CMHD Pathology Report

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Mouse Genetics Project
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ReportID: Report Date: March 19, 2014
Pathologist: Dr. H. Adissu

CMHD LabID: N13-1254

Relevant History:
Phenotype:

decreased bone mineral density
abnormal lens morphology
cataracts
increased circulating alkaline phosphatase level
decreased body weight
decreased body weight
decreased bone mineral content
kyphosis
abnormal spine curvature
abnormal incisor color
partial lethality

AnimalID: M01334749 (Male)

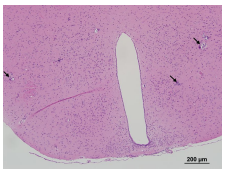
Histopathology Findings:

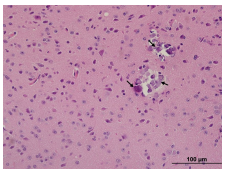
brain (MA:0000168)

Histopath Description:
There are multifocal mineralization within the forebrain, midbrain, and hindbrain. Affected regions include various areas within the basal ganglia (ventral caudoputamen, nucleus acumbens), medial septal nucleus, preoptic areas and nuclei, and substantia innominata in the forebrain, the thalmus and hypothalamus in mid brain, and the various medullary nuclei in the hind brain.

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Process Term:** mineralisation MPATH:555

Definitive Diagnosis:
Brain, multifocal mineralization


Brain, ventral thalamus and hypothalamus, mineralization, 10x, HE


Brain, ventral thalamus and hypothalamus, mineralization, 40x, HE

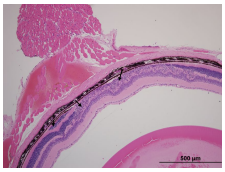
eye (MA:0000261)

Histopath Description:
Extensive displasia affecting 50% of the retina with fusion of layers and numerous rossette formations

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Process Term:** developmental dysplasia MPATH:64

Definitive Diagnosis:
Retinal dysplasia

Histopathology Comments:
The lesion is by far more severe than the level seen as a background lesion in this substarin.


Eye, retinal dysplasia, extensive, 10x, HE.

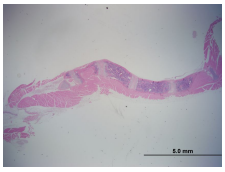
sternum (MA:0001331)

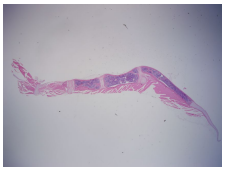
Histopath Description:
The sternum is moderately curved outwardly

Morphological Diagnosis:
Severity: moderate; **MPATH Process Term:** developmental and structural abnormality MPATH:55

Definitive Diagnosis:
Curved sternum

Histopathology Comments:
This lesion is suggestive of pectus carinatum (outward protrusion of the sternum).


Sternum, outward curvature, 1.25x, HE


Sternum, Wt, normal, 1.25x, 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: M01232872 (Male)

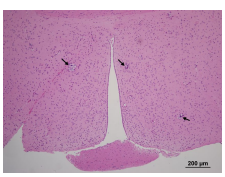
Histopathology Findings:

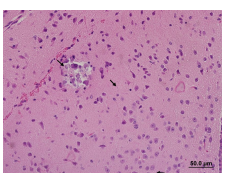
brain (MA:0000168)

Histopath Description:
There are multifocal mineralization within the forebrain, midbrain, and hindbrain. Affected regions include various areas within the basal ganglia (ventral caudoputamen, nucleus acumbens), medial septal nucleus, preoptic areas and nuclei, and substantia innominata in the forebrain, the thalmus and hypothalamus in mid brain, and the various medullary nuclei in the hind brain.

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Process Term:** mineralisation MPATH:555

Definitive Diagnosis:
Brain, multifocal mineralization


Brain, ventral thalamus and hypothalamus, mineralization, 10x, HE


Brain, ventral thalamus and hypothalamus, mineralization, 40x, HE

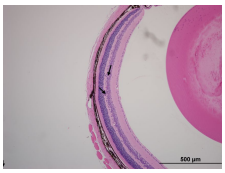
eye (MA:0000261)

Histopath Description:
Extensive displasia affecting 50% of the retina with fusion of layers and numerous rossette formations

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Process Term:** developmental dysplasia MPATH:64

Definitive Diagnosis:
Retinal dysplasia

Histopathology Comments:
The lesion is by far more severe than the level seen as a background lesion in this substarin.


Eye, retinal dysplasia, extensive, 10x, HE.

spleen (MA:0000141)

Histopath Description:
Mild erythropoiesis-erythroid and megakaryocytic

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

Definitive Diagnosis:
Mild erythropoiesis-erythroid and megakaryocytic

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: M01431073 (Female)

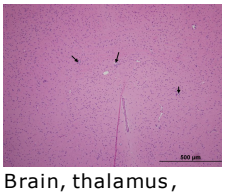
Histopathology Findings:

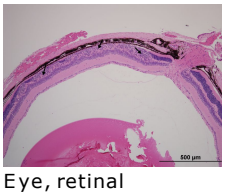
brain (MA:0000168)

Histopath Description:
There are multifocal mineralization within the forebrain, midbrain, and hindbrain. Affected regions include various areas within the basal ganglia (ventral caudoputamen, nucleus acumbens), medial septal nucleus, preoptic areas and nuclei, and substantia innominata in the forebrain, the thalmus and hypothalamus in mid brain, and the various medullary nuclei in the hind brain.

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Process Term:** mineralisation MPATH:555

Definitive Diagnosis:
Brain, multifocal mineralization


Brain, thalamus, mineralization, 10x, HE


Eye, retinal dysplasia, extensive, 10x, HE.

eye (MA:0000261)

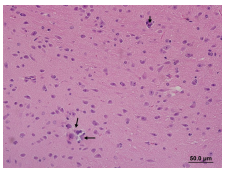
Histopath Description:
Extensive displasia affecting 50% of the retina with fusion of layers and numerous rossette formations

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Process Term:**

developmental dysplasia MPATH:64

Definitive Diagnosis:
Retinal dysplasia

Histopathology Comments:
The lesion is by far more severe than the level seen as a background lesion in this substarin.



Brain, thalamus, mineralization, 40x, 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, uterus, oviduct, and ovary, and mammary gland.

AnimalID: M01334752 (Female)

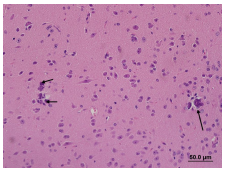
Histopathology Findings:

brain (MA:0000168)

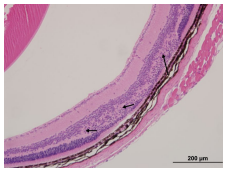
Histopath Description:
There are multifocal mineralization within the forebrain, midbrain, and hindbrain. Affected regions include various areas within the basal ganglia (ventral caudoputamen, nucleus acumbens), medial septal nucleus, preoptic areas and nuclei, and substantia innominata in the forebrain, the thalmus and hypothalamus in mid brain, and the various medullary nuclei in the hind brain.

Morphological Diagnosis:
Distribution: multifocal; **Severity:** mild; **MPATH Process Term:** mineralisation MPATH:555

Definitive Diagnosis:
Brain, multifocal mineralization



Brain, ventral thalamus and hypothalamus, mineralization, 40x, HE



Eye, retinal dysplasia, extensive, 10x, HE. 20x

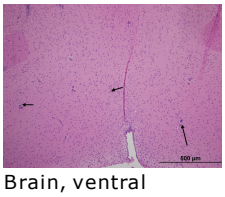
eye (MA:0000261)

Histopath Description:
Extensive displasia affecting 50% of the retina with fusion of layers and numerous rossette formations

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** severe; **MPATH Process Term:** developmental dysplasia MPATH:64

Definitive Diagnosis:
Retinal dysplasia

Histopathology Comments:
The lesion is by far more severe than the level seen as a background lesion in this substarin.



Brain, ventral thalamus and

hypothalamus, mineralization, 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, uterus, oviduct, and ovary, and mammary gland.

Report Summary and Recommendation:
Multifocal mineralization of the basal ganglia, thalamus, hypothalamus, and medulla is present in all mice. Mutation in SLC20A2 is associated with familial idiopathic basal ganglia calcification in humans (see references).

Marker retinal dysplasia was seen in all mice. The lesion is much more severe compared to the mild retinal dysplasia seen as background lesion in C57B6/N substrain. Note that ocular phenotype (ocular Albinism and hypopigmentation defects) were observed in a mouse line that is null for a related gene (Slc24a5) (Vogel et al., 2008).

Outward protrusion or curving of the sternum is present in one mouse. This sternal deformity is consistent with pectus carinatum. In humans, this deformity is associated with vertebral deformities such as scoliosis (as is the case in this mouse line).

Line summary:

Brain: Mineralization (multifocal): 4/4
Eye: Retina, extensive retinal dysplasia (4/4)
Sternum: Sternal defornmity (pectus carinatum) - 1/4

References:
1. Novel SLC20A2 mutations identified in southern Chinese patients with idiopathic basal ganglia calcification. Chen WJ, et al. Gene, 2013 Oct 15. PMID 23939468. 2. Association between a novel mutation in SLC20A2 and familial idiopathic basal ganglia calcification. Zhang Y, et al. PLoS One, 2013. PMID 23437308. 3. Reporting a new mutation at the SLC20A2 gene in familial idiopathic basal ganglia calcification. Lemos RR, et al. Eur J Neurol, 2013 Mar. PMID 23406454. 4. Mutations in SLC20A2 are a major cause of familial idiopathic basal ganglia calcification. Hsu SC, et al. Neurogenetics, 2013 Feb. PMID 23334463. 5. Mutations in SLC20A2 link familial idiopathic basal ganglia calcification with phosphate homeostasis. Wang C, et al. Nat Genet, 2012 Feb 12. PMID 22327515. 6. Vogel P. et al (2008). Veterinary Pathology. 45:264-279