



CMHD Pathology Report



CMHD Pathology Core

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Mouse Genetics Project

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CMHD LabID: N13-581

Relevant History:

Phenotypes:

preweaning lethality
embryonic lethality
abnormal optic nerve morphology
retinal degeneration

AnimalID: M00688346

Histopathology Findings:

eye (MA:0000261)

Histopath Description:

Involving one eye, there are focal clusters of external nuclear structures within the outer plexiform layer. The optic nerve is unremarkable

Morphological Diagnosis:

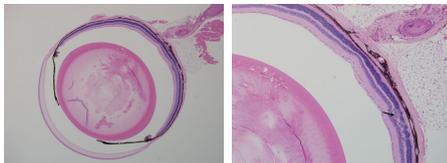
Distribution: Focal; **Severity:** mild;

Definitive Diagnosis:

Retinal dysplasia

Histopathology Comments:

Retinal dysplasia is reported as a background lesion in C57BL/6N lines (Mattapallil et al., 2012).



Eye, retinal
dysplasia, 4x, HE

Eye, retinal
dysplasia, 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 plasmotoid cells. There are prominent germinal centers within the medulla

Morphological Diagnosis:

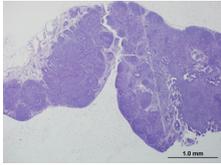
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134

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 marginal center lymphoma is suspected.



Lymph node,
lymphoid
hyperplasia, 4x, HE

liver (MA:0000358)

Histopath Description:

diffuse lipidosis

Morphological Diagnosis:

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

Definitive Diagnosis:

hepatic steatosis

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).

skin (MA:0000151)

Histopath Description:

There are clusters of mononuclear inflammatory cells within the panniculus carnosus. There is focally extensive regeneration of the skeletal muscle within the panniculus carnosus characterized by multinucleated large basophilic myotubules and central nuclear rowing. There are occasional fibers with prominent wavy fibers. The overlying dermis and hypodermis are unremarkable.

Morphological Diagnosis:

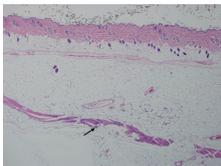
Distribution: diffuse; **Severity:** moderate;

Definitive Diagnosis:

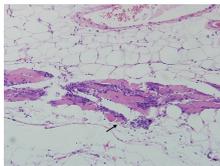
Panniculus carnosus: Degeneration with rare ragged myofibers, regeneration, mild mononuclear inflammatory infiltrates.

Histopathology Comments:

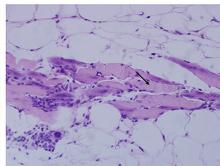
The cause for this lesion is uncertain. A deep skin wound out the field of vision is a likely cause. The wavy ragged fibers are atypical.



Panniculus
carnosus muscle:
Degeneration with
rare ragged
myofibers,
regeneration, mild
mononuclear
inflammatory
infiltrates, 4x, HE



Panniculus
carnosus muscle:
Degeneration with
rare ragged
myofibers,
regeneration, mild
mononuclear
inflammatory
infiltrates, 20x, HE



Panniculus
carnosus muscle:
Degeneration with
rare ragged
myofibers,
regeneration, mild
mononuclear
inflammatory
infiltrates, 40x, HE

AnimalID: M00688328**Histopathology Findings:****eye (MA:0000261)****Histopath Description:**

Involving one eye, there are clusters of external nuclear structures within the internal and outer plexiform layer. The optic nerve is unremarkable

Morphological Diagnosis:

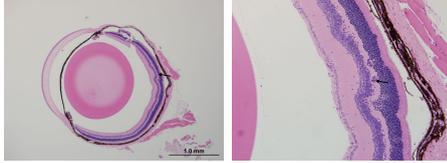
Distribution: Focal; **Severity:** mild;

Definitive Diagnosis:

Retinal dysplasia

Histopathology Comments:

Retinal dysplasia is reported as a background lesion in C57BL/6N lines (Mattapallil et al., 2012).



Eye, retinal
dysplasia, 4x, HE

Eye, retinal
dysplasia, 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 plasmotoid cells. There are prominent germinal centers within the medulla

Morphological Diagnosis:

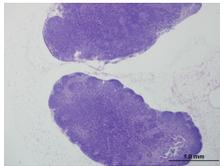
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134

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 marginal center lymphoma is suspected.



Lymph node,
lymphoid
hyperplasia, 4x, HE

liver (MA:0000358)**Histopath Description:**

diffuse lipidosis

Morphological Diagnosis:

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

Definitive Diagnosis:

hepatic steatosis

salivary gland (MA:0000346)**Histopath Description:**

There are multifocal perivascular mononuclear inflammatory cell aggregates.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Interstitial inflammatory aggregates

AnimalID: M00688331

Histopathology Findings:**eye (MA:0000261)****Histopath Description:**

Involving one eye, there are focal clusters of external nuclear structures within the outer plexiform layer. The optic nerve is unremarkable

Morphological Diagnosis:

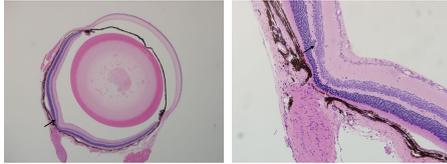
Distribution: Focal; **Severity:** mild;

Definitive Diagnosis:

Retinal dysplasia

Histopathology Comments:

Retinal dysplasia is reported as a background lesion in C57BL/6N lines (Mattapallil et al., 2012).



Eye, retinal
dysplasia, 4x, HE

Eye, retinal
dysplasia, 20x, HE

lymph node (MA:0000139)**Histopath Description:**

The mesenteric lymph node is markedly enlarged (greater than five-fold). The medulla is expanded by chords and sheets of plasmotoid cells.

Morphological Diagnosis:

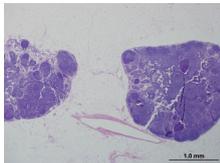
Distribution: Diffuse; **Severity:** severe; **MPATH Diagnosis:** hyperplasia MPATH:134

Definitive Diagnosis:

Lymphoid hyperplasia with medullary plasmacytosis.

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.



Lymph node,
lymphoid
hyperplasia, 4x, HE

liver (MA:0000358)**Histopath Description:**

diffuse lipidosis

Morphological Diagnosis:

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

Definitive Diagnosis:

hepatic steatosis

stomach (MA:0000353)**Histopath Description:**

mild neutrophilic gastritis; there is also mild epithelial proteinosis

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Mild neutrophilic gastritis with epithelial proteinosis

AnimalID: M00688330**Tissue Preservation and Staining:**

One of the eyes is poorly preserved and fragmented; hence not suitable for interpretation.

Histopathology Findings:**eye (MA:0000261)****Histopath Description:**

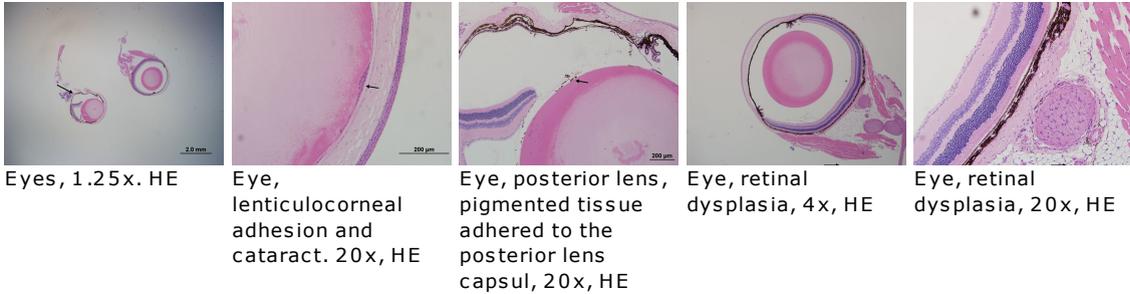
One of the eyes is poorly preserved and fragmented. This eye is smaller than the contralesional eye. The lens is adhered to the cornea. There is a focal proliferation and extension of the lens epithelium into the lens material. On the posterior aspect a fragment of pigmented tissue is intermittently attached to the posterior lens capsule. There are clusters of lens epithelial cells at the posterior margin (posterior migration of the lens epithelium). Most of the retinal structure is fragmented with marked crush artifact, hence not interpretable. The available retinal tissue within the globe is unremarkable. In the contralateral eye, there are focal clusters of external nuclear structures within the outer plexiform layer. The optic nerve is unremarkable

Morphological Diagnosis:

Severity: moderate; **MPATH Diagnosis:** cataract MPATH:29

Definitive Diagnosis:

Eye 1: Lenticulocorneal adhesion and cataract; possible microphthalmia; Eye 2: Retinal dysplasia



Eyes, 1.25x, HE

Eye, lenticulocorneal adhesion and cataract. 20x, HE

Eye, posterior lens, pigmented tissue adhered to the posterior lens capsul, 20x, HE

Eye, retinal dysplasia, 4x, HE

Eye, retinal dysplasia, 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 plasmotoid cells. There are prominent germinal centers within the medulla

Morphological Diagnosis:

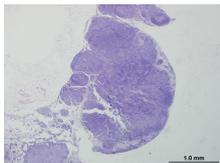
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134

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 marginal center lymphoma is suspected.



Lymph node, Lymphoid hyperplasia, 4x, HE

liver (MA:0000358)**Histopath Description:**

diffuse lipidosis

Morphological Diagnosis:

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

Definitive Diagnosis:

hepatic steatosis

Report Summary and Recommendation:

Retinal dysplasia is observed in all mice while one mouse had lesions consistent with cataract. The retinal lesion is consistent with those reported as a background lesion in C57BL/6N lines (Mattapallil et al., 2012). The optic nerve is normal in all mice observed and we did not see evidence of retinal degeneration contrary to the clinical phenotype annotation. Some of the lesions described in the clinical phenotypes (based on images on MG portal) suggest microphthalmia (another background ocular condition in B6

strains). Disorganization of the optic cup is commonly seen in microphthalmia.

Marked lymphoid hyperplasia was observed in all mice. The significance of this lesion in absence of clinical immune phenotypes is uncertain.

A unique lesion of myositis with marked muscle regeneration was seen in the panniculus carnosus. The absence of inflammatory lesions in the overlying dermis and epidermis suggests that this lesion may be primarily affecting the panniculus carnosus muscle. The muscle lesion is characterized by presence of atypical wavy ragged muscle fibers. Ragged red fibers are seen in proportion of individuals with Kearns-Sayre syndrome (KSS), mitochondrial myopathy. KSS is a more severe syndromic variant of chronic progressive external ophthalmoplegia (abbreviated CPEO), a condition associated with mutation in POGD2 gene. Inconsistent features of KSS are weakness of facial, pharyngeal, trunk, and extremity muscles. Gömöri trichrome stain and other histochemical studies such as mitochondrial enzyme stains, and electron microscopy are used to confirm mitochondrial myopathy (Sundaram et al., 2011). Note that the muscle lesion is seen focally and only in the panniculus carnosus; hence the finding should be interpreted with caution and we do not rule out the possibility that this could be an incidental finding.

There are no lesions predictive of homozygous lethality at P14. Analysis of preweaning homozygous animals is required to determine cause of mortality.

Summary:

Eye, Retina: Retinal dysplasia (4/4); lenticulocorneal adhesion and cataract; possible microphthalmia (1/4)
Lymph node: Lymphoid hyperplasia (4/4)
Panniculus carnosus muscle: degeneration with rare ragged myofibers, regeneration, mild mononuclear inflammatory infiltrates (1/4)

References:

Mattapallil MJ, Wawrousek EF, Chan CC, Zhao H, Roychoudhury J, Ferguson TA, Caspi RR. (2012). The Rd8 mutation of the Crb1 gene is present in vendor lines of C57BL/6N mice and embryonic stem cells, and confounds ocular induced mutant phenotypes. Invest Ophthalmol Vis Sci. 53:2921-2927. Sundaram C et al., 2011. Contribution of muscle biopsy and genetics to the diagnosis of chronic progressive external ophthalmoplegia of mitochondrial origin. J Clin Neurosci. 18(4):535-8.