First Description of a Congenital Choroid Plexus Papilloma in a Newborn Calf

Terim Kapakin, K. A.

Department of Pathology, Faculty of Veterinary Medicine, University of Ataturk, 25240 Erzurum, Turkey.

Corresponding author: Asst. Prof. K. A. Terim Kapakin. Department of Pathology, Faculty of Veterinary Medicine, Atatürk University, Erzurum 25240, TURKEY. Phone: +90-442-231 5531, Fax: +90-442-236 0881, email: kbraterim@gmail.com

ABSTARCT

This study reports the histopathological and immunohistochemical finding of a congenital choroid plexus papilloma in a newborn calf. Macroscopically, the mass protruded from the parietal bone and resembled the shape of a cauliflower. The tumor was 6.2 x 5 x 7.3 cm in size, pinkish in color and contained patches of hemorrhage. Histopathological examination revealed the presence of well-differentiated papillary structures of cuboidal and columnar epithelial cells enclosed by a fibrovascular stroma exhibiting branching arbiriform pattern. The tumor cells were generally large and contained brightly eosinophilic granular cytoplasm with central nuclei. There was only mild nuclear pleomorphism and mitosis was rare. The tumor cells gave positive results for pancytokeratin, S100, vimentin and the epithelial membrane antigen (EMA), but did not stain with glial fibrillary acidic protein (GFAP).

Key words: Calf, choroid plexus papilloma, congenital, immunohistochemistry.

INTRODUCTION

Tumors of the choroid plexus which arise from the neuroepithelium, are rarely observed in both humans and animals (1, 2, 3, 4). These tumors are classified under two categories, namely papillomas and carcinomas according to their histological structure. Choroid plexus papillomas (CPP) are benign intraventricular neoplasms that arise from the epithelium of the choroid plexus (1, 4, 5, 6). These tumors are generally observed in dogs, (1, 6, 7, 8, 9), but also reported to occur in domestic animals, including cattle (10, 11, 12, 13), goats (14), and horses (15), in wild animals and in ferrets (5). It is reported that these tumors arise mostly from the lateral aspect of the plexus in the fourth ventricle (1, 7, 9, 11, 14, 15, 16), however, they may also develop in the supratentorial region (1, 10). This case report provides the histopathological and immunohistochemical characterization of a congenital CPP, an uncommon tumor of both humans and animals. To the best knowledge of the author this is the first report CPP in a newborn calf.

CASE HISTORY

According to the anamnesis provided, a newborn, 12 hour-old, male, Brown Swiss breed calf was born with a well-circumscribed mass (6.2 x 5 x 7.3 cm) protruding from the parietal bone and resembling the shape of a cauliflower. The calf was reported to be unable to suckle and was reported to be ataxic. The skin in the parietal region was incomplete. The tumor had a pinkish color and contained patches of hemorrhage (Figure 1).

MATERIALS AND METHODS

The calf was referred to the Pathology Department of Atatürk University, Faculty of Veterinary Medicine, Erzurum, Turkey for examination. Study material consisted of a biopsy from the mass which protruded from the parietal bone of the newborn calf. Tissue samples were fixed in 10% buffered formaldehyde, subjected to routine tissue processing, and embedded in paraffin. Tissue sections prepared from paraffin blocks at

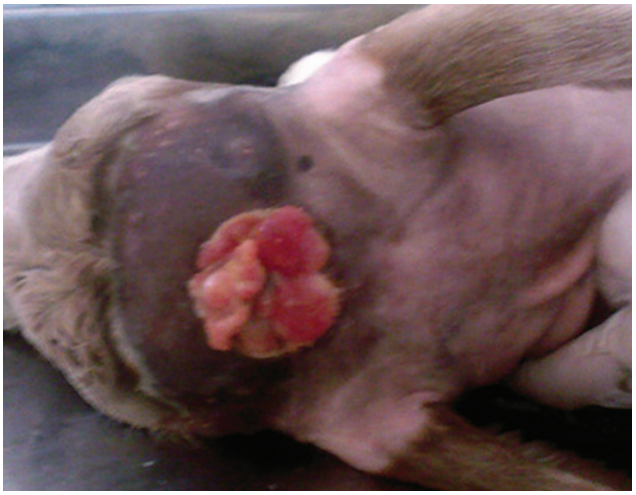


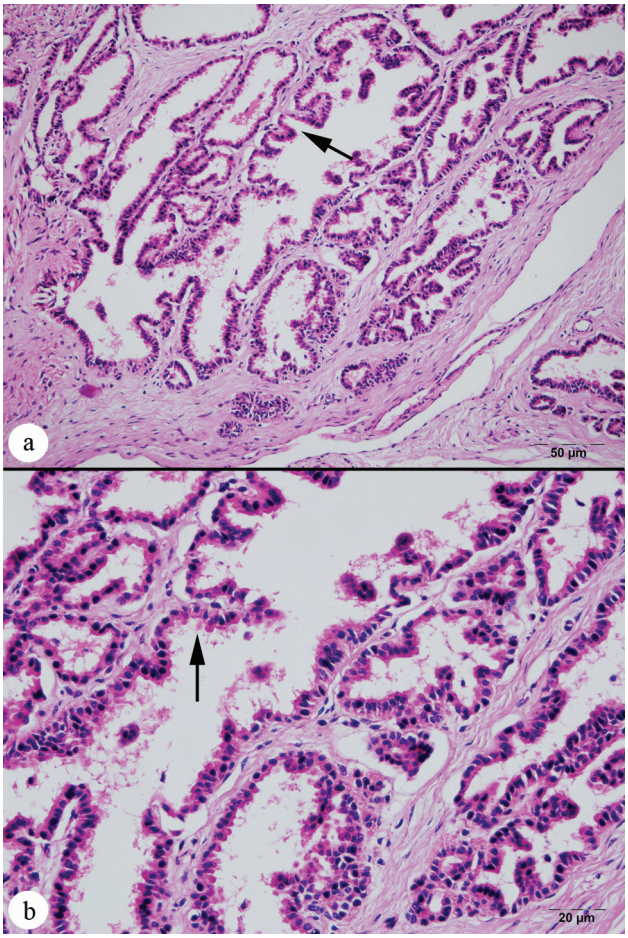
Figure 1: Macroscopic appearance of the tumoral mass.

a thickness of 4 μm were stained with haematoxylin-eosin (HE).

Immunohistochemistry

Using the avidin–biotin-complex (ABC-P) method, the antibodies used were those specific for glial fibrillary acidic protein (GFAP, Cytomation GmbH, Dako, Hamburg, Germany; diluted 1: 150), vimentin (clone Vim 3B4, Dako, Hamburg, Germany, diluted 1: 40), epithelial membrane antigen (EMA, clone E23, Dako, Hamburg, Germany, diluted 1: 200), pancytokeratin (clone AE1/AE3, Dako, Hamburg, Germany, diluted 1:500), S100 (clone Z311, Dako, Hamburg, Germany, diluted 1:1000).

After routine embedding in paraffin and preparation of sections of 4 μm, sections were then dewaxed through two xylene steps, and rinsed with a series graded alcohol solutions. Antigen retrieval was a by incubation in 0.1% trypsin reagent for 15 min at 37 ^{O}C. Endogenous peroxidase was blocked for 15 min with 3% hydrogen peroxide. Non-specific immunoglobulin binding was blocked by incubating the slides for 10 min with a protein-blocking agent before applying the primary antibody, which was then allowed to react for 30 min at room. The primary antibody was then applied together with the ABC-P. As chromagen, 3, 3-Diaminobenzidine (DAB, Dako, Hamburg, Germany) was added and sections were kept in the dark for 10 min. Sections were then stained with Mayer's hematoxylin for 8 min as counter stain. Finally, the sections were mounted with cover slips using neutral balsam (17).

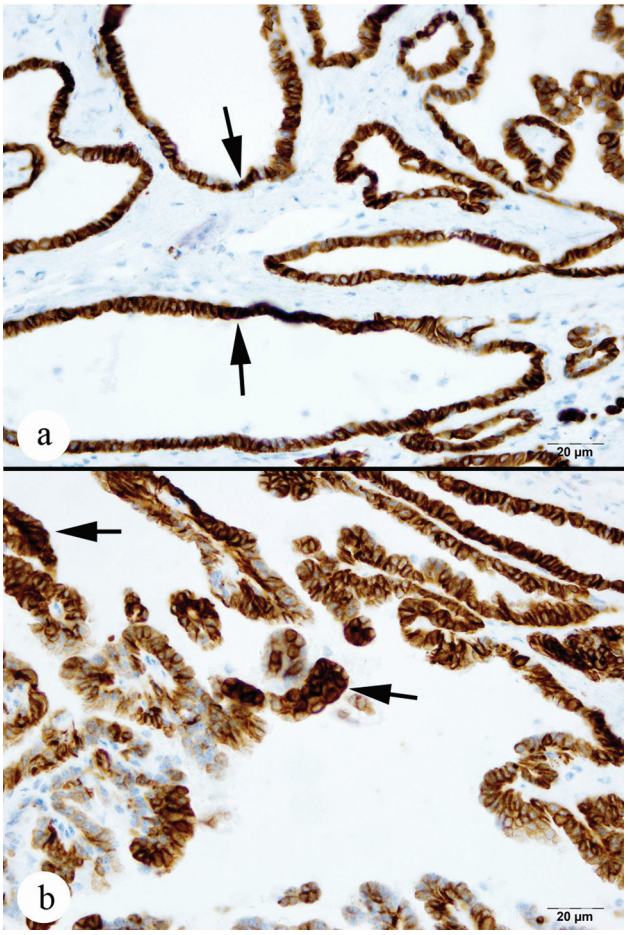


Figures 2a-b: Arboriform, densely packed papillae are composed of a vascular stroma lined by single or multiple layers of cuboidal to low columnar neoplastic epithelium, (arrows). (a) Haematoxylin - Eosin, Bar: 50 μm; (b) Haematoxylin - Eosin, Bar: 20 μm

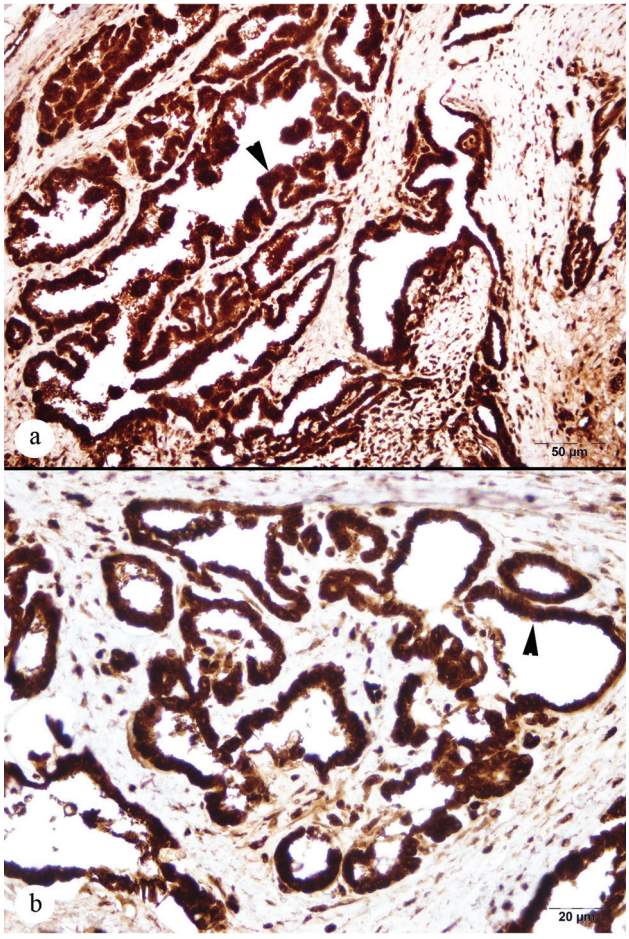
RESULTS

Microscopic examination revealed the presence of well-differentiated papillary structures of cuboidal and columnar epithelial cells enclosed by a fibrovascular stroma exhibiting branching arboriform pattern (Figure 2a-b). Multifocal hemorrhages were observed in places. The tumor cells were generally large and contained brightly eosinophilic granular cytoplasm with central nuclei. There was only mild nuclear pleomorphism and mitoses were rare.

Immunohistochemical examination revealed neoplastic cells positively labeled for antibodies against pancytokeratin (Figure 3a-b), EMA, vimentin, and S-100 (Figure 4a-b), but they were not immunoreactive for GFAP. Based on the pathomorphological and immunohistological findings of the



Figures 3a-b: Neoplastic epithelial cells are strongly immunoreactive for pancytokeratin (arrows), (a) immunohistochemistry (IHC) Bar: 50 µm; (b) immunohistochemistry (IHC) Bar: 20 µm



Figures 4a-b: Neoplastic epithelial cells are strongly immunoreactive for S-100 (arrowheads), (a) immunohistochemistry (IHC) Bar: 50 µm; (b) immunohistochemistry (IHC) Bar: 20 µm

mass, the tumor was diagnosed and classified as a choroid plexus papilloma.

DISCUSSION

This rare case presents a congenital choroid plexus papilloma in a newborn calf. Excluding medulloblastoma in calves (4, 11), primary brain tumors have been reported rarely in cattle (2, 12, 13). To date, only four cases of CPP have been reported in cattle (2, 10, 13, 18). These tumors are also uncommon in humans, and constitute only 0.4% to 0.6% of all intracranial tumors. The majority of these tumors are observed in children and they constitute 3.9% and 2.3% of the primary brain tumors in newborns and children, respectively. CPPs comprise 4-6% of the intracranial neoplasms in children younger than 2 years and 12-13% of intracranial neoplasms in children younger than 1 year (3, 19).

In animals, all CPP cases reported in the literature have been observed in middle-aged animals (1, 2, 7, 8, 13, 14, 15, 18), with the exception a few cases seen in the young (8). However, to the best of author's knowledge there are no previous reports of the occurrence of congenital CPP in animals. The age of the calf (12 hours) is significant because congenital CPP cases have been observed in children.

The common sites of origin of these tumors are the lateral ventricles in children and the fourth ventricle in adults (3, 19). The cerebellopontine angle and the third ventricle are extremely rare sites for the origin of CPP. Intraparenchymal locations of CPP have also been described (16). The localization site of the fourth ventricle (2, 13, 18), the third ventricle

(8) has been reported previously in cattle. Although genetic factors in the etiology of CCP were discussed, polyoma viruses (SV40, JC and BK) have also been considered (19, 20, 21). In the case presented here the origin of the tumor was not determined as all work was performed on biopsy material.

Grossly, CPP appear as pink or reddish globular masses with a rough, irregular surface resembling a cauliflower. They are very vascular and sometimes, significant calcification is noted. Microscopically, they resemble the normal architecture of the choroid plexus and show papillae composed of a single layer of columnar or cuboidal epithelium lining a stroma of vascularized connective tissue. Features of microscopic invasion, mitotic activity, and pleomorphism should raise the possibility of malignancy, even when the general architecture indicates a well differentiated papilloma. The macroscopic and microscopic findings obtained in the investigated case were in agreement with previous literature reports (1, 5, 6, 13, 14).

The differentiation between CPP and papillary ependymoma may be difficult since some histological features are similar for both neoplasms (1, 5). Immunohistochemistry is the most reliable diagnostic method to differentiate CCP from papillary ependymoma (22, 23). Tumor cells of choroid plexus tumors express cytokeratin while ependymoma cells will express GFAP and vimentin (1). Many reports mention the absence cytokeratin immunoreactivity in ependymomas from humans and animals (1, 22). Usually choroid plexus tumors in humans express cytokeratin, vimentin to a lesser extent, and rarely GFAP (13, 15).

Although previously conducted immunohistochemical studies report positive results to tumors for keratin, EMA and strong positive results for vimentin, cytokeratin, pancytokeratin and S-100, (4, 9, 10, 13, 15) both positive and negative results for GFAP in humans and animals (13, 15). GFAP positive cells are normally not seen in choroid plexus epithelium. However, CPP may demonstrate various types of metaplastic changes. The stroma may exhibit focal metaplastic changes such as xanthomatous change, calcification and rarely ossification. The epithelial component may show mucinous metaplasia, pigmentation with presence of neuromelanin, ependymal differentiation or oncocytic transformation. Focal positivity for GFAP has been observed in choroid plexus papillomas and choroid plexus carcinomas in 35-40% of cases. It has been suggested that focal GFAP positivity indicates glial or possibly ependymal differentiation in the choroid plexus epithelium (24, 25). Our results show strong immunohistochemical reactivity to pancytokeratin and S100 in the epithelial cell lining of the tumor, with a weak positivity for EMA and vimentin, but were not immunoreactive for GFAP.

This case suggests that in new born animals congenital choroid plexus papillomas may occur and definitive diagnosis requires histopathology and immunohistochemistry.

ACKNOWLEDGMENTS

Thanks are extended to academic staff at Departments of Surgery, Faculty of Veterinary Medicine, Atatürk University.

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