Title of Disease:  Globoid cell leukodystrophy (Krabbe disease)

Contributors:  Charles H. Vite, DVM, PhD, Dipl ACVIM Neurology

Synonyms:  GLD, Galactosylceramide Lipidosis

Disease Description:
Globoid cell leukodystrophy (GLD; Krabbe disease) is a neurological disease caused by mutations in the galactocerebrosidase (GALC) gene. GALC deficiency results in a failure to adequately degrade galactocylceramide and psychosine and a failure to produce and maintain compact, stable myelin. Affected Cairn and West Highland white terriers were the first animal model of a lysosomal storage disease described. Affected dogs show demyelination, reduced oligodendrocyte numbers, destruction of white matter, accumulation of astrocytes and globoid cells, and enlargement of the cerebral ventricles. Deficient brain GALC activity and elevations in brain and cerebrospinal fluid psychosine concentrations occur.

Description of Disease in specific Species:
GLD dogs develop signs of cerebellar dysfunction, spastic paralysis, and peripheral neuropathy and frequently die before 1 year of age.

Genetic Basis /Mode of Inheritance:
Autosomal recessive
A to C transversion at GALC cDNA position 473, changing tyr 158 to ser in both Cairn and West Highland white terriers
Insertion mutation of 78 base pairs (bp) consisting of 16 bp of insertion site duplication and 62 bp of sequence derived from the U4 small nuclear RNA in the Irish setter

Etiology:
Galactocerebrosidase (GALC) deficiency
Genetic, hereditary

Breed Predilection:
Domestic shorthair cat
miniature poodle dog
beagle dog,
blue tick hound dog
Australian working Kelpie
Irish Setters
Cairn terrier
West Highland white terrier

Sex predilection:
None

Age predilection:
Generally affects animals less than one year of age

Clinical Findings / Signs:
GLD dogs develop signs of cerebellar dysfunction, spastic paralysis, and peripheral neuropathy and frequently die before 1 year of age.

Magnetic resonance imaging (MRI) and spectroscopy (MRS) of affected dogs showed robust differences in the white matter between affected and normal dogs which included an increase in lateral and third cerebral ventricular volume on MRI; an increase in T2-weighted signal intensity of the centrum semiovale, internal capsule, and corpus callosum; a regionally-specific decrease in magnetization transfer ratio; and a decrease in N-acetylaspartate (NAA) and an increase in choline (Cho) on MRS compared to normal dogs.

Diagnostic Procedures / Diagnostic Results:
Serum GALC levels
Molecular testing

Treatment/Management/Prevention:
None

Differential Diagnosis:
Canine distemper virus infection
White shaker dog disease
Other leukodystrophies

Available Tests/Testing Facilities:
David A. Wenger, Ph.D., Director
Paola Luzi, Ph.D., Assistant Director
Lysosomal Diseases Testing Laboratory
Jefferson Medical College Department of Neurology
1020 Locust St., Room 346
Philadelphia, PA 19107

References:

OMIA/OMIM Acc. Number: