BRIEF COMMUNICATIONS and CASE REPORTS

Globoid Cell-like Leukodystrophy in a Domestic Longhaired Cat

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Abstract. Globoid cell leukodystrophy (GLD; Krabbe disease), is a rare heritable metabolic disorder in humans, dogs, mutant twitcher mice, rhesus monkeys and humans that results from a deficiency in the lysosomal enzyme galactocerebrosidase (GALC). GALC deficiency results in the accumulation of psychosine, which is toxic to oligodendrocytes and Schwann cells of the central and peripheral nervous systems. Clinical signs include hypotonia, mental regression, and death by 2 years of age in most human patients. Here we describe a domestic longhaired kitten with rapidly progressive neurologic disease and brain and spinal cord lesions characteristic of GLD. Pathologic hallmarks of the disease reflect the loss of oligodendrocytes and include myelin loss, gliosis, and the perivascular accumulation of large mononuclear cells with fine cytoplasmic vacuoles (globoid cells) in the peripheral and central nervous systems. Globoid cells were CD68 and ferritin positive, confirming their monocytic origin, and cytoplasmic contents were nonmetachromatic and periodic acid–Schiff positive.

Key words: Cat; central nervous system; demyelination; galactocerebrosidase; GLD; globoid cell leukodystrophy; Krabbe disease; macrophages; metabolism; psychosine.

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extensive myelin loss. Globoid cell cytoplasmic contents were periodic acid–Schiff stain positive and nonmetachromatic. Bodian staining demonstrated the presence of nerve fibers in all white matter areas, including those of marked pallor. By immunohistochemistry, globoid cells were CD68 and ferritin positive, suggesting an origin of bone marrow–derived macrophages. This finding is consistent with previous findings of GLD in humans. Controls used included the substitution of concentration-matched irrelevant mouse and rabbit antibodies.

GLD is an autosomal recessive disorder resulting in a deficiency of GALC enzyme activity (confirmed by enzyme analysis8). Unfortunately, enzyme analysis on this kitten was not possible because all tissues were formalin fixed. GALC is a lysosomal hydrolase that normally degrades galactolipids involved in myelin production.9 Therefore, in the absence of functional GALC, galactosphingolipids, including psychosine, accumulate. Psychosine is highly toxic to oligodendrocytes8 and myelin production and maintenance cease with degeneration of these cells.4 In GALC-deficient dogs, psychosine has been shown to accumulate during active myelination and is elevated by 4 months of age, resulting in toxicity and death of oligodendrocytes and a scarcity of myelin.7,9 Neuro-pathologic lesions of affected humans and other animals are typified by extensive demyelination, globoid cell accumulation in the white matter, and severe gliosis.2,8

In this kitten, the appearance of the globoid cells may raise the question as to the possible differential diagnosis of idiopathic granulomatous inflammation. However, the homogenous population of large globoid cells accumulating perivascularly along with the LFB stain demonstrating myelin loss characterize this disease as a myelin disorder. Moreover, the accumulation of globoid cells seen in this kitten is characteristic of GLD previously described in other species.9 In contrast to the previous report of feline GLD involving domestic shorthaired kittens, the present case involves a longhaired kitten. Unfortunately, this kitten was acquired from a pet store and we were unable to characterize the familial history. The accumulation of globoid cells in GLD differs significantly from other lysosomal storage diseases where storage of hydrophilic substrates in lysosomes occurs in many cell types.3

Recently, Im et al.1 showed the molecular target of psychosine to be a G protein–coupled receptor known as T cell death–associated gene 8. Moreover, the in vitro binding of psychosine to cells expressing this receptor leads to the formation of globoid multinuclear cells.1 Studies of humans with GLD treated early with bone marrow transplants have shown slowing of disease progression, providing hope for possible therapeutic intervention strategies.5 In summary, GLD does occur in the cat and the progression and neuropathology of the disease mirror those of the naturally occurring disease described in dogs, rhesus monkeys, mutant twitcher mice, and humans.

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