CMHD Pathology Report

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Mouse Portal
Europhenome

ReportID: Report Date: September 12, 2013
Pathologist: Dr. H. Adissu

CMHD LabID: N13-565

Relevant History:
Phenotype:
decreased lumbar vertebrae number
increased sacral vertebrae number
lumbar vertebral transformation
vertebral transformation
abnormal vertebral arch morphology
chromosomal instability

AnimalID: M00896523 (Male)

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
diffuse lipidosis

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

Definitive Diagnosis:
hepatic steatosis

brain (MA:0000168)

Histopath Description:
There is mild dilation of the lateral ventricles. The medulla is poorly preserved to assess lesions observed in M00896535 and M00896536.

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).

eye (MA:0000261)

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

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

Definitive Diagnosis:
Retinal 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: M00896524 (Male)

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
diffuse lipidosis

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

Definitive Diagnosis:
hepatic steatosis

brain (MA:0000168)

Histopath Description:
There is mild dilation of the lateral ventricles. The medulla is poorly preserved to assess lesions observed in M00896535 and M00896536.

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).

thymus (MA:0000142)

Histopath Description:
There are two 50 um diamater epithelial cysts.

Morphological Diagnosis:
Distribution: multifocal; **MPATH Diagnosis:** cyst MPATH:62

Definitive Diagnosis:
Epithelial cyst

Histopathology Comments:
This is a developmental abnormality commonly seen in mice.

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: M00896536 (Female)

Histopathology Findings:

brain (MA:0000168)

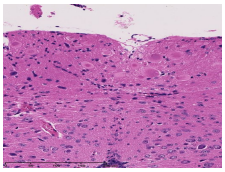
Histopath Description:
Within the neuropil of the dorsal medullary region (area posterama, solitary and cuneate nuclei) are numerous eosinophilic, amorphous granular spheroid/globular bodies that are 20-40 um in diameters. Some of the spheroids have a basophilic core. There is no cellular reaction in these areas. The lateral ventricles are mildly dilated.

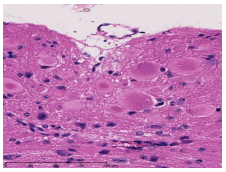
Morphological Diagnosis:
Distribution: multifocal;

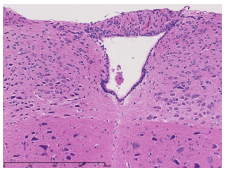
Definitive Diagnosis:
Eosinophilic spheroids in dorsal medullar nuclei

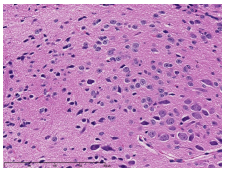
Histopathology Comments:
See line summary for comments on this lesion. Mild dilation of the lateral ventricles is a background

condition in mice of C57BL/6N background (Brayton et al., 2004).


Brain stem, spheroid bodies within the neuropil, 20x, HE


Brain stem, spheroid bodies within the neuropil, 40x, HE


Brain stem, WT, normal, 20x, HE


Brain stem, WT, normal, 40x, HE

liver (MA:0000358)

Histopath Description:
moderate lipidosis

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

Definitive Diagnosis:
hepatic steatosis

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: M00896535 (Female)

Histopathology Findings:

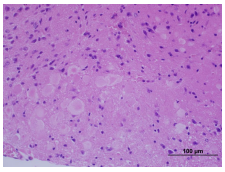
brain (MA:0000168)

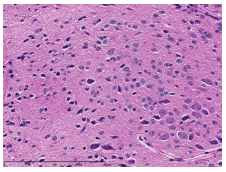
Histopath Description:
Within the neuropil of the dorsal medullary region (area posterama, solitary and cuneate nuclei) are numerous eosinophilic, amorphous granular spheroid/globular bodies that are 20-40 um in diameters. Some of the spheroids have a basophilic core. There is no cellular reaction in these areas. The lateral ventricles are mildly dilated.

Morphological Diagnosis:
Distribution: multifocal;

Definitive Diagnosis:
Eosinophilic spheroids in dorsal medullar nuclei

Histopathology Comments:
See line summary for comments on this lesion. Mild dilation of the lateral ventricles is a background condition in mice of C57BL/6N background (Brayton et al., 2004).


Brain stem, spheroid bodies within the neuropil, 40x, HE


Brain stem, WT, normal, 40x, HE

liver (MA:0000358)

Histopath Description:
diffuse lipidosis

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

Definitive Diagnosis:
hepatic steatosis

thymus (MA:0000142)

Histopath Description:
There are two 50 um diamater epithelial cysts.

Morphological Diagnosis:
Distribution: multifocal; **MPATH Diagnosis:** cyst MPATH:62

Definitive Diagnosis:
Epithelial cyst

Histopathology Comments:
This is a developmental abnormality commonly seen in mice.

thyroid gland (MA:0000129)

Histopath Description:
The thyroid gland is partially replaced by a lymphoid tissue reminiscent of thymic tissue.

Morphological Diagnosis:
Distribution: multifocal;

Definitive Diagnosis:
Ectopic thymic tissue

Histopathology Comments:
This is developmental anomaly incidentally seen in mice

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.

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 lesion in this line is the presence of eosinophilic speheroid bodies in the dorsal medullary nuclei in two female mice (M00896535 and M00896536). The brainstem ifrom the other two male mice (both males) is fragmented and poorly preserved.

The morphology and the specific location of these bodies is very similar to those described in autophagy-related 4b (Agtb4b) mutants (Read et al., 2011). In addition, mice deficient for Atg5 (autophagy-related 5) specifically in neural cells develop progressive deficits in motor function that are accompanied by the accumulation of cytoplasmic inclusion bodies in neurons (Hara et al., 2006). These types of bodies are occasionally seen in old mice so their appearance in young mice is often associated with premature senility or autophagy defects. We suspect they represent the latter stages of axonal spheroids and dystrophic axons and neurites, basically an accumulation of incompletely digested endosomal/lysosmal contents and thus the connection to autophagy defects. Based on these findings, we speculate that the Esco1gene may have a role in autophagy. We did not see similar lesions elsewhere in other tissues. Hence its role (if any) in the phenotypes observed in this line are uncertain.

It is challenging to corroborate the skeletal dysmorphologies by histopathology.

Line summary: Eosinophilic spheroids in dorsal medullary nuclei (2/4).