

Recurrent Skin Mass from the Digit of a Dog

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**What Is Your
Diagnosis?**

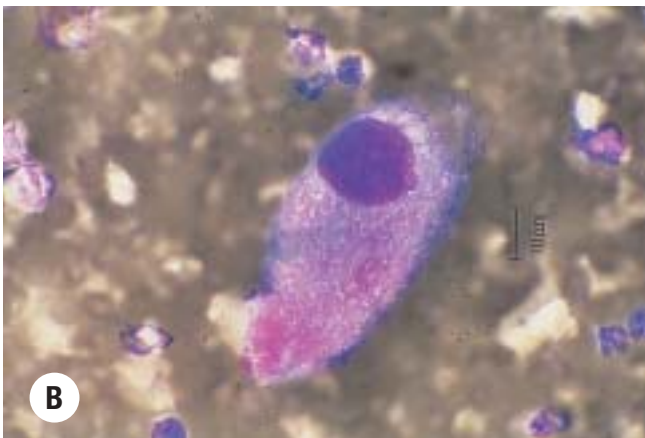
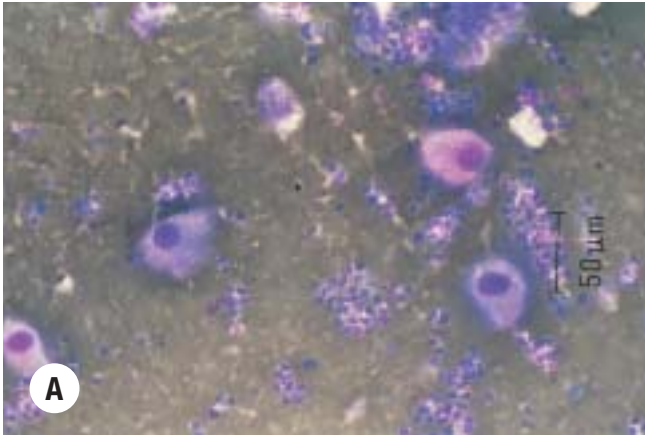


Figure 1. Fine-needle aspirate of a right forelimb digital mass from a dog. Wright-Giemsa, (A) bar=50 μm, (B) bar=10 μm.

Case Presentation

A 7-year-old neutered female Dalmatian dog was presented to the Colorado State University College of Veterinary Medicine with a recurrent 1×1×1 cm raised, reddened alopecic mass on the second digit of the right forelimb. Physical parameters were within normal limits, except for the digital mass. Results of a CBC and serum biochemical analysis were normal. History included several recurrent urinary tract infections and an episode of pyelonephritis. A fine-needle aspirate of the digital mass was submitted for cytologic evaluation (Figure 1).

(Continued on next page)

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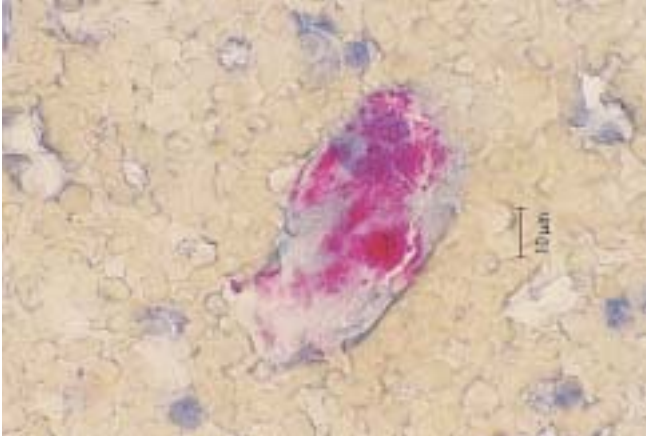


Figure 2. Immunocytochemistry of the canine digital mass aspirate using a broad-spectrum cytokeratin antibody. Cytokeratin positivity in this cell is demonstrated by bright red staining. The cell is the same as that depicted in Figure 1B. Bar = 10 μ m.

Cytologic Interpretation

Examination of the fine-needle aspirate revealed a dense population of RBCs with a slight increase in the number of nondegenerate neutrophils over that expected from peripheral blood contamination (Figure 1). A sparse population of uniform, large, polygonal to fusiform cells approximately 40 μ m in width and 40-60 μ m in length was observed. These cells had low nuclear to cytoplasmic ratios. The cytoplasm ranged from lightly basophilic and foamy to eosinophilic and granular. Nuclei were round to ovoid and eccentrically located, with a clumped chromatin pattern. Some cells had characteristics of epithelial cells, including a polygonal shape and foamy cytoplasmic vacuolation; whereas, others had characteristics of mesenchymal cells, including a fusiform shape and eosinophilic granularity. Thus, the cytologic interpretation was large individualized cells of undetermined origin, with mild suppurative inflammation and blood contamination. A biopsy with histopathology was recommended.

Immunocytochemistry was performed using a broad-spectrum cytokeratin antibody to explore the possibility that the cells were of epithelial origin. Because only 1 aspirate was submitted for cytologic evaluation, the Wright-Giemsa-stained preparation was destained with acetone prior to cytokeratin immunostaining. Most of the cells stained strongly positive for cytokeratin (Figure 2).

Histologic Interpretation

The mass was excised and submitted for histologic examination. Hematoxylin and eosin-stained sections consisted of a well-demarcated endophytic papillary mass

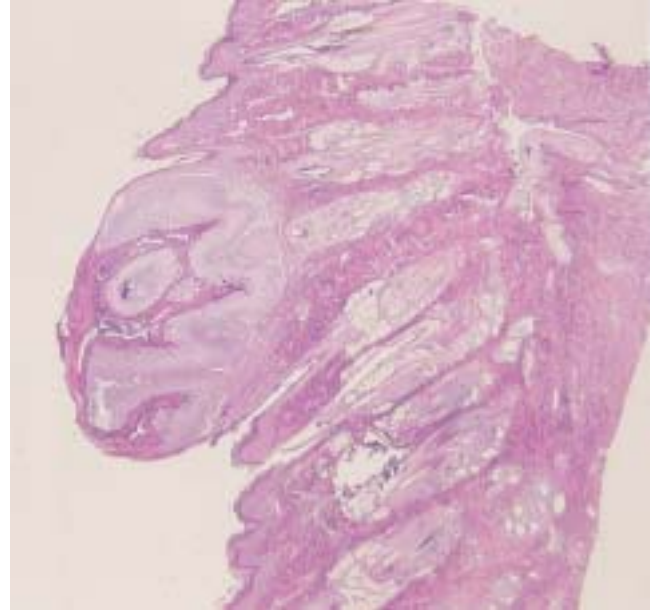


Figure 3. Histologic section of squamous papilloma in a dog. Slightly hyperplastic epidermis forming irregular rete ridges is associated with an endophytic papillary projection. Hematoxylin and eosin, $\times 40$.

contained within a slightly hyperplastic epidermis with irregular rete ridges and hypertrophied keratinocytes (Figures 3, 4). In some sections, the mass developed within hair follicles. The hypertrophied keratinocytes had amphophylic cytoplasm, prominent intercellular bridges, and large nuclei with marginated chromatin and perinuclear vacuolization. No intranuclear viral inclusions were observed. The histologic interpretation was squamous papilloma.

Immunohistochemistry was performed on paraffin-embedded sections in the laboratory of Dr Paul Sundberg (Jackson Laboratory, Bar Harbor, Maine) using a rabbit polyclonal antibody that reacts with structural proteins of a broad range of papillomaviruses (Dako Corp, Carpinteria, Calif).¹ Positive-staining cells were present within foci of the hyperplastic epidermis and were limited to the nuclei of the hypertrophied keratinocytes (Figure 5). These findings confirmed that the mass was caused by papillomavirus infection resulting in endophytic proliferation of hypertrophied keratinocytes.

Discussion

Based on the histologic interpretation of squamous papilloma and the positive staining for cytokeratin in cells of the cytologic specimen, the cells in question were identified as hypertrophied keratinocytes. Although not all cells were positive for cytokeratin, and

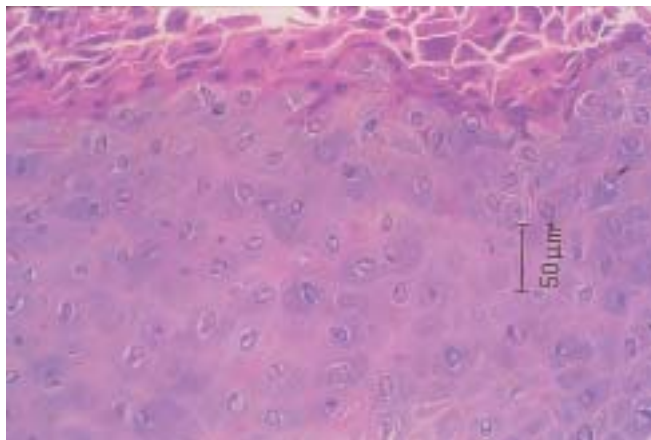


Figure 4. Hypertrophied keratinocytes (koilocytes) containing large nuclei with margined chromatin, perinuclear vacuolization, and no evidence of nuclear inclusions. Hematoxylin and eosin, bar = 50 μm .

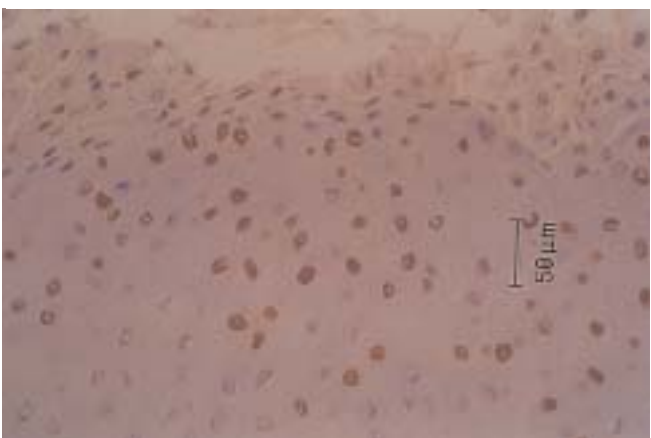


Figure 5. Hypertrophied keratinocytes with nuclei staining positive for papilloma group-specific antigens. Avidin-biotin-peroxidase complex method, Mayer's hematoxylin counterstain, bar = 50 μm .

smears were unavailable for vimentin immunostaining, it is likely that all cells were of epithelial origin based on the histopathologic appearance of the lesion. The eosinophilic granular cytoplasm in some cells may have been the result of keratin production.

Hypertrophied keratinocytes (koilocytes, defined as hollow cells) are common features of papillomavirus infections² and have a characteristic appearance in Papanicolaou-stained human vaginal cytologic specimens. These cells, which have undergone degeneration, have lost their characteristic sharp polygonal shapes and become round and blunt. The cytoplasm has variable lucency and condensation, and nuclei are often enlarged and eccentric within a halo-like intracytoplasmic space. Occasionally, bi- and trinucleate cells can be seen.

Most papillomavirus infections in dogs induce exophytic proliferations of hyperplastic and hyperkeratotic

squamous epithelium covering closely grouped papillary projections in the skin or oral and ocular mucosa.^{3,4} The less common endophytic cutaneous lesions, as seen in this dog, are also referred to as inverted papillomas. These flask-shaped lesions are composed of papillary proliferations with a thin fibrovascular stalk and can have small pore openings to the surface of the skin. These lesions occur in the skin, and no age, sex, or breed predisposition has been reported.^{3,5-7}

Although viral inclusions have not been observed in Papanicolaou-stained epithelial cells from vaginal smears of infected human patients, human papillomavirus antigens are present in 0.5-5% of these cells.⁸ Viral inclusions have also been identified in the cytoplasm, nucleus, and abnormal intermediate filament accumulations in histologic sections from other sites and species.^{2,9}

At least 4 distinct papillomaviruses, each with a specific tropism for a distinct anatomic site, are thought to infect dogs, based on experimental virus transmission, immunohistochemistry, and in situ hybridization studies;¹⁰ however, the genome of only 1 canine papillomavirus, canine oral papillomavirus, has been cloned and characterized.^{11,12} This specific viral type induces predominantly exophytic oral and cutaneous lesions in immunosuppressed dogs.^{4,5,13} More recently, a second canine papilloma viral genome was cloned. This virus induced endophytic cutaneous lesions as seen in this dog; however, this virus has not been completely characterized.³ The specific viral type in this dog was not identified because the requisite molecular typing was not available. Although no laboratory evidence of immunosuppression was identified in this dog, the recurrent urinary tract infections and pyelonephritis suggest underlying immunosuppression. \diamond

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Key Words: Cytology, dog, endophytic papilloma, immunosuppression, papillomavirus, skin

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Recurrent Skin Mass from the Digit of a Dog

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