

liver (MA:0000358)

Histopath Description:
Lipid deposition not observed

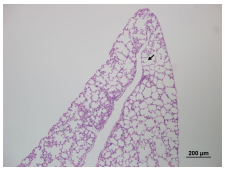
Definitive Diagnosis:
No lipid deposition in hepatocytes

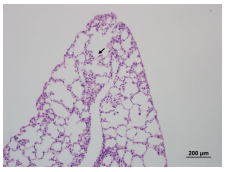
lung (MA:0000415)

Histopath Description:
No significant finding

Definitive Diagnosis:
No significant finding

Histopathology Comments:
Compare to M00743476


Lung, normal alveoli


Lung normal alveoli

brain (MA:0000168)

Histopath Description:
mild hydrocephalus of the lateral venticles

Morphological Diagnosis:
Distribution: bilateral; **Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

Definitive Diagnosis:
Mild hydrocephalus

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: M00743483 (Female)

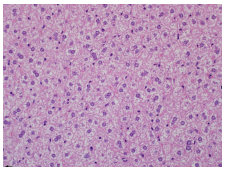
Tissue Preservation and Staining:
Thyroid and parathyroid glands are not present in section

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
Lipid deposition not observed

Definitive Diagnosis:
No lipid deposition in hepatocytes



Liver, absent lipidosis

skin (MA:0000151)

Histopath Description:
There is mild perifollicular mononuclear inflammatory infiltrates

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** dermatitis MPATH:196

Definitive Diagnosis:
Dermatitis, mild

brain (MA:0000168)

Histopath Description:
mild hydrocephalus of the lateral venticles

Morphological Diagnosis:
Distribution: bilateral; **Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

Definitive Diagnosis:
Mild hydrocephalus

Organ/Tissue Analyzed:
Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, 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: M00748102 (Female)

Histopathology Findings:

lymph node (MA:0000139)

Histopath Description:
The mesenteric lymph node is enlarged 3x than normal). There are multiple follicles with large germinal centers. The sinuses contain large numbers of mature lymphocytes.

Morphological Diagnosis:
Duration: Sub-acute; **Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lymphoid hyperplasia MPATH:147

Definitive Diagnosis:
Lymphoid hyperplasia.

Histopathology Comments:
The changes in the mesenteric lymph node are suggestive of draining of a regional inflammatory process. However, such a process was not observed in the tissues examined.

liver (MA:0000358)

Histopath Description:
Multifocal macrovesicular lipid deposition in hepatocytes

Morphological Diagnosis:
Distribution: multifocal; **Severity:** moderate; **MPATH Diagnosis:** steatosis MPATH:622

Definitive Diagnosis:
Moderate hepatic steatosis

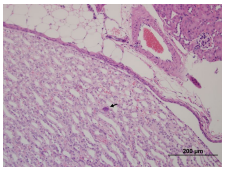
kidney (MA:0000368)

Histopath Description:
Occasional papillary tubules contain granular basophilic material that variably occludes lumina (mineral).

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

Definitive Diagnosis:
Renal papillary intratubular mineral deposits

Histopathology Comments:
This minimal level of intraluminal mineral deposites is occasionally seen in wild type mice.



Kidney, papillary tubular mineralization

brain (MA:0000168)

Histopath Description:
mild hydrocephalus of the lateral venticles

Morphological Diagnosis:
Distribution: bilateral; **Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

Definitive Diagnosis:
Mild hydrocephalus

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:
Absence of hepatic lipid deposition in 3/4 mice is consistent with decreased body weight.

The emphysematous change observed in one mouse (M00743476) should be considered with caution as described in the comment.

Minimal renal papillary tubular mineralization was observed in two mice (M00743476 and M00748102) while a focal mieralization and osseous metaplasia was observed in one mouse (M00739496). These lesions are occasionally seen in wild type controls. However, the prevalence of this lesion/s in this line (3/4) is unusual.

There are no lesions severe enough to explain reduced survival at p14. Analysis of tissues from clinically affected mice (if available) is recommended.

References:
Reference: Bhatia AL. (1985). Tritium Toxicity: Age-dependent Radiosensitivity of Mouse Testes. Bull. Environ. Contam. Toxicol. 34:803-808 Bryan JHD (1987). Spermatogenesis Revisited III. The Course of Spermatogenesis in a Male-Sterile Pink-Eyed Mutant Type in the Mouse. Cell Tiss. Res. 180, 173-186. Chinoya NJ et al. (2005). Fluoride+aluminium induced toxicity in mice testis with giant cells and its reversal by vitamin c. fluoride 38:109–114 Gordon LR, Majika JA, and Boorman GA (1996). Spontaneous Nonneoplastic and neoplastic lesions and experimentally induced neoplasms of the testes and accessory sex glands. In Pathobiology of the Aging Mouse. Mohr U et al (ed). Vol 1. ILSI, P422. Singh SK, Abe K. (1987). Light and electron microscopic observations of giant cells in the mouse testis after efferent duct ligation. Arch Histol Jpn. 50:579-85.