Neuronal Ceroid Lipofuscinosis-A/Cerebellar Ataxia – Am. Staffordshire Terrier

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Synonyms:
Ceroid Lipofuscinosis
Lysosomal storage disease
Cerebellar cortical degeneration
Cerebellar abiotrophy
Cerebellar Purkinje cell abiotrophy
Cerebellar atrophy

Disease description:
The neuronal ceroid lipofuscinoses (NCLs) are a group of lysosomal storage diseases characterized by intraneuronal accumulation of fluorescent granules and early neuronal death. Dogs with NCL4A have late-onset and slowly progressive behavioral changes, cognitive and motor degeneration, ataxia, seizures, and premature death.

CLINICAL SIGNS AND DIAGNOSIS
Signs of cerebellar degeneration are the same signs as found with any cerebellar dysfunction: head and body tremors, hypermetria, a broad base stance, truncal swaying, bunny hopping, ataxia, decreased menace response and nystagmus. In general, signs are progressive over time but speed of progression varies with breed and type of degeneration.

A tentative diagnosis is based on the signalment, the absence of other systemic diseases, the presence of progressive cerebellar signs, and MRI findings of a smaller than normal cerebellum. Cerebrospinal fluid evaluation is of value if an inflammatory disorder is one of the differential diagnoses. A definitive diagnosis requires histopathological evaluation of cerebellar tissue.

CLINICAL SIGNS AND DIAGNOSTICS
In American Staffordshire Terriers, a prevalence rate was estimated at 1 in 400 terriers. Although the age of onset of neurologic deficits varied from 18 months to 9 years, the majority of affected dogs presented between 4 and 6 years of age. The time from onset of clinical signs to euthanasia has varied from 6 months to 6.5 years. Survival time is usually 2 to 4 years. Initial neurologic findings include stumbling, truncal sway, and ataxia exacerbated by lifting the head up and negotiating stairs. Signs progress to obvious ataxia characterized by dysmetria, nystagmus, coarse intention tremor, variable loss of menace reaction, marked
truncal sway, and falling with transient opisthotonus. Clinical signs of a storage
disease (1-2-hydroxyglutaric aciduria) in this breed can appear in a similar
manner.\textsuperscript{11-12}

**Etiology:**
Autosomal recessive mutation in the ARSG gene on chromosome 9. A substitution in
the gene encoding the lysosomal enzyme arylsulfatase G. Affected dogs are deficient
in ARSG: \url{http://www.ncbi.nlm.nih.gov/gene/480460}

Genetic, hereditary

**Breed predilection:**
Am. Staffordshire terrier
Pit bull terrier

**Age predilection:**
Juvenile
Middle-aged
Young adult

**Clinical findings:**
AFEBRILE
ANOREXIA, HYPOREXIA
ATAXIA, INCOORDINATION
Cachexia, weight loss
CENTRAL NERVOUS SYSTEM (CNS) SIGNS
Cerebellar signs
Disoriented
Dysmetria
Falling
GAIT ABNORMAL
Gait bunny hopping
Head tremors
Hypermia
Intention tremors
Malaise
Menace response absent or decreased
Muscle fasciculations
NYSTAGMUS, EYE MOVEMENT RAPID
Signs progressive
Stance wide based
TREMORS
Walking difficulty
ZZZ INDEX ZZZ

**Diagnostic procedures:**
Brain CT or MRI scan
Biopsy and histopathology of the brain

**Diagnostic results:**
Cerebellar size decreased
Axonal degeneration
Degeneration of caudate nuclei
Degeneration of cerebellar granular layer
Degeneration of cerebellar molecular layer
Degeneration of cerebellar Purkinje layer
Degeneration of substantia nigra

Direct genetic test

**Treatment/Management/Prevention:**

**SPECIFIC**
1) None

**SUPPORTIVE**
1) Keep affected animal on non-slick surfaces.
2) Avoid stairwalking, swimming, and other high risk activities

**Preventive Measures:**
1) Test relatives of affected dogs, or dogs at risk, and avoid breeding carrier dogs to each other.
2) Replace carrier parents with normal testing offspring.

**Differential Diagnosis:**
1-2-hydroxyglutaric aciduria
Cerebellar hypoplasia
Storage diseases
Canine distemper encephalitis
Encephalitis
Toxoplasmosis
Neuroaxonal dystrophy
Neoplasia
Cystic structures

**Mode of Inheritance**
Autosomal Recessive

**Human Disease Homolog**
Ceroid Lipofuscinosis, Neuronal, 4a, Autosomal Recessive; Cln4a; Kufs disease: [http://omim.org/entry/204300](http://omim.org/entry/204300)

**Available Tests/Testing Facilities**
Optigen: www.optigen.com (607-257-0301)
Antagene (France): [www.Antagene.com](http://www.Antagene.com)

**OMIA:** 001503-9615, 000177-9615, 001221-9615  **OMIM:** 204300

**References:**
3) Vandevelde M: Neurodegenerative Diseases in Domestic Animals. ACVIM

