



Case report

Vaginal Fibropapilloma in a Heifer

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Abstract

The term fibropapilloma is used to refer to a papilloma virus induced benign tumor in the skin. A 6 month old Holstein calf was referred to the veterinary hospital of this school having multiple masses in the vaginal roof. The animal had 4-5 pinkish closely associated masses attached to the dorsal commissure of the vaginal roof about 5 cm deep into the vagina. Histopathological examination revealed the masses similarly consisted of abundant proliferating fibrous tissue with an epithelial covering of variable thickness. The pegs of the epithelium that typically extend into the subjacent connective tissue demonstrated papillomatous features with irregular hyperplasia and epidermal rete ridges. In the epidermis, the stratum spinosum was hyperplastic and the koilocytes included variably sized keratohyalin granules and a few intranuclear inclusion bodies were present. The dermis consisted of densely packed fibroblasts and dense irregular collagenous connective tissue. In Masson's trichrome staining, the bundles of collagen were blue in color. Immunohistochemically, the neoplastic cells were positive for cytokeratin but negative for S-100. Based on routine histopathological, special staining and immunohistochemical findings, the tumor was diagnosed as vaginal fibropapilloma.

Key Words: fibropapilloma, vagina, heifer.

Introduction

Cutaneous fibropapillomatosis is characterized by the presence of multiple benign exophytic proliferations of the epidermis and of the underlying dermis, which is commonly associated with infection with a papillomavirus. It has been described in cattle and other ungulates such as red deer, roe deer, elk, and less frequently in horses, dogs, cats, sheep, goats, pigs, and bison (3, 8, 10). Bovine papillomaviruses are divided into 6 subtypes (1-6) and 2 groups, A and B. The viruses in group A are known to transform the fibroblasts and epithelial cells and include BPV-1 and -2 (4). Genital papillomavirus infection has also been described in cows and pigs and the affected animals are young, usually in their first breeding season, and the lesions are self-limiting (5, 6). This report describes the gross, histopathological and immunohistochemical features of vaginal fibropapilloma in a heifer.

Case history, histopathological and immunohistochemical findings

A 6 month old Holstein calf was referred to the veterinary hospital due to development of multiple masses in the vaginal roof. The initial examination revealed 4-5 pinkish closely associated masses attached to the dorsal commissure of the vaginal roof about 5 cm deep into the vagina (Figure 1). Local anesthesia was obtained by epidural injection of 5 ml of lidocaine 2% between coccygeal vertebrae 1 and 2. The area was washed and prepared for sterile surgery. By two stay sutures deep into the vaginal wall, the area was exposed, and the masses were removed by scalpel, and the bleeders were controlled by electrocautery. The stay sutures were removed. The calf received an anti-inflammatory drug postoperatively. The excised masses were sent for histopathologic study. For structural differentiation, fragments of the tumoral mass were fixed in 10% neutral formalin solution for paraffin embedding. Paraffin wax sections (4 to 5 µm) were dewaxed and stained with haematoxylin and eosin

(HE) and also with Masson's trichrome for differentiation of collagen fibers from muscle fibers. The sections were also evaluated immunohistochemically for the expression of cytokeratin (clone: AE1/ AE3) which was ready to use primary monoclonal anti-human antibody and S-100 protein (polyclonal) provided by Novocastra Laboratories, Newcastle, UK. As chromogen, 3, 3-diaminobenzidine tetrahydrochloride (DAB) was used. All immunohistochemical sections were counterstained with Harris hematoxylin.



Figure 1. Gross appearance of vaginal fibropapilloma in a heifer. Multiple masses have developed in the vaginal roof.

Microscopically, there was marked proliferation of the epithelium as well as proliferation of dermal fibroblasts, giving the tumor a broad papillary pattern. The overlying epithelium was hyperplastic with prominent rete ridges. It consisted of well-differentiated and well-organized mature epithelial cells that demonstrated orderly pattern and some of them contained intranuclear inclusion bodies. Small groups of koilocytes, were characterized by large, mildly eosinophilic and vacuolated cytoplasm, and some cells contained small distorted nuclei with dense chromatin. In addition, lymphocytes mildly infiltrated dermis and to a lesser extent epidermis. The dermis consisted of mature fusiform fibrocytes having oval normochromatic nuclei and collagen fibers which were arranged in whorls. Hyperemia and hemorrhages were also present within the dermis. Hair follicle, sweat and sebaceous glands were not present in the affected dermis (Figure 2). Masson's trichrome staining (Figure 3), accentuated the bundles of blue collagen fibers. The immunohistochemistry of this tumor showed cytokeratin expression (Figure 4) but no S-100 positivity (Figure 5). Based on the routine histopathological, special staining and immunohistochemical findings, the tumor was diagnosed as vaginal fibropapilloma.

Discussion

Fibropapillomas, a papillomavirus induced, transmissible and self-limiting tumor, may occur in the skin and in different organs in animals. The exact

pathogenesis of the disease has not been elucidated. It seems the virus gains entrance into the skin through wounds and causes neoplastic growth of fibroblasts and makes up tumors in the vagina and vulva of young heifers and the glans penis of young bulls, usually in their first breeding season (4, 6, 8, 13). Macroscopically, the single or multiple gray-white warty masses have a papillary epithelial covering and a fibrous core. Surface ulceration associated with hemorrhage and secondary infection following spontaneous necrosis or trauma, is often extensive (6, 13, 14).

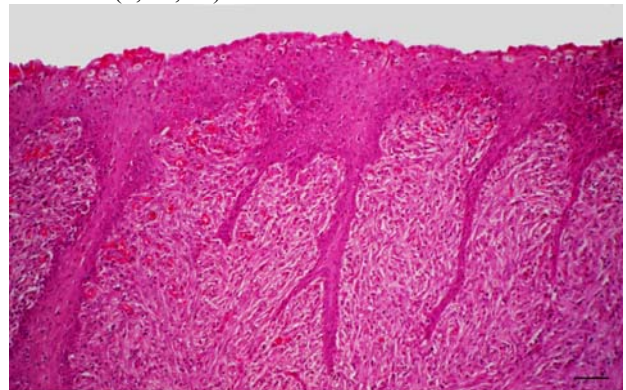


Figure 2. Fibropapilloma showing marked proliferation of the epithelium as well as proliferation of the dermal fibroblasts, giving the tumor a broad papillary pattern. Hair follicles, sweat and sebaceous glands are not present in the affected dermis (H&E, Scale bar =150 µm).

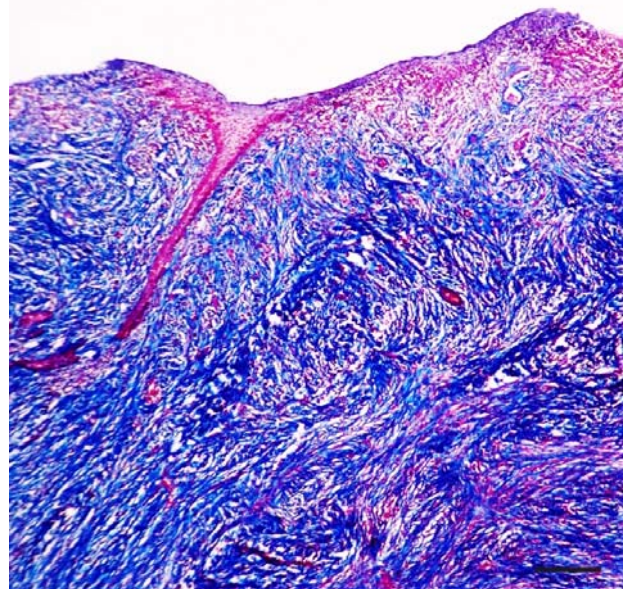


Figure 3. Blue stained collagen fibers. Masson's trichrome. (Scale bar =150 µm).

Common histologic features for spontaneous tumors included fibroblast proliferation in the superficial dermis, epidermal acanthosis and hyperkeratosis, presence of koilocytes which contain variably sized keratohyalin granules, and the occasional observation of intranuclear inclusion bodies. The nuclei in the majority of epidermal cells are vesicular, with fine chromatin and readily

apparent nucleoli. The connective tissue consists of abundant amounts of loosely arranged fibrovascular stroma with low numbers of spindle-shaped to stellate fibrocytes (7, 9, 14).

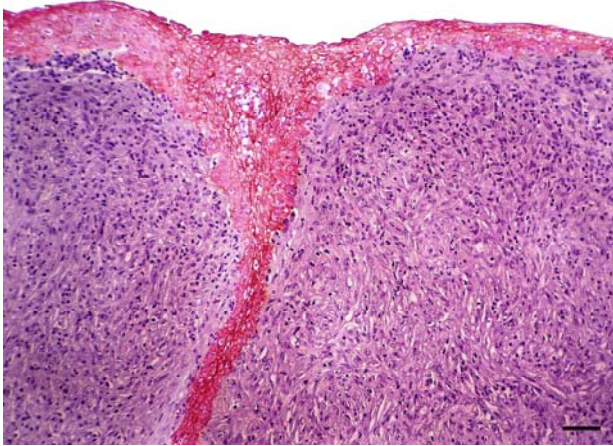


Figure 4. Fibropapilloma in vagina of a heifer showing immunoreactivity to cytokeratin protein as an epithelial marker which was ready to use primary monoclonal anti-human antibody (clone: AE1/AE3). DAB chromogen. Harris hematoxylin counterstain (Scale bar =150 μ m).

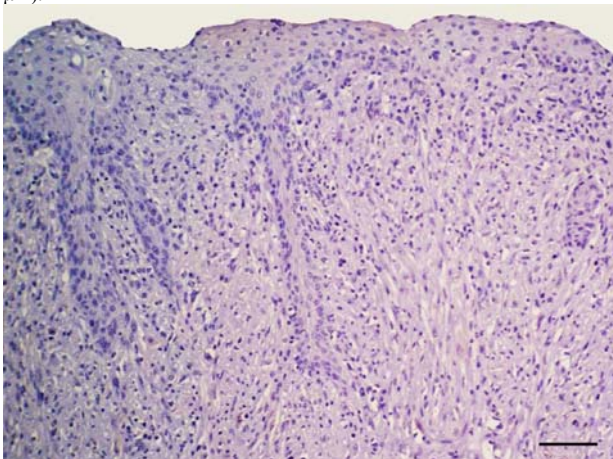


Figure 5. The immunohistochemistry of this tumor did not express S-100 protein (polyclonal). DAB chromogen. Harris hematoxylin counterstain (Scale bar =150 μ m).

Fibropapilloma should be differentiated from other spindle cell tumors such as desmoplastic melanoma, neurofibroma, schwannoma, leiomyoma, leiomyosarcoma and hemangiopericytoma. Immunohistochemical staining of the tissue sections with antibodies to different types of intermediate filaments can provide useful information for identifying and typing various tumors. Keratins are cytoplasmic intermediate filament proteins preferentially expressed by epithelial tissues in a site-specific and differentiation-dependent manner. The AE1/ AE3 keratins provide useful molecular markers for identifying the neoplasms of stratified squamous epithelial origin (2, 12). The histopathological features of the present case was supported by immunoreactivity to AE1/ AE3 keratins. S100 protein marker is widely used in diagnosis of

melanocytic neoplasms, neurofibromas and schwannomas (1). The immunohistochemistry of this tumor did not show S100 expression and ruled out tumors from neural crest origin. Masson's trichrom is used to differentially stain muscle fibers and collagenous elements which stain pink and blue respectively. In Masson's trichrome stained sections, the bundles of collagen were blue and the collagenous fibers were the major elements found in this tumor. Also hemangiopericytoma was ruled out because of its diagnostic histopathologic feature of perivascular whorls of fusiform cells (11).

In conclusion, the present case report showed that fibropapillomas should be considered as a vaginal tumor in heifers and histopathology, immunohistochemistry and special staining can help to diagnose it. It is unlikely that the transmission was venereal in the case since the heifer was sexually immature. This feature makes the report more interesting.

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