



CMHD Pathology Report



CMHD Pathology Core

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ReportID: Report Date: January 13, 2014
Pathologist: Dr. H. Adissu

Mouse Genetics Project

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CMHD LabID: N13-909

Relevant History:

increased circulating bilirubin level
hypoferraemia
increased red blood cell distribution width
decreased erythrocyte cell number
increased platelet cell number
increased mean corpuscular volume
decreased hemoglobin content
decreased hematocrit
decreased T cell number
decreased CD4-positive T cell number
increased CD4-positive
increased CD8-positive
increased susceptibility to bacterial infection induced morbidity/mortality
abnormal fertility/fecundity

AnimalID: M01026080 (Male)

Histopathology Findings:

brown fat (MA:0000057)

Histopath Description:

There is a focally extensive non suppurative inflammation of the brown fat.

Morphological Diagnosis:

Distribution: Focal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212; **MPATH Process Term:** inflammation MPATH:212

Definitive Diagnosis:

Mild lymphocytic steatitis

Histopathology Comments:

The lesion is likely an extension of an overlying dermatitis and inflammation of the subcutaneous fat (paniculitis)

spleen (MA:0000141)

Histopath Description:

marked erythropoiesis; there are numerous dark-brown pigment granules within the red pulp (hemosiderin)

Morphological Diagnosis:

Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

marked erythropoiesis with hemosiderosis

bone marrow (MA:0000134)

Histopath Description:

There is moderate erythrocytic hyperplasia. There is mild decrease in megakaryocyte numbers.

Megkaryocytes are small with decreased cytoplasm content.

Morphological Diagnosis:

Severity: moderate; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

Moderate eythroid hyperplasia; megakaryocyte hypoplasia with microytosis

testis (MA:0000411)

Histopath Description:

Multifocally seminiferous tubules are dilated and there is minimal spermiogenesis in these dilated tubules. Rare vacuolated seminiferous tubules are present. Epididymal ducts are depeleted of spermatocytes and contain abundant cellular debri and proteinaceous material.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** moderate; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:

Seminiferous dilation with minimal spermiogenesis; epididymal aspermia

eye (MA:0000261)

Histopath Description:

The outer nuclear layer is reduced in thikness to nearly half normal. The outer plexiform layer is reduced in size resulting in near-fusion of the outer and inner nuclear layers.

Morphological Diagnosis:

Distribution: diffuse; **Severity:** severe; **MPATH Process Term:** atrophy MPATH:127

Definitive Diagnosis:

Atrophy of the outer nuclear and outer plexiform layers

sternum (MA:0001331)

Histopath Description:

There is a full thickness fissure (fracture) within the sternal cartilage between the 4th and 5th sternabrae. The fractured segments are malaligned and protrude into the thoracic cavity. The fractures is accompanied by necrotic chromatin smear and multifocal degeneration and necrosis of the sternal cartilage. Within the adjacent soft tissue is focally extensive mild infiltration of neutrophils and mononuclear inflammatory cells accompanied by hemorrhage and fibroplasia. There is marked nodular hyperplasia of the cartilage tissue surrounding the fracture

Morphological Diagnosis:

Duration: chronic-active; **Distribution:** focally extensive; **Severity:** extreme; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:

Sternal osteoarthritis with sternal fracture with fibroplasia

Histopathology Comments:

lesion was likely secondary to the sternal lesion (see above).

heart (MA:0000072)

Histopath Description:

There is a focally extensive fibrosis of the right ventricular epicardium.

Morphological Diagnosis:

Distribution: focally extensive; **Severity:** mild; **MPATH Process Term:** fibrosis MPATH:181

Definitive Diagnosis:

Epicarditis, right ventricle

thymus (MA:0000142)

Histopath Description:

There is a very small piece of thymic tissue available for analysis. The available tissue is morphologically unremarkable.

Definitive Diagnosis:

Thymic hypoplasia (suspect)

Histopathology Comments:

A tentative diagnosis of thymic hypoplasia is considered. Definitive diagnosis requires gross examination (including comparison with age matched WT control) and histopathology of multiple sections. Note that small thymus (MP:0000706) was documented at necropsy for one of the mice from this line (M01112244).

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: M0112244 (Male)**Histopathology Findings:****spleen (MA:0000141)****Histopath Description:**

marked erythropoiesis

Morphological Diagnosis:

Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

marked erythropoiesis with hemosiderosis

bone marrow (MA:0000134)**Histopath Description:**

There is moderate erythrocytic hyperplasia. There is mild decrease in megakaryocyte numbers. Megakaryocytes are small with decreased cytoplasm content.

Morphological Diagnosis:

Severity: moderate; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

Moderate erythroid hyperplasia; megakaryocyte hypoplasia with microcytosis

testis (MA:0000411)**Histopath Description:**

Multifocally seminiferous tubules are dilated and there is minimal spermiogenesis in these dilated tubules. Rare vacuolated seminiferous tubules are present. Epididymal ducts are depleted of spermatozoa and contain abundant cellular debris and proteinaceous material.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** moderate; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:

Seminiferous dilation with minimal spermiogenesis; epididymal aspermia

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

The outer nuclear layer is reduced in thickness to nearly half normal. The outer plexiform layer is reduced in size resulting in near-fusion of the outer and inner nuclear layers.

Morphological Diagnosis:

Distribution: diffuse; **Severity:** severe; **MPATH Process Term:** atrophy MPATH:127

Definitive Diagnosis:

Atrophy of the outer nuclear and outer plexiform layers

thymus (MA:0000142)**Histopath Description:**

There is a very small piece of thymic tissue available for analysis. The available tissue is morphologically unremarkable.

Definitive Diagnosis:

Thymic hypoplasia (suspect)

Histopathology Comments:

A tentative diagnosis of thymic hypoplasia is considered. Definitive diagnosis requires gross examination (including comparison with age matched WT control) and histopathology of multiple sections. Note that small thymus (MP:0000706) was documented at necropsy for one of the mice from this line (M0112244).

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: M01156923 (Female)**Histopathology Findings:****spleen (MA:0000141)****Histopath Description:**

marked erythropoiesis

Morphological Diagnosis:

Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

marked erythropoiesis with hemosiderosis

bone marrow (MA:0000134)**Histopath Description:**

There is moderate erythrocytic hyperplasia. There is mild decrease in megakaryocyte numbers. Megkaryocytes are small with decreased cytoplasm content.

Morphological Diagnosis:

Severity: moderate; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

Moderate eythroid hyperplasia; megakaryocyte hypoplasia with microcytosis

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

There are rare clusters of erythropoietic cells

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

Mild extramedullary hematopoiesis, erythroid

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

The outer nuclear layer is reduced in thickness to nearly half normal. The outer plexiform layer is reduced in size resulting in near-fusion of the outer and inner nuclear layers.

Morphological Diagnosis:

Distribution: diffuse; **Severity:** severe; **MPATH Process Term:** atrophy MPATH:127

Definitive Diagnosis:

Atrophy of the outer nuclear and outer plexiform layers

thymus (MA:0000142)**Histopath Description:**

There is a very small piece of thymic tissue available for analysis. The available tissue is morphologically unremarkable.

Definitive Diagnosis:

Thymic hypoplasia (suspect)

Histopathology Comments:

A tentative diagnosis of thymic hypoplasia is considered. Definitive diagnosis requires gross examination (including comparison with age matched WT control) and histopathology of multiple sections. Note that small thymus (MP:0000706) was documented at necropsy for one of the mice from this line (M01112244).

brain (MA:0000168)**Histopath Description:**

There is mild dilation of the fourth ventricle

Morphological Diagnosis:

Severity: mild; **MPATH Process Term:** degenerative change MPATH:14

Definitive Diagnosis:

Dilation of the brain ventricles

Histopathology Comments:

Mild dilation of the ventricles is a background condition in mice of C57BL/6N background

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: M01156922 (Female)**Histopathology Findings:****brown fat (MA:0000057)****Histopath Description:**

There is a focally extensive non suppurative inflammation of the brown fat.

Morphological Diagnosis:

Distribution: Focal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212; **MPATH Process Term:** inflammation MPATH:212

Definitive Diagnosis:

Mild lymphocytic steatitis

Histopathology Comments:

The lesion is likely an extension of an overlying dermatitis and inflammation of the subcutaneous fat (paniculitis)

spleen (MA:0000141)**Histopath Description:**

marked erythropoiesis

Morphological Diagnosis:

Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

marked erythropoiesis with hemosiderosis

bone marrow (MA:0000134)**Histopath Description:**

There is moderate erythrocytic hyperplasia. There is mild decrease in megakaryocyte numbers. Megakaryocytes are small with decreased cytoplasm content.

Morphological Diagnosis:

Severity: moderate; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:

Moderate erythroid hyperplasia; megakaryocyte hypoplasia with microcytosis

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

The outer nuclear layer is reduced in thickness to nearly half normal. The outer plexiform layer is reduced in size resulting in near-fusion of the outer and inner nuclear layers.

Morphological Diagnosis:

Distribution: diffuse; **Severity:** severe; **MPATH Process Term:** atrophy MPATH:127

Definitive Diagnosis:

Atrophy of the outer nuclear and outer plexiform layers

thymus (MA:0000142)**Histopath Description:**

There is a very small piece of thymic tissue available for analysis. The available tissue is morphologically unremarkable.

Definitive Diagnosis:

Thymic hypoplasia (suspect)

Histopathology Comments:

A tentative diagnosis of thymic hypoplasia is considered. Definitive diagnosis requires gross examination (including comparison with age matched WT control) and histopathology of multiple sections. Note that small thymus (MP:0000706) was documented at necropsy for one of the mice from this line (M01112244).

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:

Various histopathological findings were documented in this line.

Marked splenic erythropoiesis and bone marrow erythroid hyperplasia were observed in all mice. These findings, together with the hematological data, suggest the presence of regenerative anemia. Increased circulating bilirubin together with marked splenic hemosiderosis is suggestive of extravascular hemolysis (splenic destruction of erythrocytes). Hemolytic anemia is not usually associated with hypoferrremia as the iron is recycled. We speculate some degree of iron sequestration (trapping) by splenic macrophages. Note that a small amount of hemosiderin within macrophages in the spleen reflects normal erythrocyte (RBC) turnover.

The decreased T cell number is likely secondary to suspected thymic hypoplasia. Note the diagnosis of splenic hypoplasia was based on the small sized sample present for examination together with gross observation (the latter in one mouse); hence should be cautiously interpreted. We recommend careful documentation and weighing of the thymus and comprehensive histological sampling and analysis.

The testicular lesion together with epididymal aspermia is consistent with abnormal fertility and fecundity in this line. Note that the testicular lesion is considered minimal and does not match the complete depletion of spermatocytes within the epididymis. We speculate underlying defective spermiogenesis (differentiation of spermatids to spermatocytes).

The retinal lesion was unexpected or unpredicted by the clinical phenotype. The atrophy of the outer plexiform layer was likely secondary to atrophy of the outer nuclear layer since the former is composed of processes (dendrites) of the latter.

Line summary:

Spleen: Extramedullary erythroid hematopoiesis (marked); Splenic hemosiderosis (4/4)

Bone marrow: Erythroid hyperplasia; megakaryocyte hypoplasia and micrococytosis (4/4)

Thymus: Hypoplasia (tentative) - (4/4)

Testis: Multifocal testicular degeneration with lack of spermiogenesis (minimal) with epididymal aspermia (4/4)

Retina: Atrophy of the outer nuclear and outer plexiform layers (4/4)