A CASE OF CHOROID PLEXUS CARCINOMA.

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CYTOLOGIC DESCRIPTION (Figures 1- 3)

A cytospin preparation of the CSF sample was examined. The preparation had a high nucleated cell count and adequate cell preservation. In the background large numbers of erythrocytes were seen. The preparation contained numerous macrophages which occasionally exhibited erythrophagia, along with a few small lymphocytes and ependymal cells. Additionally, a population of atypical epithelial cells arranged in large cohesive rafts and clusters was noted. The epithelial cells had a moderate amount of basophilic and often vacuolated cytoplasm, and a large, round to oval nucleus of coarse chromatin and a single irregular, prominent nucleolus. The N:C ratio was high and anisocytosis and anisokaryosis were moderate to marked. Occasional mitotic figures were seen.

The cytologic interpretation was abnormal CSF with increased cell count and total protein, consistent with chronic inflammation, and presence of a significant population of abnormal epithelial cells, suggestive of epithelial malignancy.

ADDITIONAL TEST RESULTS

Magnetic Resonance Imaging (Figures 4-7)

MRI scan showed multiple lesions in the neurocranium: two small focal lesions within the parenchyma of the dorsal midline cerebellum and the right occipital lobe, consistent with a mass lesion with a necrotic centre; one lesion in the right thalamus; one large intradural but extramedullary lesion extending along the right brainstem, likely arising from the pia mater and responsible for the clinical signs (Figures 4-7).

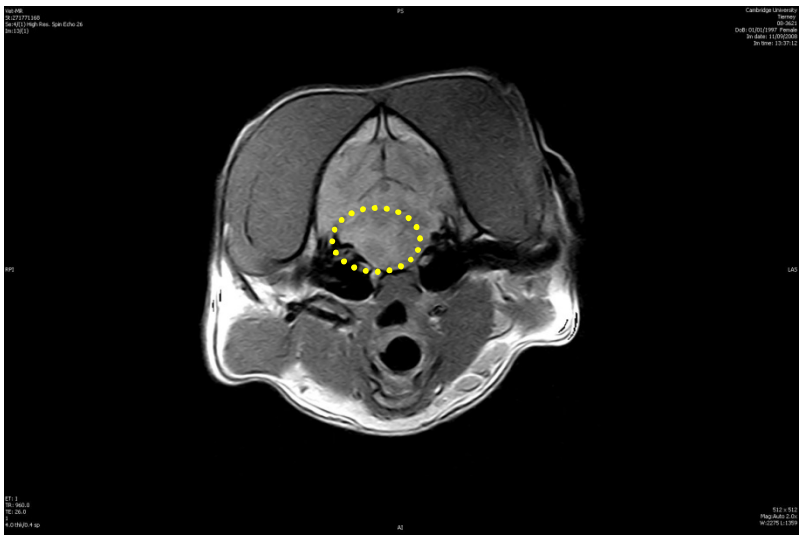

Figure 4. T1w pre contrast trans. Poorly defined hypointense lesion in the right brain stem, with a mild mass effect.

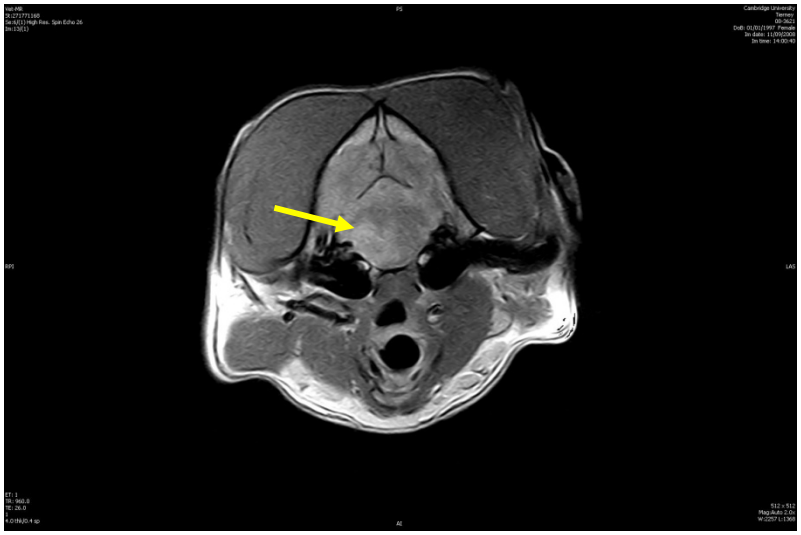

Figure 5. T1w plus contrast trans. Moderate contrast enhancement of mass with a broad base.

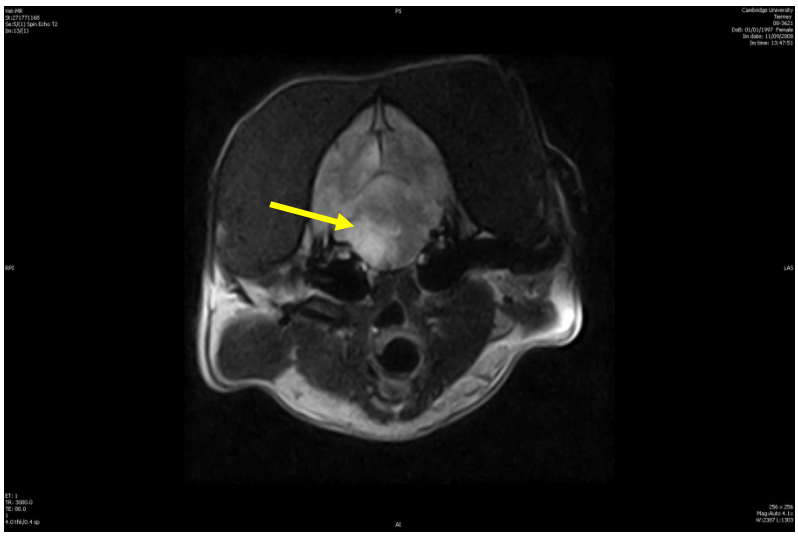

Figure 6. T2w trans. Same area appear bright and hyperintense on T2.

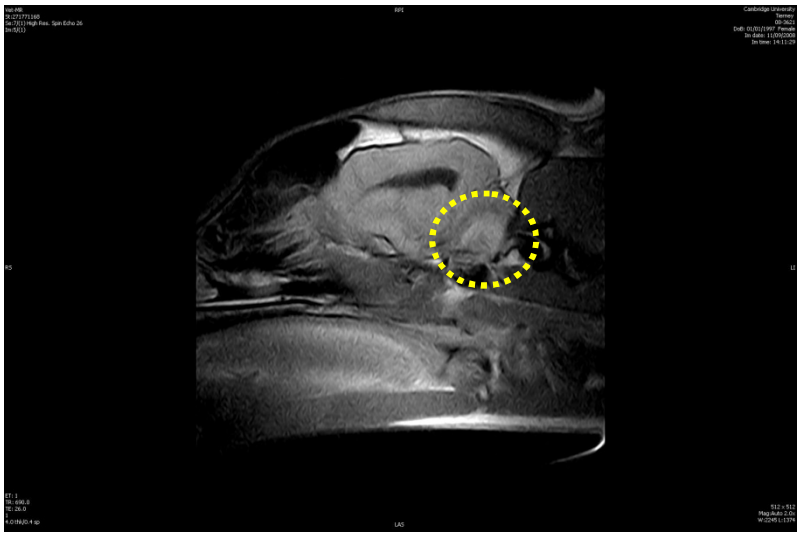

Figure 7. T1w post contrast sagittal. The mass is visible at the level of the cerebellum.

Post mortem findings

In the light of these clinical findings, the owners opted for euthanasia, and also consented to a post mortem examination. The latter revealed an asymmetrical cerebellar well-defined, non-encapsulated, red, granular mass within the choroid plexus of the fourth ventricle with local extension into the cerebellopontine angle.

The mass from the fifth right mammary gland was multinodular, firm, well-demarcated, but non-encapsulated.

Histopathology (Figures 8-10)

Both the neurocranial mass and the mammary mass were fixed in 10% buffered formalin and histopathological examinations were performed.

Histological sections of the brain mass (figures 8-10) contained branching frond-like papillary structures of fibrovascular connective stroma, covered by a single layer of cuboidal to columnar epithelium. The epithelial cells showed moderate pleomorphism and had hyperchromatic nuclei containing up to two prominent nucleoli. Occasional cells had few cilia on the baso-lateral surface. Mitoses were 4 per 10 high power fields. Within the mass there was moderate, multifocal haemorrhage and mild oedema around the blood vessels. Large cells (assumed endothelial) were seen around the blood vessels. The white matter adjacent to the mass was compressed, and numerous prominent glial cells were seen.

Histology of the mammary mass revealed two populations of neoplastic cells, epithelial and mesenchymal. The epithelial cells were arranged in ducts and solid areas, with occasional papillary structures growing into the lumina of mammary ducts, and supported by basement membrane and connective tissue stalks. The spindle-shaped mesenchymal cells were arranged in streams. The mitotic index was 1 to 2 mitoses per 10 high power fields.

The histological diagnoses were choroid plexus carcinoma with local extension into the cerebellopontine angle and complex adenoma, for the brain mass and the mammary mass respectively.

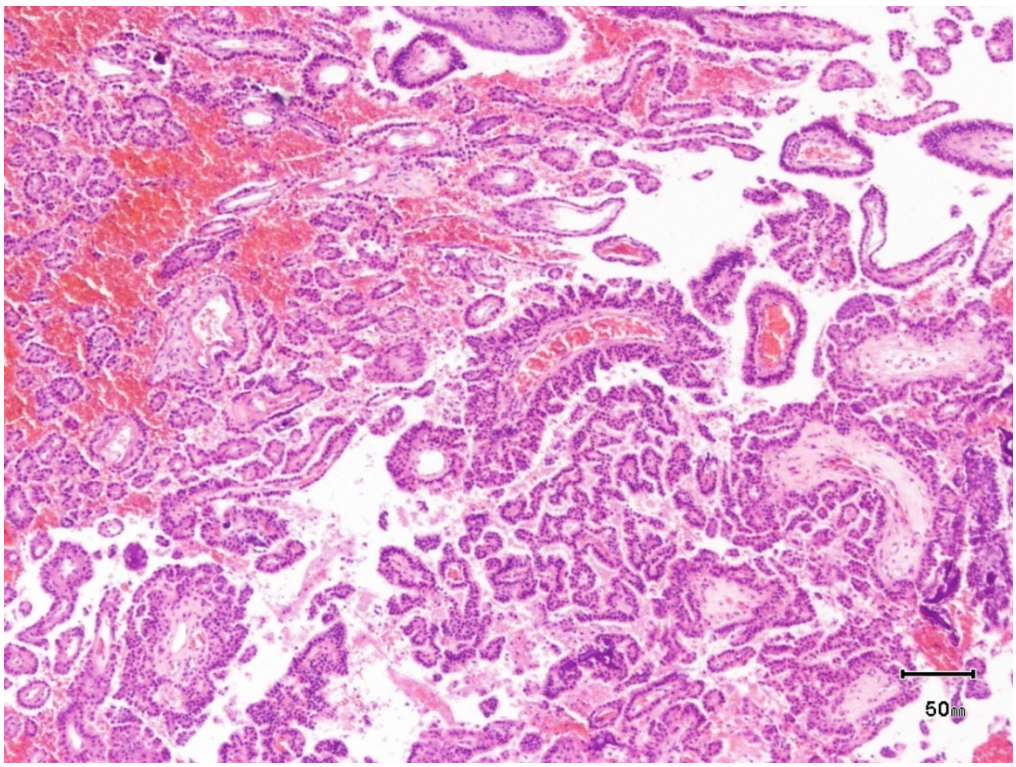

Figure 8. Choroid plexus carcinoma. Arborising to branching papillary pattern supported by fibrovascular stroma. H&E.

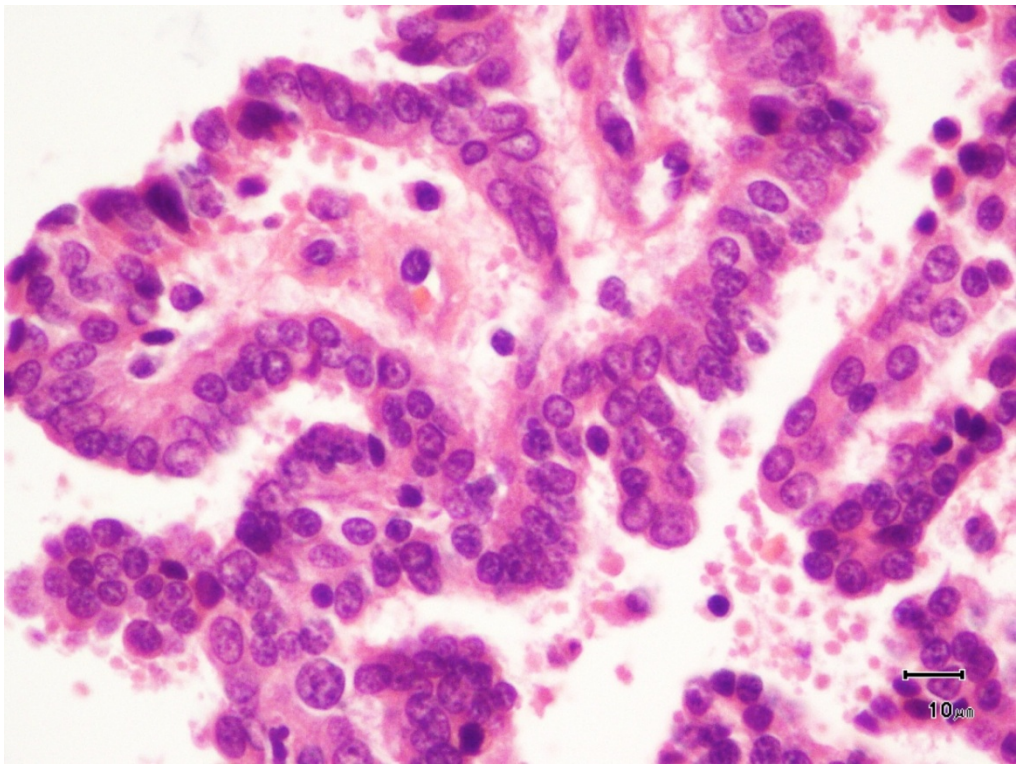

Figure 9. Choroid plexus carcinoma. Neoplastic cuboidal epithelium with cellular pleomorphism, nuclear atypia and hyperchromasia. H&E.

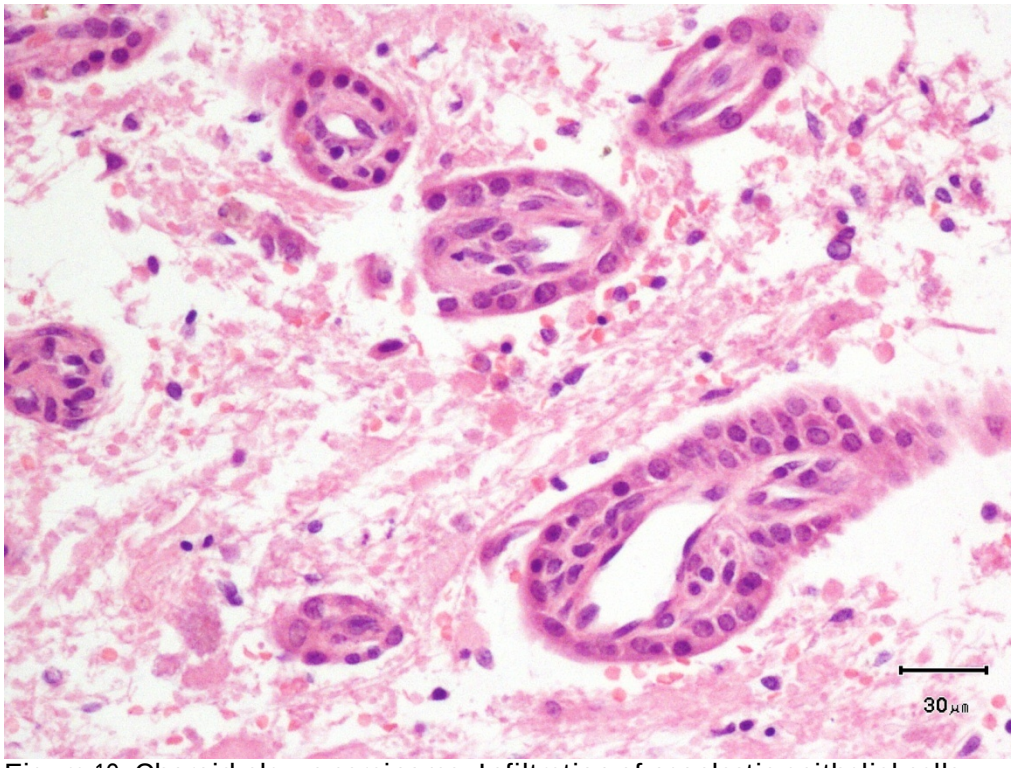

Figure 10. Choroid plexus carcinoma. Infiltration of neoplastic epithelial cells within the adjacent neuropil. H&E.

Immunohistochemistry (Figures 11 and 12)

Selected sections of the brain tumour were tested with the following antibodies: pancytokeratin, vimentin and glial fibrillary acidic protein (GFAP). Pancytokeratin binding was completely absent, while vimentin was strongly expressed by a large numbers of cells (figure 11). The staining was predominantly cytoplasmic. Occasional small clusters of cells exhibited a low positive nuclear immunolabelling for GFAP (figure 12).

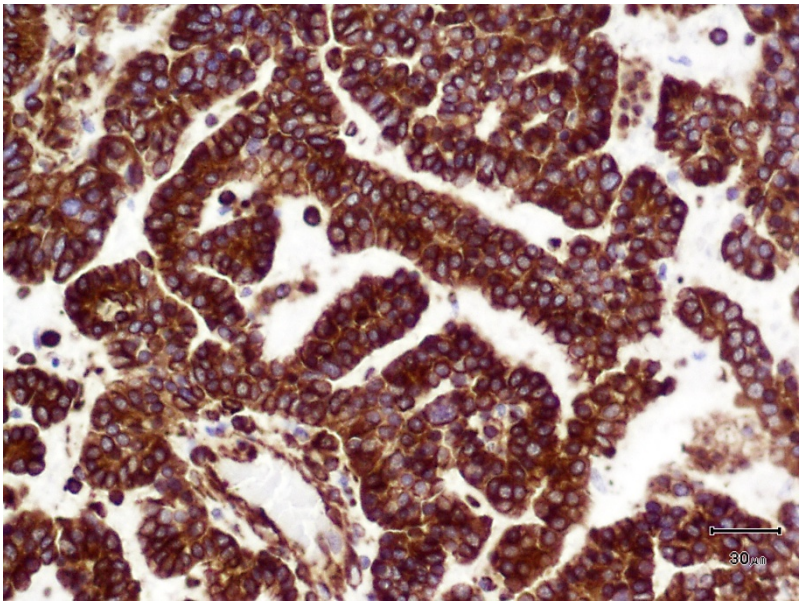

Figure 11. Choroid plexus carcinoma. Vimentin staining.

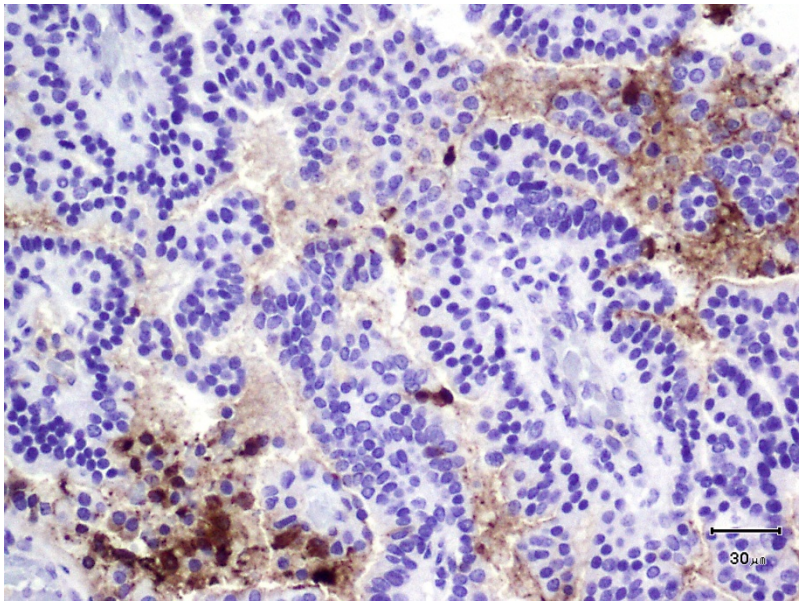

Figure 12. Choroid plexus carcinoma. GFAP staining.

DISCUSSION

Choroid plexus tumours are uncommon neoplasms derived from choroid plexus neuroepithelium which covers the surface of the ventricular cavity and the central canal of the spinal cord, and they are characterized by papillary and intraventricular growth. Within this family of tumours, there are benign and malignant variants, typically classified as choroid plexus papilloma and choroid plexus carcinoma, respectively.

Choroid plexus carcinoma is a highly aggressive malignant tumour, which must be distinguished from choroid plexus papilloma. Distinction between these two neoplasms is generally based on the histological evidence for anaplastic features and/or invasion and metastases within the ventricular system and along the neuroaxis [10].

Cantile and colleagues (2002)[1] noticed that the presence of metastases within the subarachnoid space or the ventricular system was a constant finding in choroid plexus carcinomas in the dog.

In man, choroid plexus tumours represent approximately 0.4% to 0.6% of all brain tumours [14].

Although choroid plexus tumours are rare in animals, comprising 10% of all primary intracranial central nervous system [11], several cases have been previously described. They have been reported in cats, horses, cows, goats, ferrets, and more frequently in dogs [1,2,4,8,11-13,15,17,19,21-26,]. In the latter species, middle-aged dogs appear to be more affected and, although previous literature reported that males are up to three times more predisposed than females to these tumours [13], more recent studies showed an equal male:female ratio for choroid plexus tumours in dogs [21,24].
Approximately 80% of choroid plexus tumours show benign behaviour and are classified as papillomas, while the remaining 20% are reported as carcinoma [9,18]. Conversely, in Westworth's case series [24], out of 56 choroid plexus tumours, 36% were papillomas and 64% were carcinomas.

The fourth ventricle is reported to be the most common location for the development of these tumours in dogs and man [11], while the lateral and third ventricles appear to be less frequently involved.

The previously reported cases of choroid plexus tumours were diagnosed at post mortem examination by histopathology [1,8,19,22,25,27], or by collection of wedge biopsies during neurosurgical procedures and subsequent cytologic squash preparations [4,23]. More recently, the cytological re-evaluation of archived CSF samples in a retrospective study [24] demonstrated the presence of atypical cells attributable to choroid plexus epithelium, highlighting the diagnostic value of CSF samples to recognise these tumours. Nevertheless, to date the finding of a considerable population of neoplastic choroid plexus epithelial cells in a CSF specimen, as in this case report, is quite uncommon, and reflects tumour seeding of the cerebrospinal fluid.

The post mortem and histopathological examination revealed that the mammary mass was a complex adenoma, ruling out a possible metastatic carcinoma to the choroid plexus.

There are very few reports of immunohistochemical investigations of choroid plexus tumours. Koestner and Higgins (2002)[11] consider cytokeratins as the most reliable markers for the epithelial component of choroid plexus tumours, with rare GFAP positivity. In this report, the pancytokeratin marker did not show any positive immunolabelling, while some individual cells were moderately positive for GFAP, and vimentin – a mesenchymal marker – was largely and strongly positive. Positive reactivity for vimentin has been reported in human choroid plexus tumours [5,7,16], and in Vernau's findings [23] all choroid plexus tumours (without any discrimination between papillomas and carcinomas) were positive for vimentin and negative for cytokeratin. On the other hand, two independent studies [1,3] described a stronger positive reaction for vimentin in malignant choroid plexus tumours than in the benign variant. It is possible that malignant anaplastic cells lose the ability to react with cytokeratins and synthesise atypical proteins (e.g. vimentin).

The clinical signs - head tilt, loss of equilibrium, behavioural changes - exhibited by this dog are consistent with the signs reported in previous cases [1,25,27].

Choroid plexus carcinoma has been associated with obstruction of the cerebrospinal fluid pathways and, potentially, overproduction of CSF, leading to hydrocephalus and increased intracranial pressure [18]. Increased intracranial pressure due to local compression of the ventricular lumina or increased synthesis of CSF and poor CSF

reabsorption is likely to have accounted for the right sided papilloedema observed in the dog describe in this case report.

REFERENCES

1. Cantile C., Campani D., Menicagli M., Arispici M. Pathological and immunohistochemical studies of choroid plexus carcinoma of the dog. J. Comp Path. 2002; 126:183-193.

2. Chénier M., Gosselin Y., Teuscher E., et al. Paradoxic vestibular syndrome associated with choroid plexus papilloma in a dog. J Am Vet Med Assoc 1983;182:66-67.

3. Cruz-Sanchez F. F., Rossi M. L., Hughes J. T., et al. Choroid plexus papillomas: an immunohistological study of 16 cases. Histopathology. 1989; 15: 61–69.

4. De Lorenzi D., Mandara M.T., Tranquillo M., et al. M. Squash–prep cytology in the diagnosis of canine and feline nervous system lesions: a study of 42 cases. Vet. Clin. Path. 2006; 35: 208-214

5. Doglioni C., Dell'Orto P., Coggi G., et al. Choroid plexus tumors. An immunocytochemical study with particular reference to the coexpression of intermediate filament proteins. American Journal of Pathology. 1987; 127: 519–529.

6. Indrieri R.J., Holliday T.A., Selcer R.R, et al. Choroid plexus papilloma associated with prolonged signs of vestibular dysfunction in a young dog. J. Am. Anim. Hosp. Assoc. 1980;16:263-268.

7. Kato T., Fujita M., Sawamura Y., et al. Clinicopathological study of choroid plexus tumors: immunohistochemical features and evaluation of proliferative potential by PCNA and Ki-67 immunostaining. Noshuyo Byori. 1996; 13: 99–105.

8. Klopfleisch R., Beier D., Teifke J. P. Choroid Plexus Carcinoma in a Goat. J. Comp. Path. 2006;135: 42-46.

9. Koeller K.K., Sandberg G.D. From the archives of the AFIP: Cerebral intraventricular neoplasms: radiologic-pathologic correlation. Radiographics 2002;22:1473-1505.

10. Koestner A., Bilzer T., Fatzer R., et al. Histological Classification of Tumors of the Nervous System of Domestic Animals, Armed Forces Institute of Pathology; American Registry

of Pathology; The World Health Organization Collaborating Center for Worldwide Reference on Comparative Oncology. Second Series, Vol. V, Washington D.C., 1999: 23–24.

11. Koestner A., Higgins R.J. Tumors of the ependyma and choroid plexus. In: Meuten DJ, ed. Tumors in Domestic Animals. 4th ed. IA: Blackwell Publishing, 2002:707-712.

12. Kurtz H.J., Hanlon G.F. Choroid plexus papilloma in a dog. Vet Pathol 1971;8:91-95.

13. Luginbuhl H., Frankhauser R., McGrath J.T. Spontaneous neoplasms of the nervous system in animals. Prog Neurol Surg 1968;2:85-164.

14. Paulus W., Brandner S. Choroid plexus tumours. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, eds. WHO Classification of Tumours of the Central Nervous System. Lyon, France: IARC Press 2007:81–85.

15. Pirie R.S., Mayhew I.G., Clarke C.J., et al. Ultrasonographic confirmation of a space-occupying lesion in the brain of a horse: choroid plexus papilloma. Equine Vet. J. 1998;30:445-448.

16. Radotra B. D., Joshi K., Kak V.K. and Banerjee A.K. Choroid plexus tumours—an immunohistochemical analysis with review of literature. IndianJournal of Pathology and Microbiology. 1994; 37: 9–19.

17. Ribas J.L., Mena H., Braund K.G., et al. A histologic and immunocytological study of choroid plexus tumors of the dog. Vet. Pathol . 1989;26:55-64.

18. Rickert C.H., Paulus W. Tumours of the choroid plexus. Microsc. Res. Tech. 2001;52:104–111

19. Sant'Ana F.J.F., Gabriel A.L, Kommers G.D., Barros C.S.L. Choroid plexus carcinoma in a cow. Ciencia Rural, Santa Maria, Online. 2009.

20. Summers B. A., Cummings J. F., de Lahunta A. Veterinary Neuropathology, Mosby-Year Book, Inc., St Louis, 1995: 373–375.

21. Thankey K, Faissler D., Kavirayani A., et al. Proc. ACVIM forum 2006; Abstract 266: 782-783.

22. Van Zeeland Y., Schoemaker N., Passon-Vastenburg M., Kik M. Vestibular syndrome due to a choroid plexus papilloma in a ferret. J. Am. Anim. Hosp. Assoc. 2009; 45: 97-101.

23. Vernau K.M., Higgins R.J., Bollen A.W., et al. Primary canine and feline nervous system tumours: intraoperative diagnosis using the smear technique. Vet Pathol. 2001; 38: 47-57.

24. Westworth D.R., Dickinson P.J., Vernau W, et al. Choroid plexus tumours in 56 dogs (1985-2007). J. Vet. Intern. Med. 2008; 22: 1157-1165.

25. Wilson R. B., Holscher M. A.,West W. R. Choroid plexus carcinoma in a dog. J. Comp. Path. 1989; 100: 323-326.

26. Yamada M., Nakagawa M., Yamamoto M., et al. Histopathological and immunohistochemical studies of intracranial nervous-system tumours in four cattle. J. Comp. Path. 1998;119:72-82.

27. Zaki F.A., Nafe L.A. Choroid plexus tumors in the dog. J. Am. Vet. Med. Assoc. 1980;174:328-330.