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Olgu Sunumu ***Case Report***

Histopathological and Immunohistochemical Characteristics of Ventricular Ependymoma in A Goat

Ghasem FARJANIKISH[1], Azizollah KHODAKARAM-TAFTI[2]*

[1]Department of Pathobiology, Faculty of Veterinary Medicine, Lorestan University, Khorram Abad, Iran
[2]Department of Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

****Sorumlu Yazar / Corresponding Author:***
Ghasem Farjanikish
e-mail: farjanikish.gh@lu.ac.ir

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Abstract
Ependymomas as primary central nervous system neoplasms are occasionally observed in human infants however; they are rare in animals. A three-year-old male goat was presented with clinical neurological signs. At necropsy, a 3×2×2 cm, bulging, white-grey- to red, soft mass extending into the left lateral ventricle of brain was observed. Microscopically, the mass with densely cellular population was nonencapsulated, mostly containing cuboidal-columnar neoplastic cells with pseudo-rosettes formation. Mitotic figures were rare and malignancy indexes were not observed. Neoplastic cells were immunohistochemically positive for Glial Fibrillary Acidic Protein (GFAP), S-100, and vimentin; however, they did not express Cytokeratins. On the basis of the location, histologic and immunohistochemical findings, the tumor was diagnosed as an ependymoma.

Introduction

Ependymoma is derived from the ependymal cell lining of the brain ventricle system and the central canal of the spinal cord. Among domestic animals, ependymomas are relatively rare tumors reported in a few cases including dogs, cats, cattle, horses, and rats (Carrigan et al., 1996; McGill and Wells, 1993; McKay et al., 1999; Michimae et al., 2004; Simpson et al., 1999; Vural et al., 2006). Ependymomas are occasionally reported in human infants; however, they are rarely observed in animals. Due to such rarity, the growth rate of ependymomas has not been well defined (Cordy, 1990). Two major histological subtypes of ependymomas, including cellular and papillary types contain both pseudo-rosettes and true rosettes (Koestner and Higgins, 2002; Simpson et al., 1999). These tumors are highly cellular and vascular with uniform cells (Koestner and Higgins, 2002).

The present study describes the clinical, histopathological and immunohistochemical characteristics of a ventricular ependymoma associated with hydrocephalus in a native Iranian goat.

Case

A three-year-old male native Iranian goat was presented with a history of circling, spinning, behavioral changes, and falling. Oculocephalic responses and papillary light reflex were depressed, but the vision was intact. Neurological examinations revealed some normal spinal reflexes. The goat died after two days and necropsy was performed. At necropsy, significant findings were limited to the brain. There was a 3 × 2 × 2 cm, bulging, white-grey to red, soft mass extending into the left lateral ventricle. The appropriate tissues were fixed in 10% neutral buffered formalin, dehydrated in graded Ethanol, cleared in Xylene and embedded in paraffin wax. Sections of 5 µm thickness were stained by Hematoxylin and Eosin (H & E) and examined microscopically. Immunohistochemical staining was performed on paraffin-embedded specimens based on the Labeled Polymer Technique in which Novolink along with DAB is used as chromogen and antibodies are used against glial fibrillary acidic protein (GFAP) (Biogenex, monoclonal antibody clone GA-5, USA), vimentin (Dako, monoclonal mouse antibody clone V9, Denmark), S-100 (Dako, poly clonal rabbit antibody, Denmark) and cytokeratin (Biogenex, AE1/AE3, USA).

Histopathologically, the mass was densely cellular, well-vascularized, non-encapsulated possessing perivascular zone characteristics. Moreover, there were occasional formations of some ependymal pseudo-rosettes (Figure 1). Cuboidal neoplastic cells being radially oriented around thin-walled blood vessels were observed. The neoplastic cells were usually uniform, with minimal cytoplasm, round to oval or slightly elongated granular, centrally-located round hyperchromatic small nuclei (Figure 2). Among pseudo-rosettes formations, there were thin connective tissues and solid sheets or clusters of cells with no specific pattern. Mitotic figures were rare and no malignancy characteristics were observed. Degeneration and necrosis of neurons were observed in the brain tissues near the tumoral mass. In addition, vascular endothelial cells were swollen and the vessels were congested. Immunohistochemically, about 40% of neoplastic cells were positive for S-100 and less than 20% of these cells were positive for GFAP (Figures 3 and 4). In addition, although the tumor mass was strongly positive for vimentin, they were negative for Cytokeratins (CK). Based on the locational, clinical, histopathological, and immunohistochemical findings of the mass, the tumor was diagnosed as an ependymoma.

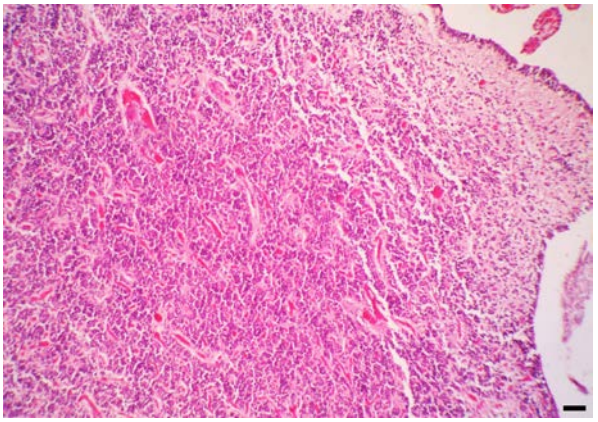

Figure 1. Ependymoma. The mass is densely cellular, well vascularized and unencapsulated (HE, Bar: 50 µm).

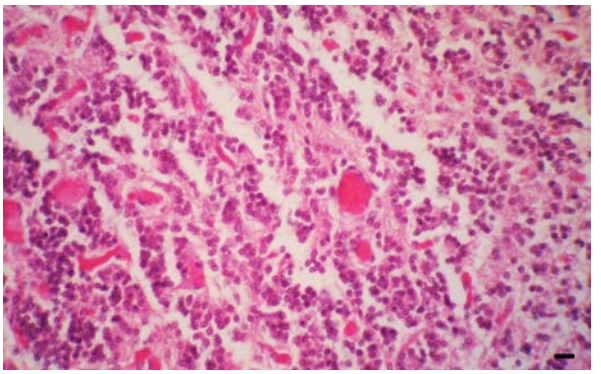

Figure 2. This photomicrograph of ependymoma illustrates the high density, cuboidal neoplastic cells. Nuclei are densely packed and the minimal cytoplasm is hard to delineate (HE, Bar: 25 µm).

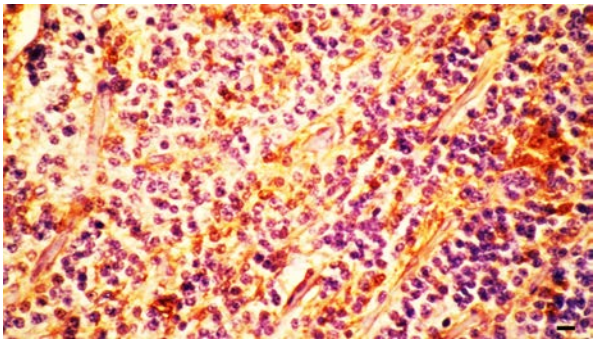

Figure 3. Neoplastic cells showing S-100 positivity (IHC, Bar: 20 µm)

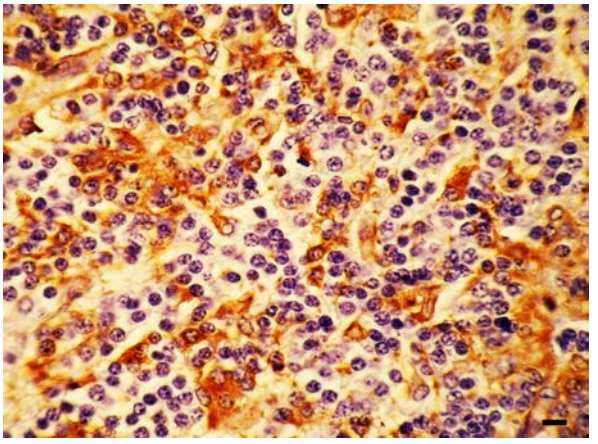

Figure 4. Neoplastic cells showing GFAP positivity (IHC, Bar: 20 µm).

Discussion

Ependymomas are primary central nervous system neoplasms in human being. They are rare in adults; however, they are more common in pediatric population (Gilbert et al., 2010). These tumors are generally hug-intra-ventricular masses, mostly well demarcated, grey to red, with a smooth texture in dogs and with much more granular textures in cats. These tumors are slow-growing, circumscribed, expansile masses mainly developing within lateral ventricles. Clinical symptoms

may vary, depending on the location and their size as well as the severity of secondary changes (Koestner and Higgins, 2002; Wiestler et al., 2000). Ependymomas are divided into two subcategories in animals: a papillary ependymoma within horses and a malignant ependymoma within cats (Carrigan et al., 1996) and atypical ependymomas are described for cattle (McGill and Wells, 1993).

For human beings, this neoplasm commonly develops in the spinal cord and the fourth ventricle (Koestner and Higgins, 2002; Michimae et al., 2004; Vural et al., 2006); however, in the case of animals, the tumor mainly develops within the lateral ventricles, less often in third or fourth ventricle and rarely in the central canal of spinal cord (Koestner and Higgins, 2002). Regarding the pediatric cases, the location is usually intracranial; however, it is spinal for adults.

The common site for intracranial ependymoma is the fourth ventricle. The cellular ependymomas are moderately to densely cellular and well-vascularized, possessing the characteristics of nuclear-free peri-vascular zones formed by tumor cell processes. These perivascular zones appear fibrillated and result in the formation of pseudo-rosettes. The tumor cells are clustered with no orientation within the blood vessels (Vernau et al., 2001). Perivascular pseudo-rosettes are formed by tumor cells radially surrounding blood vessels and appear in a majority of ependymomas. Predicting the prognosis of such a tumor is also difficult since ependymomas vary considerably both in their morphologic appearance and in their biological behavior (Metellus et al., 2010). In a majority of previous reports, it has been claimed when H&E stain is used as a diagnostic method, ependymomas can get confused with other tumors. Therefore, ultrastructural or immunohistochemical differentiation methods should be used (Carrigan et al., 1996; Koestner and Higgins, 2002). The differentiation between ependymoma and an anaplastic choroid plexus tumor may be difficult based on H&E stained sections. Moreover, the positive GFAP and negative cytokeratin immunostaining in ependymomas are the most reliable diagnosis criteria. Choroid plexus tumor contains a fibrovascular stroma and stains positively for cytokeratins (Carrigan et al., 1996).

The differentiation between ependymoma and an anaplastic choroid plexus tumor may be difficult based on H&E stained sections (Koestner and Higgins, 2002). In the present report, immunolabelling showed that the neoplastic cells were immunoreactive for GFAP, vimentin and S-100. GFAP immunoreactivity of ependymoma has been reported to be positive in cats and horses (Carrigan et al., 1996; Koestner and Higgins, 2002). There are few reports on immunolabelling of animal ependymomas and an equine papillary ependymoma was positive for GFAP and vimentinin a report of an ependymoma in the fourth ventricle of a cat as positive for GFAP, vimentin, S-100 and negative for cytokeratin (Carrigan et al., 1996; McKay et al., 1999; Vural et al., 2006) similar to the present report. In the present study, immunoreactivity for vimentin was strongly positive, which was the same as findings reported in a previous study (Cantile et al., 2002).

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