

Mammary Fibroadenoma in a Young Holstein Cow

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ABSTRACT. A mammary mass approximately 60 cm in diameter, which developed in the left udder of a 17-month-old Holstein cow, was removed surgically. The mass was well demarcated from the surrounding tissues and its cut surface was lobular in appearance. Microscopically, the mass consisted of a proliferation of well differentiated ducts and mucinous connective tissue. Immunohistochemically, the proliferative stroma contained two distinct cell types; vimentin-positive fibroblasts and spindle cells positive for vimentin and actin at the periphery of the ducts. The biological features of the present mammary tumor are thought to be generally compatible with those of mammary fibroadenoma reported in humans and dogs.—**KEY WORDS:** cattle, mammary fibroadenoma.

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Since the occurrence of mammary gland neoplasms is rare in the domestic cow as compared with dogs and cats [1, 5, 6, 8, 10], the biological nature of these neoplasms has not been clarified in detail. Ford *et al.* [3] reported that only 41 primary mammary gland neoplasms in cows had been observed between 1902–1989. Recently, a mammary carcinoma with peritoneal metastasis was recognized in a Simmental cow [9]. The present paper describes the morphological and immunohistochemical features of a fibroadenoma in a young Holstein cow.

A hard mass about 5 cm approximately in diameter was found by palpation in the rear left mammary area of a 4-month-old Holstein cow. At 13 months after onset, the mass had grown to approximately 60 cm in diameter, replacing the left udder. Surgically, the mass could be removed easily because it was well demarcated from the surrounding tissues and had a thick capsule. The mass was hard, and its cut surface was solid, pinky white in color, and lobular in appearance. The cow has since remained in good condition.

Tissue samples of the mammary mass were fixed with 10% formalin for histopathological examination. Paraffin sections were stained with hematoxylin and eosin (HE), Masson's trichrome, Watanabe's silver impregnation, alcian blue (pH 2.5) and colloidal iron. Immunohistochemical examination was performed using a kit employing the avidin-biotin-peroxidase complex (ABC) method (Vectastain, Vector Laboratories, Burlingame, CA, U.S.A.). Rabbit antiserum against keratin (prediluted, Dako, Carpinteria, CA, U.S.A.) and mouse monoclonal antibodies against vimentin (prediluted, Dako), alpha-smooth muscle actin (1:20, Dako) and proliferative cell nuclear antigen [4] (PCNA, 1:200, Novocastra Laboratories, England) were used as primary antibodies. Biotinylated goat sera against rabbit and mouse immunoglobulins (1:200, Dako) were used as secondary antibodies. Normal mammary tissues from a 1-year-old Holstein cow was used as a control for immunostaining.

Microscopically, the mass consisted of a proliferation of well differentiated ductal epithelial cells and stromal tissues, and was separated into lobules by thick fibrous connective tissue (Fig. 1). The ducts were commonly lined by stratified epithelial cells with narrowing of their lumina.

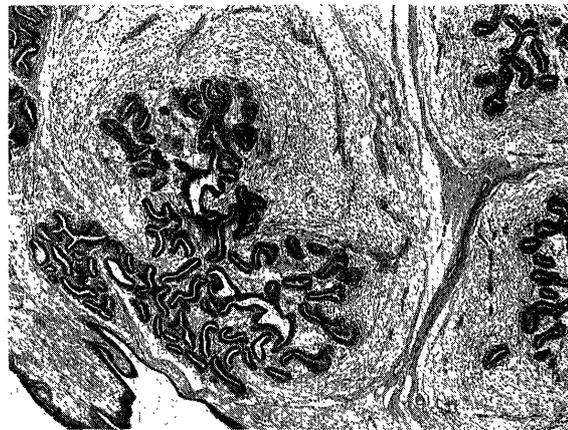


Fig. 1. Proliferation of irregular ducts and a myxomatous stroma. HE. $\times 20$.

Some ducts showed cystic dilation. The ductal epithelial cells were large, columnar or cuboidal with large round hyperchromatic nuclei, which sometimes showed mitotic figures (Fig. 2). In the stroma, small spindle-shaped fibroblasts proliferated within a mucinous or edematous stroma, showing intense reaction for alcian blue or colloidal iron. Mitotic figures were also noted in these stromal cells. Neither the proliferative epithelial nor stromal cells exhibited severe cellular atypia. Invasive proliferation and necrosis were not observed in the neoplasm.

The PCNA antibody was reactive with large numbers of nuclei of both ductal epithelial and stromal cells (about 996 nuclei/mm) in comparison with those in the control mammary gland tissue (about 256 nuclei/mm). This finding appeared to indicate proliferative activity of both the epithelial and stromal cells in this mammary tumor, as suggested previously [4]. In the proliferative ducts, epithelial cells were positive only for keratin. In contrast, small flattened cells (myoepithelial cells) located between the epithelial cells and the basal lamina of the ducts showed intense immunoreactivity for keratin, actin, and vimentin. The structural relation between ductal epithelial and myoepithelial cells was well preserved, and similar to that in the normal control. Almost all proliferating stromal

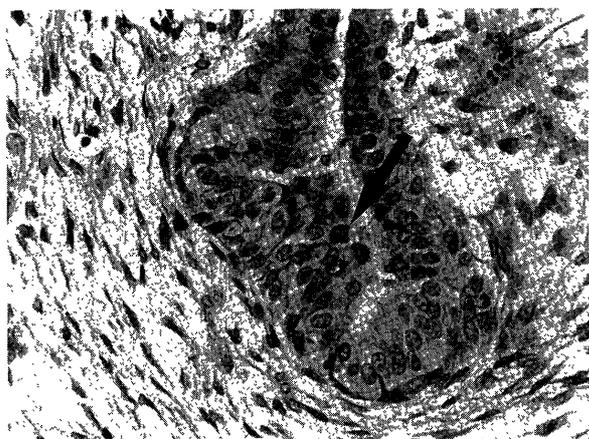


Fig. 2. Proliferative ductal epithelial cells with mitotic figure (arrow) and small spindle stromal cells. HE. $\times 100$.

cells showed intense immunoreactivity for vimentin. In addition, a subset of stromal cells proliferating in the periphery of the ducts was also positive for actin, although this reaction was relatively weak in comparison with that for vimentin. All cells proliferating in the stroma were negative for keratin.

Mammary fibroadenomas characterized by benign neoplastic proliferation of both ductal and stromal elements are known to be the most common benign breast tumors in young women [7] and have also been reported in dogs [5]. The tern bovine adenofibroma was used in a previous review of the literature by Povey and Osborne [10], but there has been little information on its biological or morphological nature. Fibroepithelial hyperplasia reported in humans and cats [7, 8] has a morphology similar to fibroadenoma, but the disorder appears commonly in multiple mammary areas without the formation of an encapsulated mass. The present tumor had several similarities to human mammary fibroadenoma, i.e. occurrence at a young age, formation of a well demarcated tumor mass, and histological features of proliferation of both ductal epithelial cells and connective tissues with a mucinous stroma. Histopathologically, human mammary fibroadenomas are classified into 2 subtypes; the pericanalicular type in which the stroma surrounds the ducts, and the intracanalicular type in which the epithelial elements are distorted, stretched, and compressed by the proliferation of stromal tissues [7]. The same histopathological classification has been proposed for mammary tumors of domestic animals [5]. The present bovine mammary

tumor, therefore, can be diagnosed as "fibroadenoma, pericanalicular type" on the basis of the histopathological features.

The present cow had not begun estrus until the removal of the tumor mass. In human mammary fibroadenomas, hormonal influences are suggested for their tumorigenesis because of the predominant occurrence in young women [7]. Similar etiological interpretation may be expected even in bovine mammary fibroadenoma.

Immunohistochemically, the proliferative stroma contained two distinct cell types; vimentin-positive fibroblasts and spindle cells positive for vimentin and actin at the periphery of the ducts. Recently, Destexhe *et al.* [2] demonstrated immunohistochemical characteristics of epithelial, myoepithelial, and connective tissue cells in several types of canine mammary tumor, and considered that the cells positive for both vimentin and alpha-actin were myofibroblasts. They reported that such myofibroblasts were present at the periphery of benign mammary tumors, but absent in fibroadenomas, unlike the present case [2]. This inconsistency might have been due to the different specificity of the antibody against actin used in this study.

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