Caudal Fossa Respiratory Epithelial Cyst in a Dog: Clinical, Magnetic Resonance Imaging, and Histopathologic Findings

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An 11-month-old female Bloodhound was presented because of progressive ataxia and head swaying with insidious onset 2 weeks before admission. On neurologic examination, the dog was bright, alert, and responsive, but showed involuntary swaying of the head to both sides and a mild head tilt to the left. Gait inspection disclosed mild ataxia. Paw placing responses were delayed in all 4 limbs. Segmental spinal reflexes and skin sensation were normal. Cranial nerve examination identified left-sided ventrolateral strabismus. Nystagmus was not seen. All other cranial nerve functions were normal. Based on the clinical findings, bilateral central vestibular disease was suspected. Hematology and serum biochemistry findings were within normal reference ranges.

For magnetic resonance imaging (MRI), the dog was premedicated with diazepam (0.5 mg/kg IV) and alfaxalone (2 mg/kg IV). Anesthesia was maintained with isoflurane. MRI was performed at the MRB using a 1.5 Tesla Siemens Magnetom Avanto and 2 purpose-built CPC coils.

Magnetic resonance imaging of the brain disclosed a well-circumscribed cystic lesion with dimensions of approximately 1.5 × 2.2 × 2.9 cm inside of the fourth ventricle, with dorsal displacement of the cerebellum, which was pushed against the osseous tentorium cerebelli, and dorsal compression of the myelencephalon (Fig 1). Both structures were decreased by >50% of their expected dorsoventral diameters (Fig 1A). Sagittal images indicated no signs of foramen magnum herniation or cervical syringomyelia (Fig 1A,B).

On close examination, the cyst appeared loculated with a large dorsomedial compartment being strongly hypointense on T2-weighted images (T2W; Fig 1C) and on fluid-attenuated inversion recovery (FLAIR) sequence (Fig 1D). Another, smaller ventrolateral compartment was hyperintense on T2W (Fig 1C asterisk) and isointense to brain parenchyma on FLAIR images (Fig 1D asterisk). The entire lesion was hypointense on precontrast T1-weighted images (T1W; Fig 1A) with slightly more extensive signal void in the smaller ventrolateral compartment.

After injection of a single bolus of gadopentetate dimeglumine (Magnograf, 0.2 mmol/kg IV), a peripheral ring enhancement with clear demarcation from neighboring neuroparenchyma and the ventricular lumen was seen (Fig 1B arrows). The rostral parts of the ventricular system were symmetrically enlarged.

Based on the imaging findings, an intraventricular cyst was diagnosed. The authors considered an epidermoid/dermoid cyst (IEDC) most likely. Additional differential diagnoses included choroid plexus cyst, ependymal cyst, and abscess bulging into the ventricle.

Upon careful risk evaluation, the dog underwent brain surgery. The dog received cefazolin (20 mg/kg IV) before surgery. Premedication, induction, and maintenance of anesthesia were performed as described above. In addition, fentanyl was given as a continuous rate infusion (CRI) (0.002 mg/kg/h). Just after craniotomy, the dog received methylprednisolone (30 mg/kg IV) before surgery. Premedication included continuous assessment of cardiorespiratory function by pulse oximetry, electrocardiography, and expired gas analysis.

The caudal fossa was approached through a central suboccipital craniotomy. After durotomy, a cyst was identified within the fourth ventricle, confined by an opaque, yellowish-white capsule. The cyst wall was incised, after which approximately 6 mL of yellowish-brown mucoid fluid was removed with a syringe. The cyst then was removed in total by blunt
dissection without obvious damage to the neuroparenchyma.

Approximately 10 minutes after extirpation, the dog experienced acute respiratory arrest. With recurrence of spontaneous breathing, after 3–4 minutes, the dog developed persistent ataxic respirations characterized by exaggerated laryngeal and tongue movements and the dog’s lips were pulled back. Because spontaneous breathing did not restore physiological oxygen saturation of the blood, oxygen was supplied. The gag reflex remained absent after withdrawal of anesthesia. All other cranial nerve functions were within normal limits. Intravenous injection of naloxone hydrochloride (0.04 mg/kg) did not result in improvement. The dog did not regain consciousness and died of apnea 12 hours after surgery.

Cytologic examination of the cyst contents identified paucicellular mucoid material containing necrotic cellular debris, keratin flakes, cholesterol crystals, fibrin, some free red blood cells, mixed degenerate mixed leukocytes, and xanthomatous macrophages. Histologically, the inner surface of the cyst wall was lined by pseudostratified squamous epithelium interrupted by segments of 2-layered, ciliated, cuboidal, or columnar respiratory epithelium (Fig 2A). The transition between the 2 types of epithelium was gradual and some keratinized foci very present. Either type of epithelium was present on a partially ruptured (Fig 2B), fibrovascular capsule with multiple perivascular lymphoid aggregates and diffusely scattered lymphocytes and plasma cells (Fig 2C). Focal neutrophilic infiltrates were seen in areas of squamous metaplasia and keratinization (Fig 2D). In addition, the stroma of the cyst wall contained several microhemorrhages with hemosiderophage aggregation.

Although no goblet cells were evident on conventional stains, the secretory activity of the epithelium was demonstrated by a large number of epithelial cells containing cytoplasmic periodic acid-Schiff (PAS)-positive droplets (Fig 2D). Immunohistochemically, epithelial cells stained strongly for cytokeratin (CK), weakly for S-100 protein (if compared to attaching meningothelial cells), and negative for vimentin and glial fibrillary acidic protein (GFAP; Fig 2E–H). Based on these results, the ventricular mass lesion was diagnosed as a respiratory subtype of an intracranial neuroenteric cyst (RE-INC).

Neuroenteric cysts are rare CNS lesions that result from segmental persistence of the neuroenteric canal that transiently connects the yolk sac to the amniotic cavity in the trilaminar germ disk or from impaired ventral separation of the endoderm from the neural plate. Being related to the embryonic foregut, INC are lined by a mucin-secreting epithelium, similar to that found in the respiratory and gastrointestinal tract. To date, approximately 140 INC cases have been described in the human medical literature, but no such cases have been reported in the veterinary literature. Basically, INC can occur throughout the neuroaxis. Most INC in humans affect the spinal cord with a predominance in the lower cervical and upper thoracic segments. INC are uncommon and usually occur in the caudal fossa. Therefore, most reports describe midline lesions cranial to the brain stem. Other rare localizations comprise the cranio cervical junction, cerebellopontine angle (CPA), cerebellum, and fourth ventricle.
The clinical presentation of INC, as of other expansive mass lesions, is related to pressure on the adjacent neural structures and blood vessels and to inflammatory changes, such as leukocyte-mediated injury, release of neurotoxic factors, and vasogenic edema. Neurologic dysfunction in the caudal fossa may arise from lesions of the cerebellum, peduncles, brainstem, and nuclei and roots of cranial nerves V, VII, VIII, and IX. With ventricular and CPA masses, the vestibular system is particularly susceptible because of its superficial nuclear placement and its connections involving the brainstem and caudal cerebellar peduncles. Accordingly, the left-sided predominantly ventrolateral strabismus and head tilt, the bilateral swaying of the head and delayed paw placing in this dog were compatible with an asymmetric, bilateral brainstem lesion affecting the vestibular and proprioceptive pathways.

Magnetic resonance imaging confirmed compression of both brainstem and cerebellum by a cystic mass lesion of the fourth ventricle. Previously reported fourth ventricle and CPA cysts in dogs consisted of arachnoid diverticula, IEDC, choroid plexus cysts and cysts arising from the ependyma. In agreement with previous reports in people, the RE-INC appeared hypointense compared to gray matter on T1W images and hyperintense on T2W and FLAIR sequences. Thus, the pattern is nonspecific and overlaps with the MRI features of the most prevalent canine IEDC and much more rare choroid plexus cysts and ependymal cysts in dogs.

Based on experience in human medicine, intracranial epithelial cysts appear hypo-, iso-, or hyperintense...
compared to CSF on both T1W and T2W sequences depending on their protein content that results from intracystic hemorrhage, secretary activity, and breakdown products related to degeneration and desquamation of the cellular lining.11

The distinction of nonsecretory and nondegenerate cysts, such as arachnoid diverticula may be facilitated by FLAIR sequence, on which hyperintensity may persist if the protein, cholesterol, keratin content, or some combination of these are increased.3,12 As in the present case, postcontrast peripheral ring enhancement on T1W occasionally is seen in both INC2 and in IEDC of dogs.3,6 It is attributed to abundance of blood vessels within the cyst wall or vascular leakage.9 Peripheral ring enhancement also is a frequent finding in brain abscesses. This differential diagnosis was considered unlikely because of the intraventricular location of the lesion, lack of perilesional edema in the adjacent neuroparenchyma, absence of penetrating injuries to the calvarium or infection of the inner ear, maxillary sinus and dental alveoli and no indications of a compromised immune system.13 In humans, neurocystercerosis could have been considered a relevant differential diagnosis.13–15 Among the more likely differential diagnoses, cystic neoplasms such as meningioma were excluded because of lack of neoplastic growth.13

Because the MR features provided nonspecific findings, the definite diagnosis relied on histologic examination, by which the mass lesion was classified as a cyst of epithelial origin. Apical cilia, PAS-positive basement membrane and the secretory activity of CK-positive epithelial cells were findings compatible with origin from endoderm rather than from neuroepithelium. Most conspicuously, the ciliated pseudostratified columnar epithelium resembled upper airway epithelium and led to the final diagnosis of a respiratory neuroenteric cyst type A.2,11,16–18

Multifocal transition into keratinized squamous epithelium represents a metaplastic adaptation to chronic physical and inflammatory irritation of the cyst wall.16 As a consequence, leakage of cyst contents resulted in aseptic meningitis. In particular, keratin flakes have been associated with PMN-mediated recurrent meningitis in humans with INC.1,16 similar to the reactions seen in dogs with IEDC.6

Ontogenetically, respiratory epithelium is a hallmark of the nasopharynx, paranasal sinuses, and middle ear cavities. In hypophyseal and parahypophyseal areas, Rathke’s cleft would be considered most likely among the likely origins of the cyst.18,19 The caudal fossa, caudal nasopharynx, and middle ear would be more probable sources. In the absence of a patent connection to these compartments on MRI, a misplaced vesicle or cell raft from the primitive endoderm very likely could have given rise to the cyst wall that was disconnected to or later entrapped in the course of neurocranium development. The normal derivatives of the foregut include the upper and lower respiratory tract (causing RE-INC) and the proximal gastrointestinal tract, including the esophagus, stomach, duodenum, liver, and pancreas (causing GI-INC). To the authors’ knowledge, this report represents the first documented case of a RE-INC in a dog.

Regardless of their benign character, INC incite neurologic deficits either by impingement on neural structures or by the recurrent aseptic meningitis or both.1,16 Additionally, malignant transformation of INC and other epithelial inclusions into carcinoma or adenocarcinoma has been reported occasionally.1 Therefore, complete surgical excision of the cyst is the treatment of choice whereas cyst fenestration and partial removal of the cyst wall for mass reduction carry the risk of recurrence and progression to malignancy.1 The surgical outcome of extirpation was good in most reported human cases. Aseptic meningitis is a considerable but usually transient complication.1,2

Surgical exploration of the caudal fossa carries some procedural risks. Fatal cardiorespiratory impairment (as occurred in this case) has been reported in a child and a young woman with IEC in the pons and medulla.2,17 Similar cases of apnea and acute respiratory arrest after suboccipital craniectomy or cranioplasty for caudal fossa decompression and cerebellar ptosis from Arnold Chiari malformation have been reported in the human medical literature; in particular in pediatric patients.20,21 Intraoperative injury to the brainstem, secondary compression or cerebellar ptosis from postoperative hematoma and acute obstructive hydrocephalus as well as loss of respiratory center neurons caused by chronic brainstem compression are possible pathogenetic mechanisms.21 It also may be hypothesized that sudden decompression triggered reperfusion injury. Unfortunately, the owners declined postmortem evaluation.

In summary, this is the first report on an INC and, in particular, its respiratory subtype (RE-INC) in a dog. Hence, endodermal cysts should be considered among the differential diagnoses for cystic lesions of the caudal fossa. Their radiologic appearance may be misleading owing to variable protein content of INC and the existence of similar intracranial lesions, in particular IEDC, from which they can only be distinguished by histopathologic examination. Complete surgical removal is the treatment of choice, but can be associated with critical cardiorespiratory center dysfunction. Aside from the mass effect, morbidity by INC may arise from aseptic chemical meningitis that may even become apparent after surgical removal.

Footnote

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References

1. Gauden AJ, Khurana VG, Kaye AH. Intracranial neuroenteric cysts: A concise review including an illustrative patient. J Clin Neurosci 2012;19:352–359.
2. Bejjani G, Wright D, Schessel D, et al. Endodermal cysts of the posterior fossa. Report of three cases and review of the literature. J Neurosurg 1998;89:326.
3. Steinberg T, Matiasek K, Bruhnschwein A, et al. Imaging diagnosis—Intracranial epidermoid cyst in a Doberman Pinscher. Vet Radiol Ultrasound 2007;48:250–253.
4. Ho NC, Wu HY. Ependymal cyst with hemorrhage in the cerebellopontine angle. J Clin Neurosci 2009;16:127–129.
5. Galano HR, Platt SR, Neuwirth L, et al. Choroid plexus cyst in a dog. Vet Radiol Ultrasound 2002;43:349–352.
6. Platt SR, Graham J, Chrisman CL, et al. Canine intracranial epidermoid cyst. Vet Radiol Ultrasound 2005;40:454–458.
7. MacKillop E. Magnetic resonance imaging of intracranial malformations in dogs and cats. Vet Radiol Ultrasound 2011;52: S42–S51.
8. De Decker S, Davies E, Benigni L, et al. Surgical treatment of an intracranial epidermoid cyst in a dog. Vet Surg 2012;41:766–771.
9. Brewer D, Cerda-Gonzalez S, Dewey C, et al. Diagnosis and surgical resection of a choroid plexus cyst in a dog. J Small Anim Pract 2010;51:169–172.
10. Wyss-Fluehmann G, Konar M, Jaggy A, et al. Cerebellar ependymal cyst in a dog. Vet Pathol Online 2008;45:910–913.
11. Elmadbouh H, Halpin SFS, Neal J, et al. Posterior fossa epithelial cyst: Case report and review of the literature. Am J Neuroradiol 1999;20:681–685.
12. Kitagawa M, Kanayama K, Sakai T. Quadrigeminal cisterna arachnoid cyst diagnosed by MRI in five dogs. Aust Vet J 2008;86:340–343.
13. Costanzo C, Garosi LS, Glass EN, et al. Brain abscess in seven cats due to a bite wound: MRI findings, surgical management and outcome. J Feline Med Surg 2011;13:672–680.
14. James FM, da Costa RC, Fauber A, et al. Clinical and MRI findings in three dogs with polycystic meningiomas. J Am Anim Hosp Assoc 2012;48:331–338.
15. Buback JL, Schulz KS, Walker MA, et al. Magnetic resonance imaging of the brain for diagnosis of neurocysticercosis in a dog. J Am Vet Med Assoc 1996;208:1846–1848.
16. Bigio M, Jay V, Drake J. Prepontine cyst lined by respiratory epithelium with squamous metaplasia: Immunohistochemical and ultrastructural study. Acta Neuropathol 1992;83:564–568.
17. Schelper RL, Kagan-Hallet KS, Huntington HW. Brainstem subarachnoid respiratory epithelial cysts: Report of two cases and review of the literature. Hum Pathol 1986;17:417–422.
18. Hirai O, Kawamura J, Fukumitsu T. Prepontine epithelium-lined cyst. J Neurosurg 1981;55:312–317.
19. Hasegawa D, Uchida K, Kobayashi M, et al. Imaging diagnosis—Rathke’s cleft cyst. Vet Radiol Ultrasound 2009;50:298–300.
20. Tubbs RS, McGirt MJ, Oakes WJ. Surgical experience in 130 pediatric patients with Chiari I malformations. J Neurosurg 2003;99:291–296.
21. Di X, Luciano MG, Benzel EC. Acute respiratory arrest following partial suboccipital cranioplasty for cerebellar ptosis from Chiari malformation decompression. Neurosurg Focus 2008;25:E12.