CMHD Pathology Report

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ReportID: Report Date: August 22, 2013
Pathologist: Dr. H. Adissu

CMHD LabID: N13-492

Relevant History:
Phenotypes:

hypoferremia
mydriasis
impaired pupillary reflex
abnormal placement of pupils
abnormal iris morphology
eyelids fail to open
corneal opacity
abnormal cornea morphology
decreased body length
decreased mean corpuscular volume
decreased mean corpuscular hemoglobin
vertebral fusion
scoliosis
abnormal spine curvature
partial lethality
eye development abnormalities
fetal edema
partial lethality
abnormal cornea morphology
abnormal vitreous body

AnimalID: M00633323 (Male)

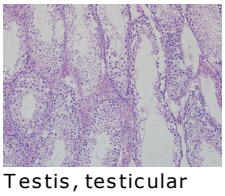
Histopathology Findings:

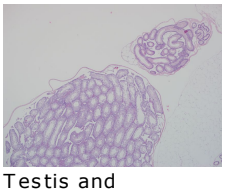
testis (MA:0000411)

Histopath Description:
The seminiferous tubule is multifocally vacuolated. Spermatozoa are absent in the lumen and there is no evidence of differentiation of spermatids to spermatozoa. There are numerous apoptotic spermatids and occasional multinucleated spermatids. The epididymis is devoid of spermatozoa and contains cytoplasmic and nuclear debris.

Morphological Diagnosis:
Distribution: diffuse; **Severity:** extreme;

Definitive Diagnosis:
Testicular degeneration and atrophy with absence of spermiogenesis; epididymal aspermia


Testis, testicular degeneration and atrophy with absence of spermiogenesis,


Testis and epididymis, degeneration and atrophy and epididymal

20x, HE aspermia, 4x, HE

liver (MA:0000358)

Histopath Description:
diffuse lipidosis

Morphological Diagnosis:
Distribution: diffuse; **Severity:** severe; **MPATH Diagnosis:** steatosis MPATH:622

Definitive Diagnosis:
Hepatic lipidosis

brain (MA:0000168)

Histopath Description:
There is mild dilation of the lateral ventricles

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

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).

aorta (MA:0000062)

Histopath Description:
The base of the aorta is segmentally thickened by fibroplasia and the wall is disrupted by deeply eosinophilic hyaline to fibrinoid material (fibrinoid necrosis).

Morphological Diagnosis:
Distribution: focally extensive; **Severity:** moderate; **MPATH Diagnosis:** vasculitis MPATH:201

Definitive Diagnosis:
Aortitis, proliferative and necrotizing

Histopathology Comments:
Inflammatory lesions of small and medium-sized arteries are common in many strains of laboratory mice. The distribution of affected vessels is quite variable and could involve arteries of the heart among others. Lesions may involve multiple vessels, hence termed "polyarteritis." The etiology of polyarteritis is not known, but thought to be immune complex-mediated. It is common in mice that are prone to autoimmune disease, including MRL and NZB mice. Polyarteritis is usually an incidental finding (Percy and Barthold. 2007).

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: M00589354 (Male)

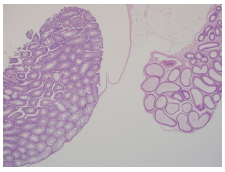
Histopathology Findings:

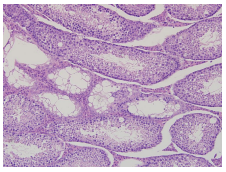
testis (MA:0000411)

Histopath Description:
The seminiferous tubule is multifocally vacuolated. Spermatozoa are minimal to absent in the lumen and there is minimal differentiation of spermatids to spermatozoa. There are numerous apoptotic spermatids and occasional multinucleated spermatids. The epididymis is devoid of spermatozoa and contains cytoplasmic and nuclear debris.

Morphological Diagnosis:
Distribution: diffuse; **Severity:** extreme;

Definitive Diagnosis:
Testicular degeneration and atrophy with absence of spermiogenesis; epididymal aspermia


Testis and epididymis, degeneration and atrophy and epididymal aspermia, 4x, HE


Testis, testicular degeneration and atrophy with absence of spermiogenesis, 20x, HE

liver (MA:0000358)

Histopath Description:
diffuse lipidosis

Morphological Diagnosis:
Distribution: diffuse; **Severity:** severe; **MPATH Diagnosis:** steatosis MPATH:622

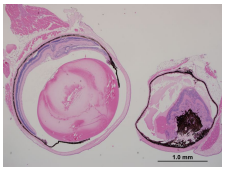
Definitive Diagnosis:
Hepatic lipidosis

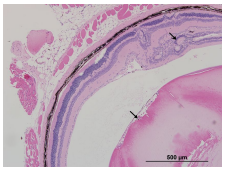
eye (MA:0000261)

Histopath Description:
The posterior retina is dysplastic with extensive multifocal retinal folding and rossette formation. There is mild cataractous change at the posterior margin of the lens

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** severe;

Definitive Diagnosis:
Retinal dysplasia; cataract


Two eyes, microphthamia (right); retinal dysplasia (left), 4x, HE


Marked retinal dysplasia with rossette formation; mild posterior cataract, 10x, HE

eye (MA:0000261)

Histopath Description:
The other eye is small (nearly half the normal size). The retinal is thrown into folds and disorganized mass and is adhered to a small piece of lens material (containing degenerate lens proteins or Morgagnian globules). Other ocular structures including the anterior uvea are disorganized.

Morphological Diagnosis:
Distribution: diffuse; **Severity:** extreme;

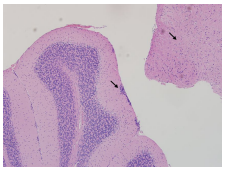
Definitive Diagnosis:
Microphtalmia

brain (MA:0000168)

Histopath Description:
There are three foci of aggregates of granular cells in the within the outer aspect of the molecular layer.

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

Definitive Diagnosis:
Cerebellar granular cell heterotopia


Brain, cerebellum,

heterotopic granular cells, 10x, 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: M00547941 (Male)

Histopathology Findings:

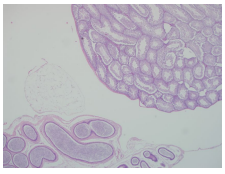
testis (MA:0000411)

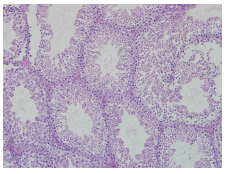
Histopath Description:
Normal

Morphological Diagnosis:
Severity: no lesions;

Definitive Diagnosis:
Normal testis

Histopathology Comments:
compare to the other two male mice


Testis and epididymis, normal,4x, HE


Testi, mormal, 20x, HE

lymph node (MA:0000139)

Histopath Description:
The mesenteric lymph node is markedly enlarged (greater than four fold). The medulla is particularly expanded by chords and sheets of plasmatoid cells. There are promient germinal centers within the medulla

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134

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. Early maginal center lymphoma is suspected.

liver (MA:0000358)

Histopath Description:
diffuse lipidosis

Morphological Diagnosis:
Distribution: diffuse; **Severity:** severe; **MPATH Diagnosis:** steatosis MPATH:622

Definitive Diagnosis:
Hepatic lipidosis

retina (MA:0000276)

Histopath Description:
Involving one eye, there are clusters of external nuclear structures within the internal plexiform layer.

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

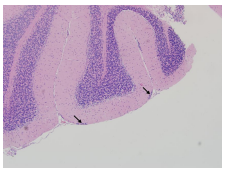
Definitive Diagnosis:
Retinal dysplasia

brain (MA:0000168)

Histopath Description:
There are two small foci of aggregates of granular cells in the within the outer aspect of the molecular layer.

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

Definitive Diagnosis:
Cerebellar granular cell heterotopia



Brain, cerebellum, heterotopic granular cells, 10x, 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: M00736694 (Female)

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
mild lipidosis

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

Definitive Diagnosis:
mild hepatic lipidosis

lymph node (MA:0000139)

Histopath Description:
The mesenteric lymph node is markedly enlarged (greater than four fold). The medulla is particularly expanded by chords and sheets of plasmatoid cells. There are promient germinal centers within the medulla

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134

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. Early maginal center lymphoma is suspected.

brain (MA:0000168)

Histopath Description:
There is mild dilation of the lateral ventricles

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

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).

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:
Three male mice are submitted. The two homozygotes show severe seminiferous degenerative and atrophic changes with absence of spermatogenesis. This is unexpected phenotype in absence of reported infertility in this line. The heterozygous male mice has no testicular lesion.

Two mice have cerebellar granule cell heterotopia. The lesions are mild and their functional effect (if any) is doubtful. Aberrant granule cells in the cerebellar molecular layer are rare in C57BL/6J mice. They have been described in 'nervous' (nr/nr) mutant mice of the Balb/cGr strain. Similar heterotopic cells are also present in normal mice of the Balb/cGr and C3Heb/FeJ strains, although to a much lesser degree (Landis, 1973).

One of the homozygous mouse has severe ocular abnormalities (unilateral microphtalmia and marked retinal dysplasia with cataractous lenticular changes in the contralateral eye). Lesion may explain the ocular abnormalities in this line.

Aortic vasculitis is seen in one of the homozygotes - in view of fetal edema and partial lethality, this lesion may signify vascular abnormality in homozygotes. Note that this lesion may rarely be seen in WTcontrols.

Line summary
1. Testicular degeneration and atrophy with epididymal aspermia (2/3 male mice)
2. Cerebellar granular cell heterotopia (2/4)
3. Micropthalmia (1/4); Retinal dysplasia (2/4); Cataract (2/4)
4. Aortic vasculitis (1/4)

Other lesions are attributable to diet or strain background.

References:
S.C. Landis, Granule cell heterotopia in normal and nervous mutant mice of the BALB/c strain, Brain Research, Volume 61, 26 October 1973, Pages 175-189