CMHD Pathology Report

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ReportID: Report Date: November 23, 2011
Pathologist: H. Adissu

CMHD LabID: N11-183

Relevant History:

Viability at postnatal day 14; Fertility; Body Weight Curves; Grip Strength; Dysmorphology; Indirect Calorimetry; Glucose Tolerance (ip); Body Composition (DEXA); X-ray Imaging; Eye Morphology; Plasma Chemistry;Haematology (CBC); Skin Histopathology) Partial lethality, decreased fertility, decreased body fat, decreased % body fat, decreased grip strength, abnormal snout/cranium/tooth morphology, abnormal joint and spinal column morphology, decreased BMC, abnormal humerus morphology, decreased body weight/length, increased erythrocyte number, decreased MCV and MCH, decreased cholesterol, FFA, amylase, and glycerol, abnormal hair shedding and hair cycling, abnormal cornea/lens and cataract

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AnimalID: M00230163 Nsun2 homo

Tissue Preservation and Staining:

A scant amount of thyoid gland is present in section; the parathyroid gland is unilaterally present. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

kidney (MA:0000368)

Histopath Description:

Extending from a focally depressed renal capsule into the superficial cortex is present a linear discrete focus (0.5x1mm) of tubular hyperplasia characterized by numerous small tubules lined by basophilic hypertrophic cuboidal epithelial cells. Protein casts are present within some of these tubules. Glomerulus associated with this focus is atrophic.

Morphological Diagnosis:

Distribution: Focal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

Definitive Diagnosis:

Tubular regenerative hyperplasia and interstitial fibroplasia

Histopathology Comments:

The lesion is suggestive of a previous tubular damage restricted to a single nephron. The cause if not obvious at this stage; the glomerulus associated with this nephron is unremarkable.

testis (MA:0000411)

Histopath Description:

Multifocally, the seminiferous tubules are vacuolated and hypocellular with fewer spermatids and no or minimum numbers of spermatocytes. Apoptotic bodies and multinucleated cells are frequent.

Morphological Diagnosis:

Distribution: Multifocal; **Severity:** moderate; **MPATH Diagnosis:** degenerative change MPATH:14

Definitive Diagnosis:

Testicular degeneration and atrophy with apoptosis and multinucleated cells.

Histopathology Comments:

The lesions are similar to those observed in M00258035 Nsun2 homo mouse.

epididymal duct (MA:0001735)

Histopath Description:

The epididymal duct in all segments contains cellular contain very few spermatocytes.

Morphological Diagnosis:

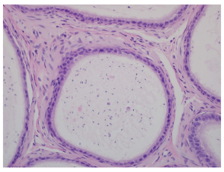
Distribution: Diffuse; **Severity:** severe;

Definitive Diagnosis:

Epididymal hypospermia.

Histopathology Comments:

The low spermatocyte number in the epididymis is consistent with the changes in the seminiferous tubules.



Epididymal duct, Tail of epididymis, hypospermia, 40x, HE.

brain (MA:0000168)

Histopath Description:

There is a mild enlargement of the third ventricle.

Morphological Diagnosis:

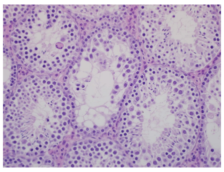
Severity: mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

Definitive Diagnosis:

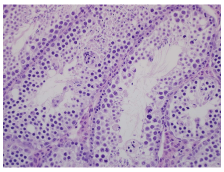
hydrocephalus, third ventricle

Histopathology Comments:

Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.



Testis, Testis , testicular degeneration and atrophy with apoptosis and multinucleated cells.40x, HE.



Testis, Testis , testicular degeneration and atrophy with apoptosis and multinucleated cells.40x, HE.

Organ/Tissue Analyzed:

There were no significant findings in the following tissues: Calvarium, brain, eyes, ears, tongue, Harderian gland, zymbal gland, salivary glands, nasal sinuses, teeth, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, liver, gall bladder, exocrine and endocrine pancreas, esophagus, stomach, intestines, adrenal gland, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

AnimalID: M00258035 Nsun2 homo

Tissue Preservation and Staining:

Thyroid not present in section. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

testis (MA:0000411)

Histopath Description:

Multifocally, the seminiferous tubules are vacuolated and hypocellular with fewer spermatids and no or minimum numbers of spermatocytes. Apoptotic bodies and multinucleated cells are frequent.

Morphological Diagnosis:

Distribution: Multifocal; **Severity:** moderate; **MPATH Diagnosis:** degenerative change MPATH:14

Definitive Diagnosis:

Testicular degeneration and atrophy with apoptosis and multinucleated cells.

epididymal duct (MA:0001735)

Histopath Description:
Very few spermatocytes are present within the tail of epididymis admixed with abundant proteinaceous material and cell debri.

Morphological Diagnosis:
Distribution: Diffuse;

Definitive Diagnosis:
Epididymal hypospermia

Histopathology Comments:
This is consistent with the testicular degeneration.

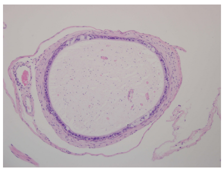
epididymal duct (MA:0001735)

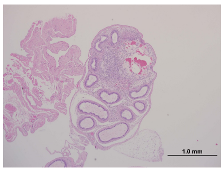
Histopath Description:
The tail of epididymis is focally disrupted by hemorrhage, edema, and a proteinaceous fluid in which are foamy macrophages, low number of neutrophils, lymphocytes, and few spermatocytes. This focus is surrounded by granulation tissue and fibrosis. The epididymal duct in all segments contains cellular contain very few spermatocytes.

Morphological Diagnosis:
Distribution: Focal; **Severity:** severe; **MPATH Diagnosis:** necrosis MPATH:4

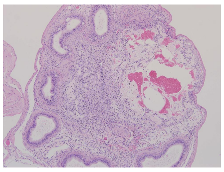
Definitive Diagnosis:
Epididymal duct necrosis and rupture with hemorrhage and fibrosis; epididymal hypospermia.

Histopathology Comments:
The lesion was likely of traumatic origin.


Tail of epididymis, hypospermia, 40x, HE.



Tail of epididymis, epididymitis, 4x, HE


Tail of epididymis, epididymitis, 10x, HE

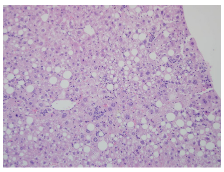
liver (MA:0000358)

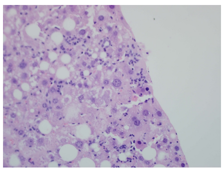
Histopath Description:
The overall hepatic lobular architecture is normal. Nearly 30% of hepatocytes mainly within the mid zone region contain large (8-15 um in diameter) intracytoplasmic clear vacuoles (macrovesicular lipid). Apoptotic cells (hepatocytes) are frewuently seen. Hepatocytes with binucleation and karyomegally are frequently seen. Mitotic figures are also frequent. Numerous single to clusters of neutrophils and lymphocytes are present randomly and around portal areas.There is a increased cellularity of sinusoidal lining cells reflecting proliferation of oval cells, Kuppfer cells, and Ito cells. Occasional intranuclear cytoplasmic inclusion bodies are present.

Morphological Diagnosis:
Duration: Chronic-active; **Distribution:** Multifocal; **Severity:** moderate; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
Neutrophilic and lymphocytic, with hepatocellular single cell necrosis, regeneration, and ito cell hyperplasia.

Histopathology Comments:
The lesion is suggestive of bacterial hepatitis. Special staining to rule out Helicobacter infection is recommended.


Liver, lipidosis and multifocal lymphocytic and neutrophilic hepatitis, 20x, HE.


Live, Multifocal chronic active hepatitis with increased sinusoidal lining cells and occasional apoptotc bodies, HE.

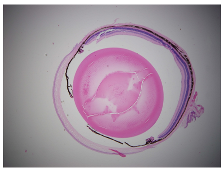
eye (MA:0000261)

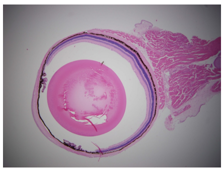
Histopath Description:
In one of the eyes, most of the iris is attached to the corneal endothelium (anterior synechia). The other eye is unremarkable (see images)

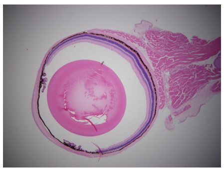
Morphological Diagnosis:
Distribution: diffuse; **MPATH Diagnosis:** synechia MPATH:623

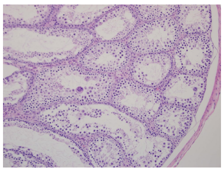
Definitive Diagnosis:
Anterior synechia

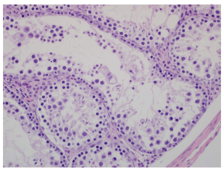
Histopathology Comments:
The lesion may explain the abnormality in eye morphology in some mice from this line. The cause for synechia is not evident.


Eye-1, anterior synechia, 4x, HE


Eye-1, anterior synechia, 20x, HE


Eye-2, normal, 4x


Testis, testicular degeneration and atrophy with apoptosis and multinucleated cells. 20x, HE.


Testis , testicular degeneration and atrophy with apoptosis and multinucleated cells.40x, HE.

Organ/Tissue Analyzed:
There were no significant findings in the following tissues: Calvarium, brain, eyes, ears, tongue, Harderian gland, zymbal gland, salivary glands, nasal sinuses, teeth, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, gall bladder, exocrine and endocrine pancreas, esophagus, stomach, intestines, urinary organs and tract, adrenal gland, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

AnimalID: M00249573 Nsun2 homo

Tissue Preservation and Staining:
Thyroid gland is not present in section; the parathyroid gland is unilaterally present. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Organ/Tissue Analyzed:
There were no significant findings in the following tissues: Calvarium, brain, eyes, ears, tongue, Harderian gland, zymbal gland, salivary glands, nasal sinuses, teeth, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, liver, gall bladder, exocrine and endocrine pancreas, esophagus, stomach, intestines, urinary organs and tract, adrenal gland, reproductive organs, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

AnimalID: M00258036 Nsun2 homo

Tissue Preservation and Staining:
Thyroid gland is not present in section. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
There are rare small mononuclear inflammatory cells within the liver. Lipidosis is not seen.

Morphological Diagnosis:
Duration: Chronic; **Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
Multifocal mononuclear inflammatory cell aggregates.

Histopathology Comments:
Hepatic lipidosis is not present in this mouse in contrast to its cohorts.

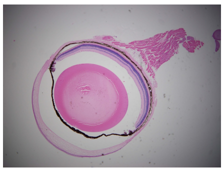
salivary gland (MA:0000346)

Histopath Description:
There is a focal interstitial aggregate of histiocytes and lymphocytes.

Morphological Diagnosis:
Duration: Chronic; **Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
Interstitial histiocytic and lymphocytic sialadenitis

Histopathology Comments:
This is a common and insignificant incidental finding in mice.



Eye, normal, 4x, HE

Organ/Tissue Analyzed:
There were no significant findings in the following tissues: Calvarium, brain, eyes, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, gall bladder, exocrine and endocrine pancreas, esophagus, stomach, intestines, urinary organs and tract, adrenal gland, reproductive organs, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

Summary:
In this line, there are degenerative and atrophic changes within the testis accompanied by decreased spermatogenesis. This lesion is expected to compromise fertility.

Report Summary and Recommendation:
In this line, there are degenerative and atrophic changes within the testis that are accompanied by decreased spermatogenesis. This lesion is expected to compromise fertility. One mouse had unilateral anterior synechia; lesion may be consistent with ocular abnormality observed in this line. We did not observe microscopic abnormalities within the hair follicles and other adnexal structures. Occasional patchy anagen and telogen stage hair follicles were observed. This was considered normal for an adult mice as hair in the adult cycles in domains and less so in wave patten (as in the case in young animals) (Plikus and Chuong, 2008; Sundberg and Silva, 2012). Humerus was not collected for histology, hence we could not confirm abnormal humerus morphology observed during in-life phenotyping.

Testis: Degenerative change : MPATH:14

References:
Plikus MV, Chuong CM. Complex hair cycle domain patterns and regenerative hair waves in living rodents. J Invest Dermatol. 2008;128:1071–1080. J. P. Sundberg andK. A. Silva. What Color Is the Skin of a Mouse? Vet Pathol 2012 49: 142-145.