

Astrocytoma in an African Hedgehog (*Atelerix albiventris*) Suspected Wobbly Hedgehog Syndrome

Makoto NAKATA^{1,2)*}, Yasutsugu MIWA^{1,3)}, Takuya ITOU²⁾, Kazuyuki UCHIDA⁴⁾, Hiroyuki NAKAYAMA⁴⁾ and Takeo SAKAI²⁾

¹⁾Miwa Exotic Animal Hospital, 1–25–5 Komagome, Toshima-ku, Tokyo 170–0003, ²⁾Nihon University Veterinary Research Center, 1866 Kameino, Fujisawa, Kanagawa, 252–0880 and Laboratories of ³⁾Veterinary Surgery and ⁴⁾Veterinary Pathology, Graduate School of Agricultural and Life Sciences, The University of Tokyo, 1–1–1 Yayoi, Bunkyo-ku, 113–8657 Tokyo, Japan

(Received 9 August 2010/Accepted 16 May 2011/Published online in J-STAGE 30 May 2011)

ABSTRACT. A 28-month-old African hedgehog was referred to our hospital with progressive tetraparesis. On the first presentation, the hedgehog was suspected as having wobbly hedgehog syndrome (WHS) and the animal was treated with medication and rehabilitation. The animal died 22 days after onset. Pathological examination revealed that the animal was involved in astrocytoma between the medulla oblongata and the spinal cord (C1). This report indicates that a primary central nervous system tumor should be considered as one of the differential diagnoses for hedgehogs presenting with progressive paresis, together with WHS.

KEY WORDS: astrocytoma, hedgehog, primary central nervous system tumor, progressive paresis, wobbly hedgehog syndrome (WHS).

J. Vet. Med. Sci. 73(10): 1333–1335, 2011

African hedgehogs (*Atelerix albiventris*) are member of the order Insectivora and are popular pets in Japan, North America, Europe and some Asian countries. Although there has been increased the literature of hedgehog diseases [5, 6, 8], there is still a lot of uncertainty surrounding hedgehog diseases.

Progressive paresis or tetraparesis in African hedgehogs has been noted by some practitioners. This condition has been reported as wobbly hedgehog syndrome (WHS) in both the African and European hedgehog species recently [2, 4, 11]. The onset of WHS commonly occurs under 2 years of age, and the characteristic histopathology of WHS is vacuolization of white matter of the brain and spinal cord, and associated neurogenic muscle atrophy. However, the cause still has not been clarified in detail. Viral encephalopathy and nutritional deficiency causing degeneration of the white matter of the brain was identified. Moreover, it should be mentioned that hedgehogs are susceptible to rabies, Baylisascaris migration and polioencephalomyelitis [9]. However, there are few reports of central nervous system (CNS) tumors in hedgehogs. Two cases of pituitary adenomas are reported in both species (the African or European) [1, 12], and a case of astrocytoma is reported [3]. Astrocytomas originate from glia cells and are one of the common primary brain tumor in human and dogs [10, 13]. Prognosis of the astrocytomas varies depending on age and histopathological grade.

A 28-month-old female African hedgehog was referred to our hospital with progressive tetraparesis. The animal presented with sudden onset of paresis of the hindlimbs 10 days ago, which progressed to the forelimbs several days later. Emaciation was seen and it became gradually difficult to

raise the upper half of its body.

Initial physical examination revealed tetraparesis and muscle wasting. No abnormal radiography results were observed. WHS was suspected at first and a prescription of prednisolone (Prednisolone, Mitaka Pharmaceutical Co., Ltd., Tokyo, Japan) 1 mg/kg once a day, cyproheptadine hydrochloride (Periactin, Banyu Pharmaceutical Co., Ltd., Tokyo, Japan) 0.4 mg/kg once a day, enrofloxacin (Baytril, Bayer Health Care, Tokyo, Japan) 5 mg/kg, vitamin B complex preparation (Vitamedin, Sankyo Pharmaceutical Co., Ltd., Tokyo, Japan) was given, along with forced feeding and rehabilitation as supportive therapy. However, there were no signs of clinical improvement for nine days. Although treatments continued, the hedgehog died 12 days from time of the first presentation (22 days from disease onset). And then, necropsy was performed.

Grossly there was a hemorrhagic focus approximately 3–5 mm in diameters in the medulla oblongata (Fig. 1) and malacia in the spinal cord (C1). In the visceral organs other than CNS, there were congestion of the lung and vesical calculi.

Histologically, the medulla oblongata and the spinal cord lesions were consisted of a proliferation of pleomorphic cells with central hemorrhagic necrosis. The neoplastic cells diffusely infiltrated from the medulla oblongata to the spinal cord (C1). The neoplastic cells varied in size, and the nuclei were varied from round, elliptical to spindle-shaped with distinct cytoplasmic processes (Fig. 2A). Mitotic figures of the neoplastic cells were rare. The tumor cells demonstrated moderate cellular and nuclear pleomorphism with bilobed nuclei. Immunohistochemically, the cytoplasm and processes of some tumor cells were intensely positive for glial fibrillary acidic protein (GFAP) antibody (1:400; DAKO) (Fig. 2B), but some pleomorphic neoplastic cells were completely negative for GFAP. Moreover, these cells were negative for human leukocyte antigens (HLA) -DR.

*CORRESPONDENCE TO: NAKATA, M., Nihon University Veterinary Research Center, 1866 Kameino, Fujisawa, Kanagawa, 252–0880, Japan.
e-mail: azu05pooh@hotmail.com

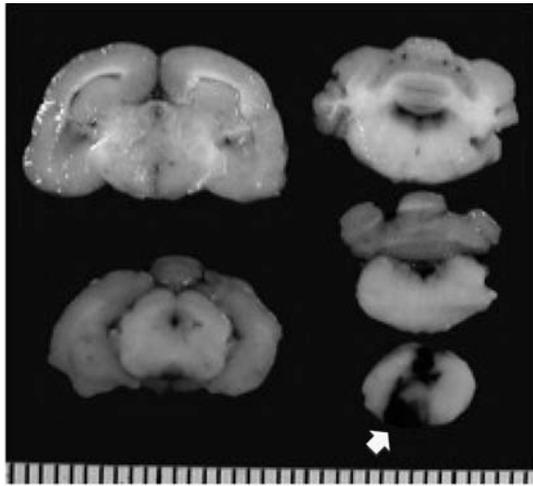


Fig. 1. Gross lesions of medulla oblongata hemorrhagic focus. Hemorrhagic focus was noted in the lateral aspect of the medulla oblongata (arrow), as seen in transverse section. Scale interval=1 mm.

Based on these pathological findings, the medulla oblongata and spinal lesion was diagnosed as astrocytoma (middle grade). Around the neoplastic lesions of the medulla oblongata and the spinal cords, there were quite number of vacuolated myelin sheaths. In the visceral organs other than the CNS, the expansion and vacuolation of nuclei were observed frequently in the renal tubular epithelial cells, and intranuclear inclusions were formed (Fig. 3). This intranuclear inclusion was positive to Periodic Acid-Schiff (PAS) staining. Additionally, hepatocyte was slightly swelling and hepatocellular vacuolation was also noted in cytoplasm.

In 1999, the classification of tumors of neuroepithelial tissue was reorganized by WHO in animals, and astrocytoma was subdivided into three grades [7]: low (well-differentiated astrocytoma), middle (anaplastic astrocytomas) and high (glioblastoma), based on their degree of differentiation or malignancy. Anaplastic astrocytomas have increased cellularity, nuclear pleomorphism, nuclear atypia, and mitotic activity. GFAP expression varies, but in foci it may be similar to that present in low-grade astrocytoma. Anaplastic astrocytoma may be focally difficult to distinguish from high-grade astrocytoma, although vascular proliferation and necrosis are absent [7]. Since present case had moderate cellular pleomorphism and necrosis with hemorrhage, the medulla oblongata and the spinal tumor could be diagnosed as middle grade (anaplastic) astrocytoma according to the criterion.

WHS is one of the most important differential diagnoses of the tetraparesis in hedgehogs. This disease has been reported in African [4] and European hedgehogs [11]. Clinically, WHS begins with mild ataxia and progresses to more severe neurologic signs such as falling consistently to one side, tremors, scoliosis, seizures, muscle atrophy, dysphagia, emaciation, ascending paresis or tetraparesis, and, rarely, self-mutilation. However, these observations are not

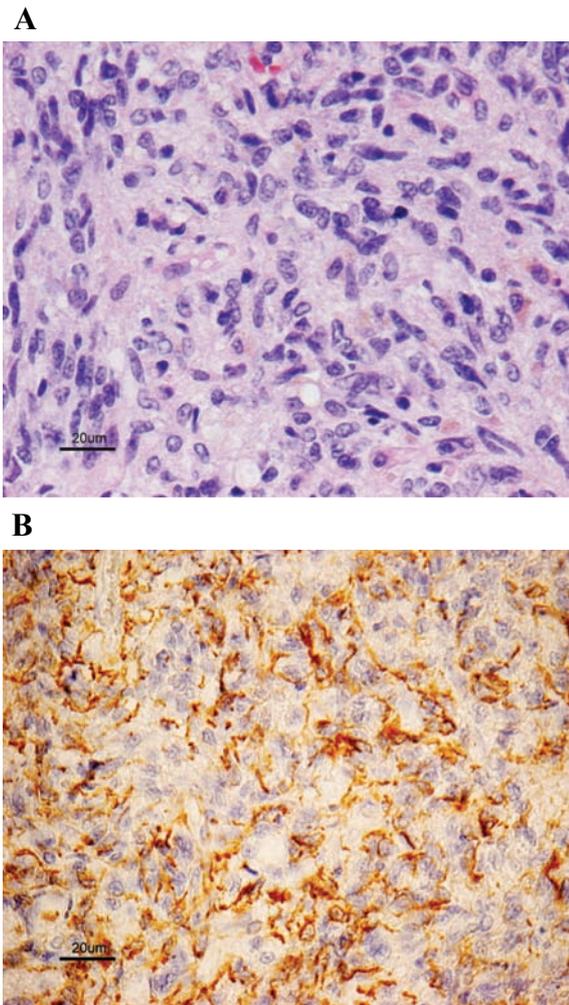


Fig. 2. Histopathology findings in the medulla oblongata. (A) A proliferation of pleomorphic cells and diffuse infiltration of the neoplastic cells in the medulla oblongata were identified (HE stain). Bar=20 μ m. (B) Positive immunohistochemical staining using anti glial fibrillary acidic protein (GFAP) antibody (Counterstained with hematoxylin). Bar=20 μ m.

specific to WHS. Characteristic histopathological lesions of WHS include spongiform changes in the white matter of the cerebrum and brain stem, as well as the white matter tracts of the spinal cord at all levels. There appears to be a loss of myelin first, then secondary degeneration and loss of the axon, followed by neuronal degeneration. There is no evidence of peripheral neuropathy. Inflammation is not a feature in the brain or spinal cord. Demyelination, axonal degeneration, and occasional neuronal necrosis are also observed [2, 4, 5, 11]. An antemortem diagnosis of WHS is difficult by only the clinical findings because diagnosis needs to be conducted histopathological examination of the central nervous system. Clinical onset of the WHS most commonly occurs at 1 to 36 months of age [2, 5]. The survival period is usually within 15 to 25 months after initial

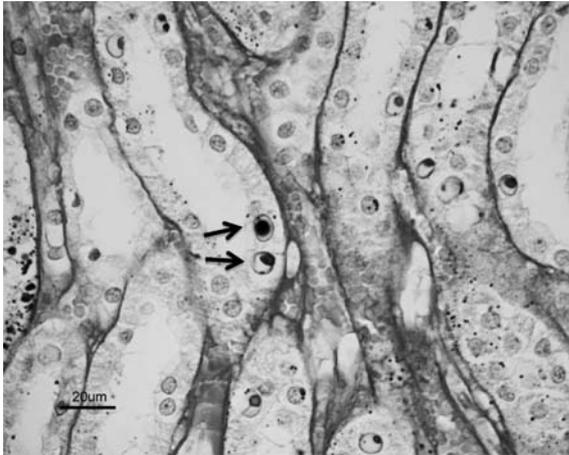


Fig. 3. Histopathology findings in the kidney. The expansion and vacuolation of nuclei and intranuclear inclusions (arrows) were observed in renal tubular epithelial cells (PAS stain). Bar=20 μ m.

presentation [4, 5]. The age of our case was 28 months and it was the same as WHS. This case was, however, observed acute progression and death at 22 days after onset. This survival period is an only difference of the clinical findings between this case and WHS patients. Based on the gross findings, the cause of the death on this case was suspected to be a sudden hemorrhage due to the tumor in the medulla oblongata.

In addition, pathological examinations revealed the vacuolar changes of the nuclei in renal tubular epithelial cells, probably resulting by intranuclear glycogen accumulation because of positive to PAS staining. These findings are very similar to a previous report of renal lesions suspected as being WHS specific [2]. Present findings indicate that the vacuolation of the nuclear lesions of the renal tubular epithelial cells may not be specific for WHS in African hedgehogs. The relevance of these renal findings and the CNS lesions is unidentified at present, and more cases of various CNS diseases of hedgehogs are necessary.

In conclusion, this paper indicates the clinicopathological features of astrocytoma in a hedgehog. The authors suggested that primary CNS tumors should be included in the

list of differential diagnosis of hedgehogs presenting with tetraparesis, together with WHS.

REFERENCES

1. Campbell, D. and Smith, W. 1966. A pituitary adenoma in a hedgehog (*Erinaceus europaeus*). *Endocrinology* **79**: 842–844.
2. Garner, M. M. 2006. Wobbly hedgehog syndrome. *Exotic DVM* **8**: 57–59.
3. Gibson, C. J., Parry, N. M., Jakowski, R. M. and Eshar, D. 2008. Anaplastic astrocytoma in the spinal cord of an African pygmy hedgehog (*Atelerix albiventris*). *Vet. Pathol.* **45**: 934–938.
4. Graesser, D., Spraker, T. R., Dressen, P., Garner, M. M., Raymond, J. T., Terwillinger, G., Kim, J. and Madri, J. A. 2006. Wobbly hedgehog syndrome in African pygmy hedgehogs (*Atelerix spp.*). *J. Exot. Pet Med.* **15**: 59–65.
5. Ivey, E. and Carpenter, J. W. 2003. African hedgehogs. pp. 339–353. *In: Ferrets, Rabbits, and Rodents Clinical Medicine and Surgery*, 2nd ed. (Quesenberry, K. E. and Carpenter, J. W. eds.), W. B. Saunders, Philadelphia.
6. Keymer, I. F., Gibson, F. A. and Reynolds, D. J. 1991. Zoonoses and other findings in hedgehogs (*Erinaceus europaeus*): a survey of mortality and review of the literature. *Vet. Rec.* **128**: 245–249.
7. Koestner, A., Bilzer, T., Fatzer, R., Schulman, F. Y., Summers, B. A. and Van Winkle, T. J. 1999. Tumors of neuroepithelial tissues. pp. 17–19. *In: Histological Classification of Tumors of the Nervous System of Domestic Animals*, 2nd series, vol. 5, The Armed Forces Institute of Pathology, Washington D.C.
8. Larsen, R. S. and Carpenter, J. W. 1999. Husbandry and medical management of African hedgehogs. *Vet. Med.* **94**: 877–890.
9. Lightfoot, T. L. 2000. Therapeutics of African pygmy hedgehogs and prairie dogs. *Vet. Clin. North Am. Exot. Anim. Pract.* **3**: 155–172.
10. Mahaley, M. S. Jr., Mettlin, C., Natarajan, N., Laws, E. R. Jr. and Peace, B. B. 1989. National survey of patterns of care for brain-tumor patients. *J. Neurosurg.* **71**: 826–836.
11. Parmer, A. C., Blakemore, W. F., Franklin, R. J. M., Frost, R. E., Gough, R. E., Lewis, J. C., Macdougall, D. F., O'Leary, M. T. and Stocker, L. R. 1998. Paralysis in hedgehogs (*Erinaceus europaeus*) associated with demyelination. *Vet. Rec.* **15**: 550–552.
12. Raymond, J. T. and Garner, M. M. 2001. Spontaneous tumors in captive African hedgehogs (*Atelerix albiventris*): a retrospective study. *J. Comp. Pathol.* **124**: 128–133.
13. Snyder, J. M., Shofer, F. S., Van Wi, T. J. J. and Massicotte, C. 2006. Canine intracranial primary neoplasia: 173 cases (1986–2003). *J. Vet. Intern. Med.* **20**: 669–675.