NOTE *Wildlife Science*

Porencephaly in a fennec fox (*Vulpes zerda*)

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ABSTRACT. A postmortem examination revealed a large brain cavity in the right cerebral hemisphere of a 9-year-old male fennec (*Vulpes zerda*). The cavity was filled with cerebrospinal fluid and extended to the right lateral ventricle. Swelling and displacement of the right hippocampal area were also observed. Histologic examination revealed no evidence of previous infarct lesions, hemorrhage, inflammation or invasive tumor cells. Observation of the defective part suggested a local circulatory disorder during the fetal stage, although the cause was not detected. No neurological symptoms that could enable a provisional diagnosis were observed during the course of his life. This is the first report of asymptomatic porencephaly in a fennec fox.

KEY WORDS: asymptomatic, cortex, fennec fox, porencephaly, spontaneousness

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Porencephaly is a rare morphological abnormality of the brain, characterized by cerebral cavities or cysts, and sometimes spreads to the ventricular system or subarachnoid space [2, 4, 11, 17]. Unlike hydranencephaly, the brain defect in porencephaly is limited to the cerebral hemisphere [12]. In humans, porencephaly commonly manifests in infants as a congenital disorder [4], but in animals, it often occurs in livestock (e.g., cattle, sheep and goats) where prenatal virus infections may represent a predisposing factor [3, 5, 6, 12, 16]. In dogs and cats, porencephaly occurs sporadically, and the cause remains unknown [1, 2, 9, 10, 11, 17].

Generally, anatomical brain anomalies are often associated with seizures; however, porencephaly can be an incidental finding in asymptomatic animals as well. Here, we report a case of a 9-year-old male fennec fox that suddenly presented with anorexia, unsteady gait and jaundice of the visible mucous membranes. He was treated with a liver tonic, prednisone and ampicillin, resulting in alleviation of symptoms. Unfortunately, after one week, signs of jaundice reappeared, accompanied by loss of appetite. He died a month later and was found to have lost more than 200 g of body weight before death. On postmortem examination, jaundice of the oral mucosa and subcutaneous tissue was observed. Swelling of the superficial cervical, axillary, inguinal, mesenteric, pancreaticoduodenal and anterior mediastinal lymph nodes was significant. Also seen were right ventricular dilatation, myocardial degeneration and cicatrices of the external surfaces in both kidneys. The liver and spleen were also swollen, and the parenchyma of the liver was fragile. Gross examination of the head revealed asymmetry of the skull and a large cavity in the right cerebral cortex. The maxilla had a small dent on the right side and a bulge on the lateral side of it. In the brain, the frontal lobe and only part of the parietal lobe along the central groove were left, whereas most of the right cortical cortex was replaced by a cavity filled with cerebrospinal fluid (CSF) (Figs. 1 and 2). The cerebellar vermis also showed asymmetry. On the formalin fixed brain cut sections, the cavity extended to the dilated right lateral ventricle. Swelling and displacement of the right hippocampus were also observed (Fig. 3).

For histologic analysis, major organs were fixed in a 10% phosphate-buffered formalin solution. The brain was cut into 5-μm-thick sections from the frontal plane, embedded in paraffin, and stained with hematoxylin and eosin (HE) according to standard procedures. The brain sections were also stained with Kluver-Barrera (KB). Immunohistochemistry (IHC) staining was also performed on paraffin wax sections of other organs, such as lymph nodes. The sections were first incubated with primary antibodies to CD3 (Dako, Carpinteria, CA, U.S.A.) and CD20 (Thermo Fisher Scientific, Waltham, MA, U.S.A.), followed by peroxidase-conjugated secondary antibody (Nichirei, Tokyo, Japan). The IHC signal was visualized using diaminobenzidine. Histologic examination of a cross section of the thalamus and cerebral peduncle revealed atrophy of the choroid plexus in the right lateral ventricle and marked edema in the neuropil beneath the cyst, including the right hippocampus (Fig. 4); myelinoclasis was also detected in the same area by KB staining. However, we did not observe any abnormal nerve cells, neuronal necrosis, fibrosis or aberrant structure of the cortex layer. We also confirmed the cyst wall as a membraneous structure contiguous with the arachnoid (Fig. 4). The swelling of mesenteric and other lymph nodes appeared to indicate evidence of lymphocytic infiltration. Tumor cells were also seen in the capsule and adipose tissue around the lymph nodes. The tumor cells appeared round or ellipsoid in shape with an eosinophilic cytoplasm, an atypical nucleus and clear multiple nucleoli.

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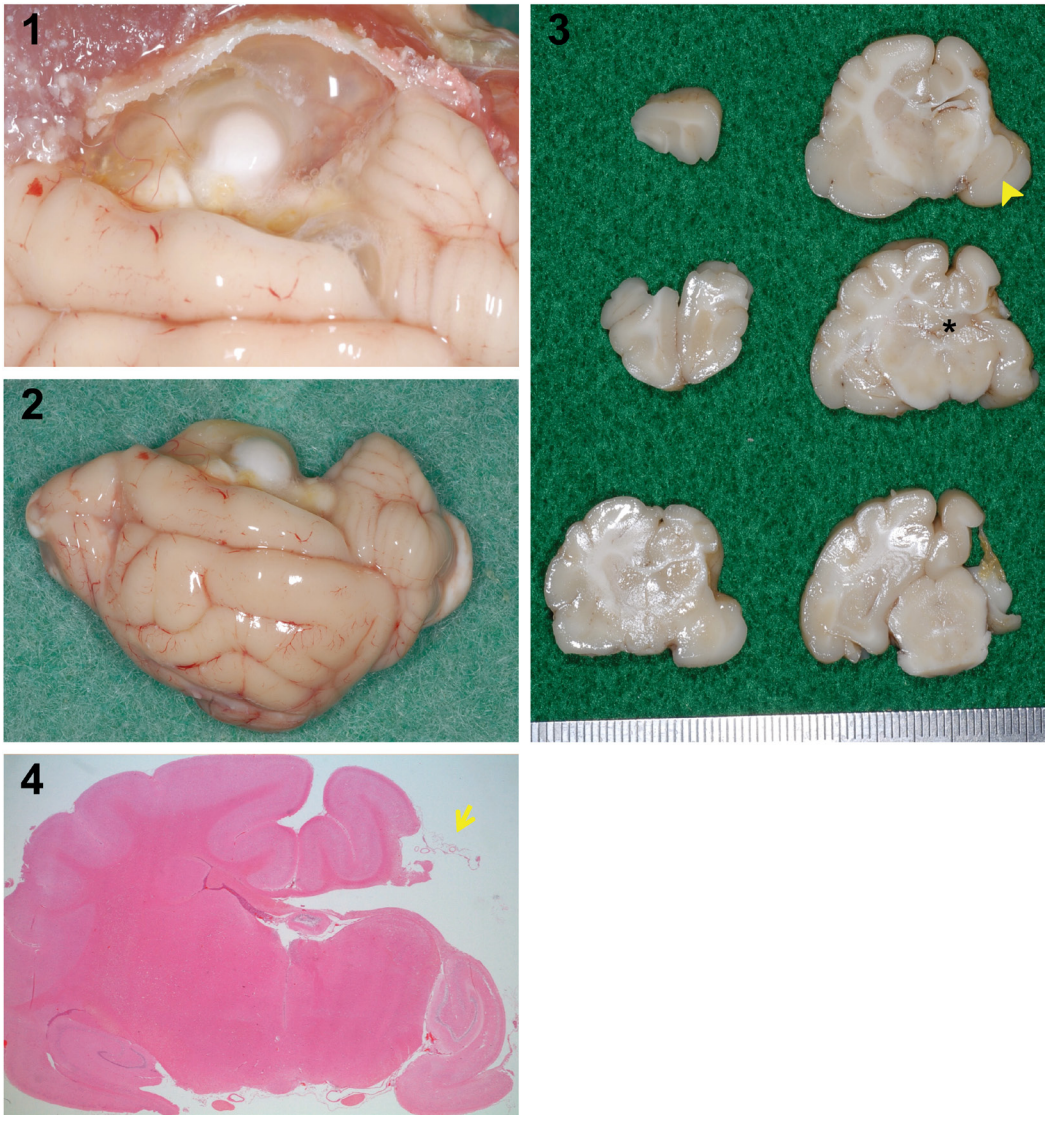

Fig. 1. The cavity in the affected region of the brain: Most of the right cortical cortex was replaced by a cavity filled with cerebrospinal fluid (CSF). The cavity decreased in size due to outflow of CSF.
Fig. 2. Excised brain: The frontal region and a part of the parietal lobe along the central groove remained. A part of the corpus callous and the brainstem can be seen. The cavity decreased in sign due to defluxion of CSF.
Fig. 3. A serial frontal plane section of the brain: The cavity extends to the right lateral ventricle (asterisk), which may have resulted in swelling and displacement of the right hippocampal aspect (arrowhead).
Fig. 4. Hematoxylin and eosin image of a cross-section of the thalamus and cerebral peduncle: Atrophy of the choroid plexus in the right lateral ventricle is observed, along with marked edema in the neuropil beneath the cyst. The cyst wall is contiguous with the arachnoid (arrow).

Many mitotic and apoptotic cells were also detected in the tumor tissue as well. Moreover, tumor cells were observed in the parenchyma of the lung, heart, liver, kidneys and testicles. These tumor cells were phenotypically positive for CD3 and negative for CD20 antibodies. Histologic examination also revealed that the cicatrices in both kidneys were fibrotic.

With respect to this case, the cavity was present in the right cerebral hemisphere and extended to the right lateral ventricle and into the subarachnoid space. In addition, no abnormal nerve cells or unusual cortex layer was seen. Moreover, the animal did not show any neurological manifestations during his lifetime. Because of these reasons, we diagnosed this case as a porencephaly. It is worth noting that hydranencephaly and schizencephaly are differential diagnosis for porecephaly. However, hydranencephaly is characterized by the complete or almost complete absence of the cerebral hemispheres, leaving only membranous sacs

filled with CSF and enclosed by leptomeninges [12]. By contrast, schizencephaly is characterized by full thickness clefts spanning the wall of the cerebral hemispheres that are lined and surrounded by polymicrogyric cortex [13].

Porencephaly is more commonly seen in livestock animals, but it is rarely reported in dogs and cats. In exotic animals, porecephaly is also rare, although a few cases have been reported in cynomolgous monkeys [7, 14]. Therefore, this article is the first to report a case of porencephaly in a fennec fox. Although hippocampal atrophy was previously observed in porencephaly of humans and dogs [8, 9], only advanced hydropic degeneration of the cortex and hippocampal neuropils beneath the cyst was found in this case. Furthermore, necrosis and fibrosis of neurons did not occur in these areas, suggesting that the hydropic degeneration may be an acute response. Remarkably, this fennec did not show any signs of seizure or neurologic manifestation over the course of his life, and these results indicated that the animal was well-adapted. In canine, brain anomalies like porencephaly have been shown to have some correlation with seizures [2, 10, 15], giving us reason to believe that this may be an asymptomatic case of the abnormality.

The risk factors for porencephaly include ischemia, hemorrhage, inflammation, infection, trauma and abnormal development of CNS during the prenatal period. In humans, virus infection or vascular insufficiency has been implicated as major causes of secondary porencephaly. While a mutation in the procollagen type IV α 1 gene (Col4a1) was reported in mice with porencephaly [4], a similar genetic correlation has not been noted in other animals [10]. In many humans and animals, the actual cause is unclear; therefore, a study of a large number of cases is useful for elucidation of the cause of porencephaly.

In this report, any cause of secondary porencephaly including invasive tumor cells was not detected in the brain. There was also no clinical sign of seizure or neurologic manifestation and malformation of the skull that was also detected in this fennec, leading to the speculation that this case of porencephaly may be a congenital one. The defective regions (the right occipital lobe and part of the temporal lobe) are predominantly supplied by the right middle cerebral artery. Thus, the cause may be a local circulatory disorder in the fetal stage. However, we could not establish the cause of porencephaly. The cause of death could have been related to severe multiple organ failure due to the multicentric and disseminated T-cell lymphoma.

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REFERENCES

1. Cantile, C., Chianini, F., Arispici, M. and Fatzer, R. 2001. Necrotizing meningoencephalitis associated with cortical hippocampal hamartia in a Pekingese dog. *Vet. Pathol.* **38**: 119–122. [Medline] [CrossRef]
2. Davies, E. S., Volk, H. A., Behr, S., Summers, B., de Lahunta, A., Syme, H., Jull, P. and Garosi, L. 2012. Porencephaly and hydranencephaly in six dogs. *Vet. Rec.* **170**: 179. [Medline] [CrossRef]
3. Garigliany, M. M., Hoffmann, B., Dive, M., Sartelet, A., Bayrou, C., Cassart, D., Beer, M. and Desmecht, D. 2012. Schmallenberg virus in calf born at term with porencephaly, Belgium. *Emerg. Infect. Dis.* **18**: 1005–1006. [Medline]
4. Gould, D. B., Phalan, F. C., Breedveld, G. J., van Mil, S. E., Smith, R. S., Schimenti, J. C., Aguglia, U., van der Knaap, M. S., Heutink, P. and John, S. W. 2005. Mutations in Col4a1 cause perinatal cerebral hemorrhage and porencephaly. *Science* **308**: 1167–1171. [Medline] [CrossRef]
5. Herder, V., Wohlsein, P., Peters, M., Hansmann, F. and Baumgärtner, W. 2012. Salient lesions in domestic ruminants infected with the emerging so-called Schmallenberg virus in Germany. *Vet. Pathol.* **49**: 588–591. [Medline] [CrossRef]
6. Hewicker-Trautwein, M. and Trautwein, G. 1994. Porencephaly, hydranencephaly and leukoencephalopathy in ovine fetuses following transplacental infection with bovine virus diarrhoea virus: distribution of viral antigen and characterization of cellular response. *Acta Neuropathol.* **87**: 385–397. [Medline] [CrossRef]
7. Hirowatari, C., Kodama, R., Sasaki, Y., Tanigawa, Y., Fujishima, J., Yoshikawa, T., Yabuuchi, K., Kuwamura, Y., Hirakawa, K., Kamimura, Y. and Maeda, H. 2012. Porencephaly in a cynomolgus monkey (macaca fascicularis). *J. Toxicol. Pathol.* **25**: 45–49. [Medline] [CrossRef]
8. Ho, S. S., Kuzniecky, R. I., Gilliam, F., Faught, E., Bebin, M. and Morawetz, R. 1998. Congenital porencephaly: MR features and relationship to hippocampal sclerosis. *AJNR Am. J. Neuroradiol.* **19**: 135–141. [Medline]
9. Hori, A., Hanazono, K., Miyoshi, K. and Nakade, T. 2015. Porencephaly in dogs and cats: relationships between magnetic resonance imaging (MRI) features and hippocampal atrophy. *J. Vet. Med. Sci.* **77**: 889–892. [Medline] [CrossRef]
10. Machado, G. F., Laranjeira, M. G., Schweigert, A. and de Melo, G. D. 2012. Porencephaly and cortical dysplasia as cause of seizures in a dog. *BMC Vet. Res.* **8**: 246. [Medline] [CrossRef]
11. MacKillop, E. 2011. Magnetic resonance imaging of intracranial malformations in dogs and cats. *Vet. Radiol. Ultrasound* **52** Suppl 1: S42–S51. [Medline] [CrossRef]
12. Maxie, G. M. and Sameh, Y. 2007. Malformations of the central nervous system. pp. 298–321. *In*: Jubb, Kenedy, and Palmer's Pathology of Domestic Animals, 5th ed. (Maxie, G. M. ed.), Saunders Elsevier, Amsterdam.
13. Merello, E., Swanson, E., De Marco, P., Akhter, M., Striano, P., Rossi, A., Cama, A., Leventer, R. J., Guerrini, R., Capra, V. and Dobyns, W. B. 2008. No major role for the EMX2 gene in schizencephaly. *Am. J. Med. Genet. A.* **146A**: 1142–1150. [Medline] [CrossRef]
14. Myers, R. E., Valerio, M. G., Martin, D. P. and Nelson, K. B. 1973. Perinatal brain damage: porencephaly in a cynomolgous monkey. *Biol. Neonate* **22**: 253–273. [Medline] [CrossRef]
15. Pákozdy, A., Leschnik, M., Tichy, A. G. and Thalhammer, J. G. 2008. Retrospective clinical comparison of idiopathic versus symptomatic epilepsy in 240 dogs with seizures. *Acta Vet. Hung.* **56**: 471–483. [Medline] [CrossRef]
16. Parsonson, I. M., Della-Porta, A. J. and Snowdon, W. A. 1977. Congenital abnormalities in newborn lambs after infection of pregnant sheep with Akabane virus. *Infect. Immun.* **15**: 254–262. [Medline]
17. Schmidt, M. J., Klumpp, S., Amort, K., Jawinski, S. and Kramer, M. 2012. Porencephaly in dogs and cats: magnetic resonance imaging findings and clinical signs. *Vet. Radiol. Ultrasound* **53**: 142–149. [Medline] [CrossRef]