Case #4

Slide #: 16-417

Institution: North Carolina State University

Signalment: 2.5-year-old, intact male, white-bellied hedgehog (*Atelerix albiventris*)

History: This animal initially presented to the NCSU-CVM Exotic Animal Medicine Service with a 7-day history of ataxia and lethargy. The ataxic gait was confirmed during the physical exam but an underlying cause was not identified. A complete blood count and chemistry panel were within normal limits and a CT scan failed to identify any abnormalities within the central nervous system. An incidental nodule in the right kidney was identified on the initial CT scan. At that time, the animal was presumptively diagnosed with Wobbly Hedgehog Syndrome. Two months later, the animal was euthanized due to progression of clinical signs.

Gross findings: There was diffuse, mild, symmetrical skeletal muscle atrophy but no remarkable gross abnormalities within the central nervous system. Additional lesions included a 1.5 cm in diameter nodule in the right kidney; a 5 mm splenic nodule; and complete absence of dentition.

Histopathology:
Central nervous system (brain, spinal cord): Multiple sections are examined. Throughout all sections (spinal cord > cerebellum > brainstem ~ cerebral cortex) are multifocal, moderate to marked, foci of white matter vacuolation. Vacuoles are variably sized, round, well-demarcated, and up to 200 um in diameter. Associated with these foci are moderately increased numbers of oligodendrocytes, hypertrophied and occasionally binucleated astrocytes, and mildly increased numbers of microglial cells (gliosis). Rare digestion chambers and spheroids are present within these foci.

Morphologic Diagnosis:

1. Brain and spinal cord: white matter vacuolation (demyelination), multifocal, moderate to marked with moderate gliosis and mild axonal degeneration (Wobbly Hedgehog Syndrome)

Discussion: Wobbly Hedgehog Syndrome (WHS) is a progressive, idiopathic, neurologic disease affecting both African and European Hedgehogs (*A. albiventris* and *Erinaceus europaeus*, respectively). It was initially described in the mid-1990's and since then, increasing numbers of cases have been reported. Currently, approximately 10% of hedgehogs are estimated to be affected by this syndrome in North America. Hedgehogs most commonly present with clinical symptoms around two years of age, though they can present at any age. Initially, hedgehogs are unable to ball up, and then progress to relapsing episodes of incoordination and mild ataxia; more severe ataxia, tremors, scoliosis, seizures, muscle atrophy, and self-mutilation; and eventually, complete paralysis. In 70% of cases, paralysis is reported to ascend from hindlimbs to forelimbs. Significant weight loss has been reported with this syndrome, although affected hedgehogs frequently maintain a good appetite until the onset of dysphagia.

On gross examination, affected hedgehogs exhibit no remarkable abnormalities within the central nervous system. Gross lesions most suggestive of a neurologic abnormality are symmetrical skeletal muscle atrophy (neurogenic) and abrasions on the dorsal aspects of the paws due to the ataxic gait. Additional lesions reported in affected hedgehogs include enlarged, pale livers (steatosis), renal

infarcts, and incidental neoplasms in other organ systems. The relationship of these lesions with WHS has not been described.

Histologically, the lesions within the central nervous system vary in severity, depending on the extent of disease progression. WHS is a primary demyelinating lesion and therefore is characterized predominantly by vacuolation of white matter tracts with less common secondary axonal degeneration (Wallerian degeneration). In areas of neuropil vacuolation, gliosis may also be present. In the late stages of disease, neuronal necrosis may occur. Inflammation is not present.

The underlying etiology for WHS is currently unknown, with the primary hypotheses including (1) an infectious agent or (2) a genetic abnormality. In one case series of 14 hedgehogs, canine distemper virus (CDV) titers were performed in 6 of 14 animals but were not suggestive of infection. Immunohistochemistry or in situ hybridization for CDV in the CNS of 8 of the animals were similarly negative. Pneumonia virus of mice (PVM) has also been investigated as a potential cause for WHS. In a case report, PVM was identified by RNA sequencing and immunohistochemistry in formalin-fixed, paraffin-embedded tissues from a hedgehog suspected to have WHS. However, this animal exhibited mononuclear inflammation concurrent with the classic vacuolization lesions in the CNS. The authors attributed the inflammation to PVM, but did not further speculate on the relationship between the two histologic lesions, and did not conclude a causal effect for PVM in WHS. With regards to a genetic abnormality, no specific mutations have been identified, though disease cluster patterns in pedigree analyses have been reported, potentially suggestive of a heritable component.

Important differential diagnoses to rule out in hedgehogs with neurologic signs include intervertebral disc disease and neoplasms. In one case report, a hedgehog suspected to have WHS in fact was diagnosed with an astrocytoma by gross and histopathological examination. In the presented case, the CT scan results were not consistent with either of these two differentials, and therefore the hedgehog was presumptively and correctly diagnosed antemortem with WHS.

References

1. Graesser D, Spraker TR, Dressen P, Garner MM, Raymond JT, Terwilliger G, Kim J, Madri JA. Wobbly hedgehog syndrome in African pygmy hedgehogs (*Atelerix* spp.). *J Exot Pet Med.* 2006; 15:59-65.
2. Madarame H, Ogihara K, Kimura M, Nagai M, Omatsu T, Ochiai H, Mizutani T. Detection of a pneumonia virus of mice (PVM) in an African hedgehog (*Atelerix arbiventris*) with suspected wobbly hedgehog syndrome (WHS). *Vet Microbiol*. 2014; 173:136-40.
3. Nakata M, Miwa Y, Itou T, Uchida K, Nakayama H, Sakai T. Astrocytoma in an African Hedgehog (*Atelerix albiventris*) suspected wobbly hedgehog syndrome. *J Vet Med Sci.* 2011; 73:1333-5.
4. Palmer AC, Blakemore WF, Franklin RJM, Frost LM, Gough RE, Lewis JCM, Macdougall DF, O'Leary MT, Stocker LR. Paralysis in hedgehogs (*Erinaceus europaeus*) associated with demyelination. *Vet Rec.* 1998; 143:550-2.
5. Quesenberry K, Carpenter JW eds. *Ferrets, rabbits, and rodents: clinical medicine and surgery.* 3rd ed. St. Louis, MO: Elsevier Saunders; 2012.

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