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.

KEYWORDS: asymptomatic, cortex, fennec fox, porencephaly, spontaneousness

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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); myelinolysis 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 membranous 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.
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 porencephaly. 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, porencephaly 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 neuropil 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 α1 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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