Myofibroblastoma of the Neck in a Heifer

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(Received 28 April 1999/Accepted 11 June 1999)

ABSTRACT. A 1.5-year-old Holstein heifer had a subcutaneous tumor mass (20 cm diameter) on the ventral portion of the neck, and the tumor was diagnosed as a locally invasive myofibroblastoma. It consisted of moderately cellular fibrous tissue, and the interlobular septum of the thymus was invaded by tumor cells. The neoplastic cells were positive for alpha smooth muscle actin and vimentin, but not for desmin. Electron microscopy disclosed the presence of moderately developed rough endoplasmic reticulum and microfilaments with focal densities.—KEY WORDS: bovine, myofibroblastoma, subcutis.

Myofibroblasts are spindle-shaped cells that secrete collagen, but also have well defined contractile properties similar to those of smooth muscle [10]. Myofibroblasts may be contained in various fibroblastic tumors [3], and tumors consisting predominantly or most entirely of myofibroblasts exist in human beings [5, 13]. A vulval myofibroblastoma has been reported in a cow [1], and sarcomas of myofibroblastic origin have been described in two cats [2, 6] and a horse [9]. This paper reports a myofibroblastoma in a heifer, whose myofibroblastic nature was confirmed immunohistochemically and ultrastructurally.

A 1.5-year-old Holstein heifer had a large tumor mass on the ventral portion of the neck, causing compression of the esophagus, ruminal tympany, and subcutaneous edema in the mandibular region. The animal was considered to have a poor prognosis, and was euthanatized. At necropsy, the subcutaneous tumor, 20 cm in diameter, was fairly well demarcated from the thymus but not encapsulated. The tissue in the cut surface was grayish white with red areas of hemorrhage, and was traversed by bands of fibrous tissue, but its consistency was somewhat soft. There were no metasteses.

Tissues were fixed in 10% buffered formalin and embedded in paraffin. Sections of 4 µm thickness were prepared for staining with hematoxylin-eosin (HE) and immunohistochemistry. Immunohistochemical staining was carried out by an avidin-biotin-peroxidase complex (ABC) method with an ABC kit (BioGenex Laboratories, San Ramon, CA, U.S.A.). The primary antibodies used were mouse monoclonal antibodies to alpha smooth muscle actin (SMA) (DAKO A/S, Glostrup, Denmark), desmin (Bio-Science Products, Emmenbrücke, Switzerland), vimentin (Dako Corporation, Carpinteria, CA, U.S.A.), and proliferating cell nuclear antigen (PCNA) (BioGenex). For electron microscopy, small pieces taken from formalin-fixed tissues were post-fixed in 1% osmium tetroxide, embedded in epoxy resin, stained with uranyl acetate and lead citrate, and examined by electron microscopy (EM). For immunohistochemical comparison, a case of uterine leiomyoma in a 9-year-old Japanese Black cow was examined using the same procedures.

Histologically, the tumor tissue was composed of moderately cellular fibrous tissue (Fig. 1) with widespread areas of hemorrhage, and invaded into the thymic interlobular septa but not into the parenchyma. The tumor cells were large, plump, and spindle-shaped or stellate, and had ovoid to fusiform nuclei and inconspicuous nucleoli. Mitoses were at times seen.

Immunohistochemically, almost all tumor cells were positive for SMA (Figs. 2, 3) and vimentin and negative for desmin, although the control leiomyoma cells were immunoreactive for desmin as well as for SMA and vimentin. The majority of the tumor cells stained intensely for PCNA (Fig. 4), whereas only a few cells in the control case.

Although the tumor tissue was inadequately preserved for electron microscopy, neoplastic cells containing both moderate quantities of rough endoplasmic reticulum (RER) and fine cytoplasmic filaments with focal densities could be confirmed (Fig. 5). The RER tended to be localized to one pole of the cytoplasm.

In conventional histological sections myofibroblasts can not be readily distinguished from fibroblasts, but immunohistochemical detection of their content of SMA and desmin (not seen in fibroblasts) or ultrastructural demonstration of contractile proteins shows that they are distinct [10]. The present neoplasm displaying SMA positivity in almost all cells was clearly different from a fibroma [3]. Although myofibroblasts, smooth muscle cells and pericytes in the bovine tissues were all positive for SMA, myofibroblasts and pericytes showed minimal or absent staining with the same anti-desmin antibody as we utilized in the present study [11]. The present tumor showed no detectable staining for desmin unlike the control case of leiomyoma. The neoplastic cells in our case had microfilaments with focal densities that were characteristic of bovine tumors of smooth muscle or myofibroblast derivation [1, 4], being discernible from hemangiopericytoma cells devoid of this feature [8].

A bovine myofibroblastoma was reported in the vulva [1], and proliferating pluripotent myofibroblasts have been discovered in a wide variety of lesions of the female...
Fig. 1. Moderate cellularity in tumor tissue. Cytoplasmic borders are difficult to distinguish from stroma. HE. × 400.

Fig. 2. SMA-positive tumor cells with fairly dense population. Immunostaining. × 200.

Fig. 3. Cytoplasmic reactivity of neoplastic cells for SMA, intensely along the cell membrane and less in the other portion of the cytoplasm. Vascular smooth muscle cells (arrows) are strongly and diffusely immunoreactive. Immunostaining. × 400.

Fig. 4. Intense positivity for PCNA in the vast majority of tumor cells. Immunostaining. × 200.

Fig. 5. Fairly well developed RER (right) and filaments with focal densities (arrows) in a tumor cell. EM. × 7,500.
reproductive tract [7]. Since the cervical subcutis is composed mainly of fibroblasts, it is most probable that the present case is associated with fibroblasts.

In the bovine case of vulval myofibroblastoma, the tumor was presumably regressive [1]. The present tumor, by contrast, showed intense PCNA positivity in most neoplastic cells, and was locally aggressive, seemingly having a biological behavior intermediate between the benign fibroblastic tumors and fibrosarcoma. Malignant tumors of myofibroblasts are rare in humans [3, 12] and animals, but sarcomas of myofibroblasts or probable myofibroblastic origin have been recorded in some animal species [2, 6, 9].

REFERENCES