



## CMHD Pathology Report

### CMHD Pathology Core

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Pathologist: H. Adissu

CMHD LabID: N12-1511

### History:

decreased body weight  
partial lethality  
abnormal fertility/fecundity  
decreased body weight  
decreased platelet cell number  
decreased circulating amylase level  
hypocalcemia  
decreased heart weight  
complete postnatal lethality  
abnormal brainstem auditory evoked potential

AnimalID: M002803333

### Histopathology Findings:

#### heart (MA:0000072)

##### Histopath Description:

There are occasional large myocardiocytes with gigantic vesicular nuclei (Anitschkow cells). Some of these cells have vacuolated cytoplasm. Low numbers of mononuclear inflammatory cells are present within the interstitium.

##### Morphological Diagnosis:

**Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** degenerative change MPATH:14

##### Definitive Diagnosis:

Myocardial regeneration, mild

#### adrenal gland (MA:0000116)

##### Histopath Description:

here is a small, well-circumscribed mass in the cortex. It is encapsulated by a thin layer of pale eosinophilic material and fusiform cells (connective tissue with fibroblasts) and is made of nests of polygonal cells interspersed by a very thin fibrovascular membrane. The architecture is reminiscent of the zona glomerulosa and zona fasciculata of the mature adrenal gland.

##### Morphological Diagnosis:

**Distribution:** focal;

##### Definitive Diagnosis:

accessory adrenal cortical tissue

#### liver (MA:0000358)

##### Histopath Description:

The overall hepatic lobular architecture is normal. Diffusely, hepatocytes contain intracytoplasmic clear vacuoles (lipid). The lipid vacuoles within the midzonal and periportal regions are small (2-3 um in diameter) and surround a central nucleus (interpreted as microvesicular lipid). The lipid vacuoles within the portal areas are large (8-12 um in diameter) and displace the nucleus to the margin (macrovesicular lipid).

##### Morphological Diagnosis:

**Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42

##### Definitive Diagnosis:

Hepatic lipidosis

##### Histopathology Comments:

Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet.

#### bone marrow (MA:0000134)

##### Histopath Description:

megakaryocytes are fewer than expected. Nearly half of megakaryocytes have vacuolated cytoplasm

##### Morphological Diagnosis:

**Distribution:** multifocal; **MPATH Diagnosis:** hypoplasia MPATH:133

##### Definitive Diagnosis:

Megakaryocyte hypoplasia and vacuolation

##### Histopathology Comments:

Changes may explain thrombocytopenia

#### pancreas (MA:0000120)

##### Histopath Description:

Nearly % of the acini are small and appear atrophic

##### Morphological Diagnosis:

**Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** atrophy MPATH:127

**Definitive Diagnosis:**

Exocrine pancreatic atrophy, mild

**stomach (MA:0000353)****Morphological Diagnosis:****Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212**Definitive Diagnosis:**

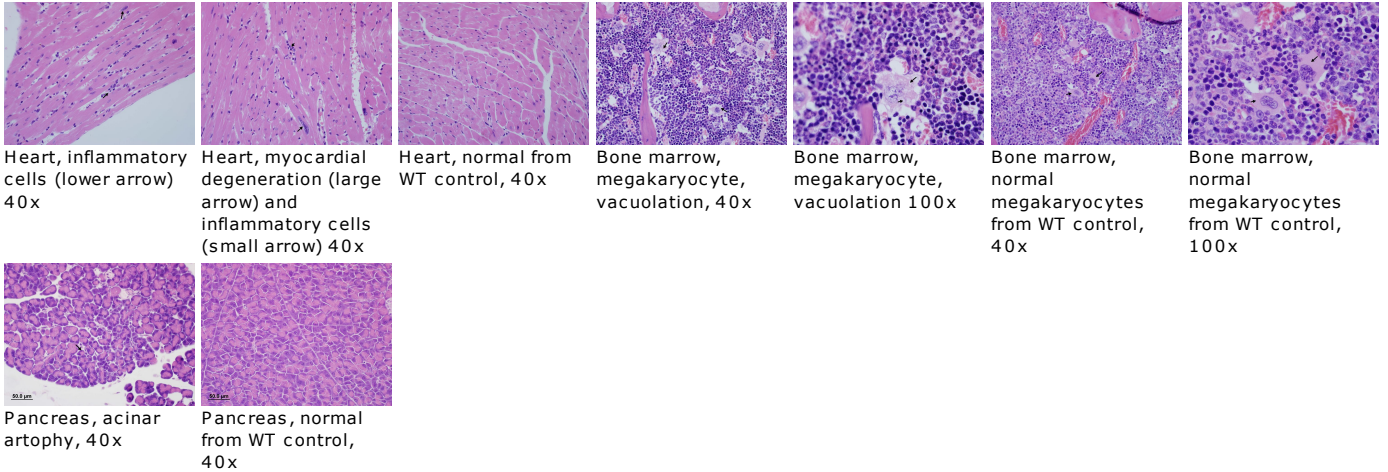
Neutrophilic gastritis

**brain (MA:0000168)****Morphological Diagnosis:****Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639**Definitive Diagnosis:**

Hydrocephalus, third ventricle, mild

**Histopathology Comments:**

No lesion is found to explain the abnormal brainstem auditory evoked potential



Heart, inflammatory cells (lower arrow) 40x

Heart, myocardial degeneration (large arrow) and inflammatory cells (small arrow) 40x

Heart, normal from WT control, 40x

Bone marrow, megakaryocyte, vacuolation, 40x

Bone marrow, megakaryocyte, vacuolation 100x

Bone marrow, normal megakaryocytes from WT control, 40x

Bone marrow, normal megakaryocytes from WT control, 100x

Pancreas, acinar atrophy, 40x

Pancreas, normal from WT control, 40x

There were no significant findings in the following tissues: eyes, tongue, Harderian gland, zymbal gland, salivary glands, nasal sinuses, teeth, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, gall bladder, endocrine pancreas, esophagus, intestines, urinary organs and tract, reproductive organs, lymph nodes, spinal cord, bones, skeletal muscles, brown fat, and skin.

**AnimalID: M002803332****Histopathology Findings:****heart (MA:0000072)****Histopath Description:**

There are occasional large myocardiocytes with gigantic vesicular nuclei (Anitschkow cells). Some of these cells have vacuolated cytoplasm. Low numbers of mononuclear inflammatory cells are present within the interstitium.

**Morphological Diagnosis:****Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** degenerative change MPATH:14**Definitive Diagnosis:**

Myocardial degeneration, mild

**liver (MA:0000358)****Morphological Diagnosis:****Distribution:** diffuse; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42**Definitive Diagnosis:**

Hepatic lipidosis

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

megakaryocytes are fewer than expected. Nearly half of megakaryocytes have vacuolated cytoplasm

**Morphological Diagnosis:****Distribution:** multifocal; **MPATH Diagnosis:** hypoplasia MPATH:133**Definitive Diagnosis:**

Megakaryocyte hypoplasia and vacuolation

**Histopathology Comments:**

Changes may explain thrombocytopenia

**brain (MA:0000168)****Morphological Diagnosis:****Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639**pancreas (MA:0000120)****Histopath Description:**

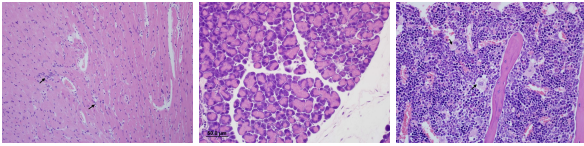
Nearly % of the acini are small and appear atrophic

**Morphological Diagnosis:****Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** atrophy MPATH:127**Definitive Diagnosis:**

Exocrine pancreatic atrophy, mild

**Histopathology Comments:**

The multifocal pancreatic exocrine atrophy may explain the low amylase level detected.



Heart, inflammatory cells (lower arrow) 40x

Pancreas, acinar atrophy, 40x

Bone marrow, megakaryocyte vacuolation, 40x

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

**AnimalID: M01159528**

**Histopathology Findings:**

**lung (MA:0000415)**

**Histopath Description:**

There are single to clusters of macrophages (histiocytes) within the interstitium.

**Morphological Diagnosis:**

**Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** histiocytosis MPATH:146

**Definitive Diagnosis:**

Pulmonary histiocytosis

**adrenal gland (MA:0000116)**

**Morphological Diagnosis:**

**Distribution:** focal; **MPATH Diagnosis:** developmental and structural abnormality MPATH:55

**Definitive Diagnosis:**

accessory adrenal cortical tissue

**liver (MA:0000358)**

**Definitive Diagnosis:**

Absence of hepatic lipidosis

**Histopathology Comments:**

Hepatic lipidosis is not present

**brain (MA:0000168)**

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

Triventricular hydrocephalus

**bone marrow (MA:0000134)**

**Histopath Description:**

megakaryocytes are fewer than expected. Nearly half of megakaryocytes have vacuolated cytoplasm

**Morphological Diagnosis:**

**Distribution:** multifocal; **MPATH Diagnosis:** hypoplasia MPATH:133

**Definitive Diagnosis:**

Megakaryocyte hypoplasia and vacuolation

**Histopathology Comments:**

Changes may explain thrombocytopenia

There were no significant findings in the following tissues: eyes, tongue, Harderian gland, zymbal gland, salivary glands, nasal sinuses, teeth, trachea, 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, skeletal muscles, brown fat, and skin.

**AnimalID: M00914551**

**Histopathology Findings:**

**liver (MA:0000358)**

**Histopath Description:**

Minimal lipidosis affecting 10% of hepatocytes

**Morphological Diagnosis:**

**Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42

**Definitive Diagnosis:**

Minimal lipidosis

**cornea (MA:0000266)**

**Definitive Diagnosis:**

corneal deformity with polypoid ingrowth and epithelial migration

**brain (MA:0000168)**

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

Triventricular hydrocephalus

**bone marrow (MA:0000134)**

**Histopath Description:**

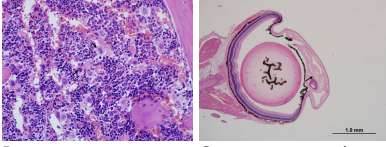
Megakaryocytes are increased in numbers. Most are smaller than normal. There is also increased proportion of erythroid cells (myeloid to erythroid ratio is estimated at 1:1)

**Morphological Diagnosis:****Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134**Definitive Diagnosis:**

Megakaryocyte and erythroid hyperplasia

**Histopathology Comments:**

The increased numbers in erythroid and megakaryocytes suggests regenerative response by the bone marrow (likely a response to decreased platelet number in the peripheral blood)



Bone marrow, megakaryocyte and erythroid hyperplasia, 40x  
 Cornea, stromal polyp and epithelial downgrowth, 4x

There were no significant findings in the following tissues: 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, skeletal muscles, brown fat, and skin.

**Summary and Recommendation:**

- No lesion found to explain phenotype abnormal fertility/fecundity
- Minimal hepatic lipidosis is consistent with decreased body weight
- Megakaryocyte vacuolation may suggest degenerative changes - may lead to ineffective platelet production --> decreased platelet cell number -
- Mild pancreatic exocrine atrophy in 2/4 mice may explain reduced amylase production and decreased circulating amylase level. This may explain decreased body weight as a sequela poor intestinal absorption of nutrients. Pancreatic exocrine atrophy and reduced amylase production was noted in E2f1/E2f2 mutant mice (Feng et al., 2003). Non-inflammatory pancreatic atrophy of the exocrine pancreas associated with decreased amylase and weight loss was also reported in young Beagle dogs (Prentice et al., 1980). Note that the pancreatic exocrine atrophy in this line is very mild to account for changes in serum amylase levels with confidence. Hypocalcemia could be caused by multitude of factors and conditions. Potential intestinal malabsorption may also explain hypocalcemia
- Mild myocardial degeneration and interstitial inflammation suggests cardiomyopathy - may explain decreased heart weight
- Complete postnatal lethality - No single lesion was considered severe to cause postnatal lethality
- Abnormal brainstem auditory evoked potential - No lesion was found to explain this phenotype. The ears are not present for analysis. No lesion was found to explain this phenotype

**References:**

D. E. Prentice, R. W. James and P. F. Wadsworth. 1980. Pancreatic Atrophy in Young Beagle Dogs. *Vet Pathol* 17: 575  
 Feng et al., 2003. *PNAS*. 100:12935-12940