Cutaneous mass aspirate from a Golden Retriever: "glandular guile"

What Is Your Diagnosis?

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Case Presentation

A 3-year-old, neutered male Golden Retriever was presented to the University of Wisconsin-Madison Veterinary Medical Teaching Hospital (VMTH) for evaluation of a cutaneous mass located over the left cranial thorax. The mass was an incidental finding by the owner, and its duration was unknown. The dog had been presented to the VMTH twice in the previous year: once for elective castration and once for a single episode of diarrhea. No cutaneous masses had been found during the previous physical examinations.

The mass was $10 \times 9 \times 5$ mm and was firm, non-ulcerated, red, raised, and nonpruritic. Regional lymphadenopathy was absent, and there were no other clinical signs. Fine-needle aspiration of the mass was performed, and the specimen was submitted for cytologic evaluation (Figure 1). Based on the cytologic findings, thoracic radiographs were taken, and excisional biopsy of the mass was performed.

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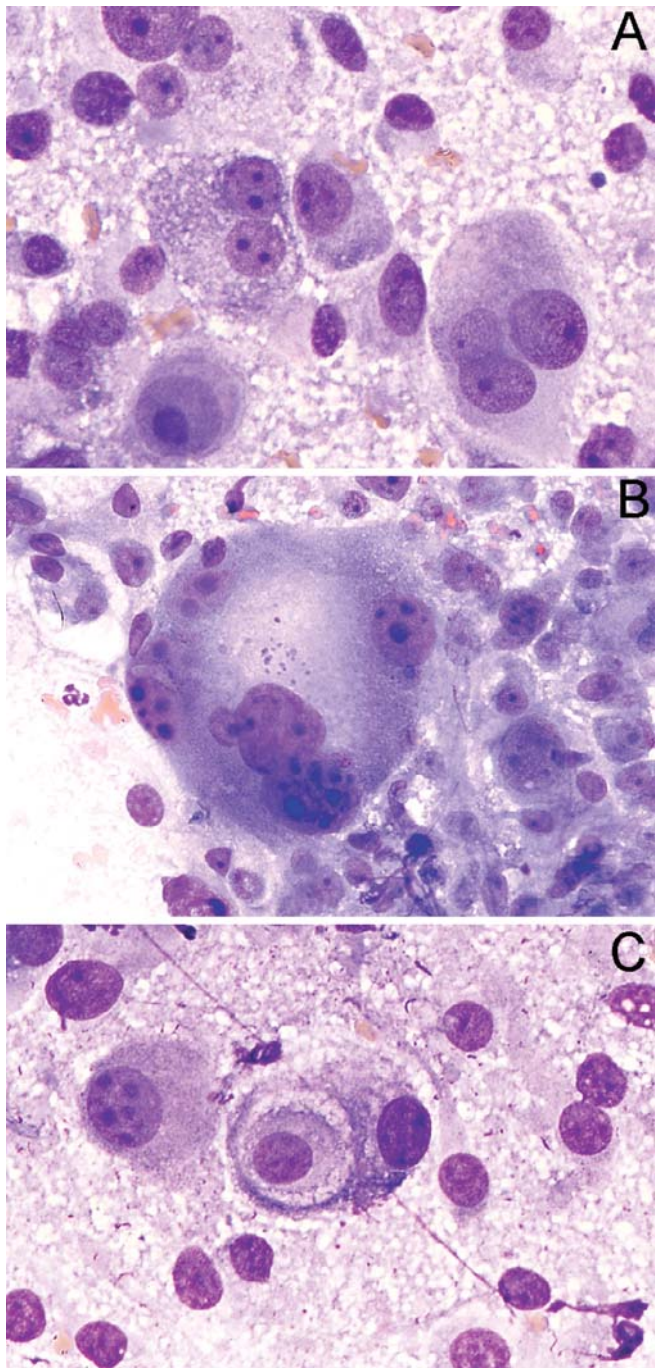

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Figure 1. (**A–C**) Three areas from a fine-needle aspirate of a cutaneous mass from a dog. Modified Wright's, ×60 objective.

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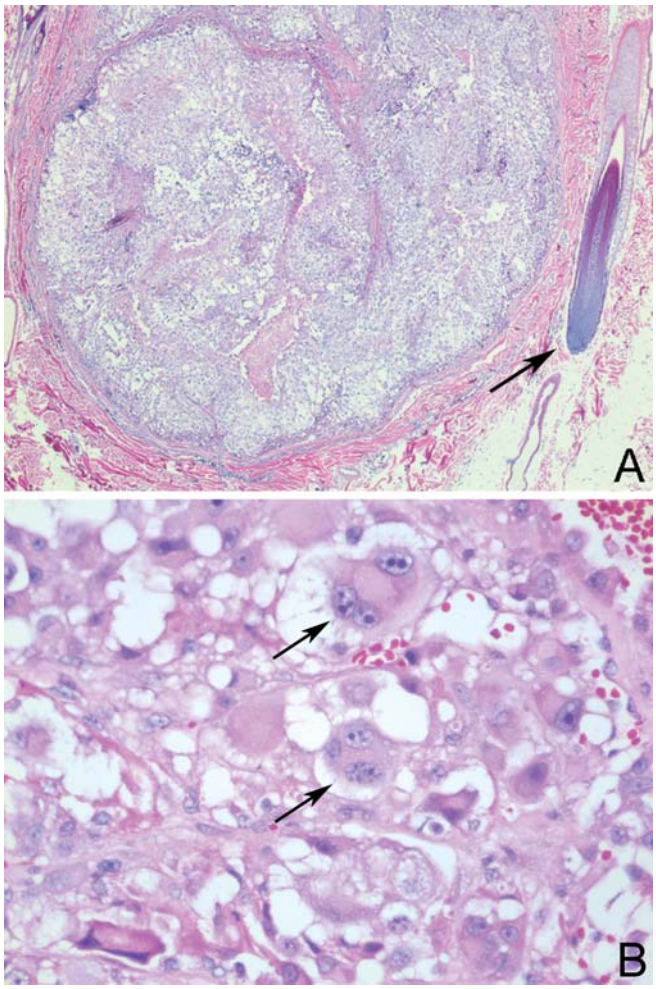

Figure 2. Histologic section of the completely excised cutaneous mass. (**A**) Multiple irregular lobules of sebaceous epithelial cells adjacent to a primary hair (arrow) opening to the surface. H&E, ×4 objective. (**B**) Pleomorphic, sebaceous epithelial cells with eosinophilic, glassy cytoplasm containing variable numbers of vacuoles. Note multinucleated forms (arrows). H&E ×40 objective.

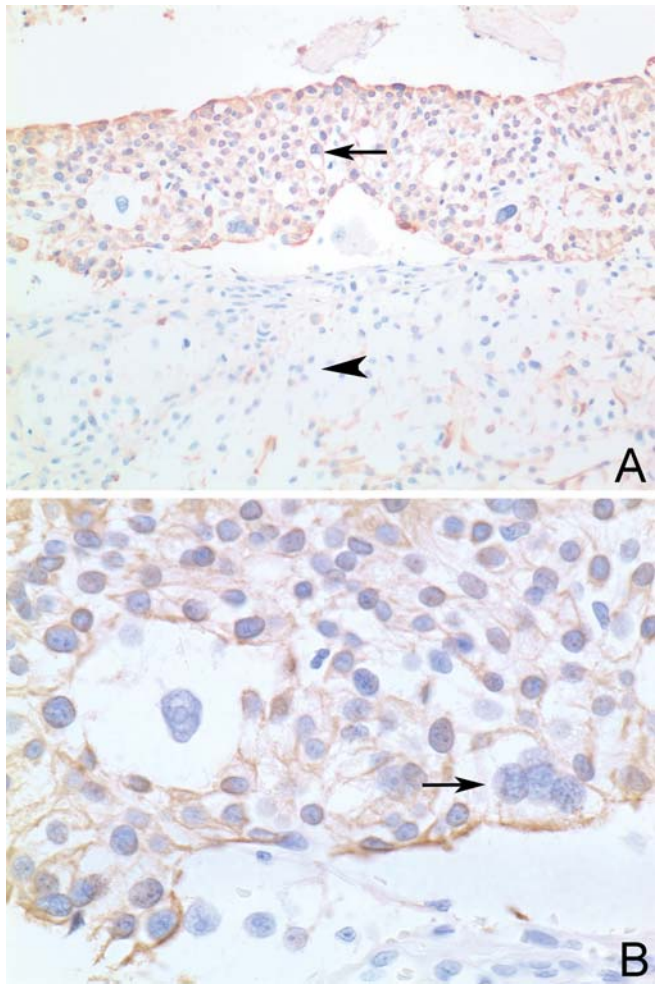

Figure 3. Histologic section of a cutaneous mass stained for pancytokeratin. (**A**) Note peripheral pancytokeratin-positive staining in the tumor cells (arrow) and the negative, adjacent, connective tissue cells below (arrowhead). Horseradish peroxidase-streptavidin, ×20 objective. (**B**) Note multinucleated cell (arrow). Horseradish peroxidase-streptavidin, ×60 objective.

Cytologic Interpretation

The sample was highly cellular with large numbers of pleomorphic, individualized, round to polygonal cells having variable N:C ratios (Figure 1). Anisocytosis and anisokaryosis were marked. Cell margins typically were distinct. The cytoplasm was basophilic and finely granular with occasional cells containing a prominent, perinuclear clear zone. A few cells contained small numbers of clear vacuoles, and infrequently, cells had intracytoplasmic secretory vacuoles. Rarely, large cells contained other similar intact cells (Figure 1C), and rare cells had a moderate amount of amorphous, magenta, glassy material within the cytoplasm. Nuclei had fine chromatin with multiple prominent nucleoli that varied markedly in size and shape. Multinucleated cells were found in moderate numbers, and there was marked variation of nuclear size within the same cell. Mitotic figures, including bizarre forms, were found in small numbers, and rarely, mitotic figures coexisted with intact nuclei within a multinucleated cell. There were a few small cellular aggregates with an acinar-like appearance. Cytoplasmic debris from ruptured cells and clear droplets were present. The background contained small numbers of nondegenerate neutrophils and vacuolated macrophages. The cytologic interpretation was malignant tumor with mild, mixed inflammation. With the exception of occasional acinar-like formations, the features were most typical of a tumor of mesenchymal origin. Differential diagnoses included liposarcoma, atypical amelanotic (balloon cell) melanoma, anaplastic sarcoma, and anaplastic carcinoma.

Additional Test Results

Following excision of the intradermal mass, the mass was placed in 10% buffered formalin and submitted for histopath-

ologic examination. A section of the mass, stained with H&E, consisted of haired skin with multiple irregular lobules of pleomorphic, sebaceous epithelial cells adjacent to a primary hair follicle (Figure 2A). The lobules were unencapsulated, yet well-circumscribed and frequently subdivided by bands of fibrous connective tissue. Many cells contained large single or multiple clear vacuoles, and others had sparse, clear vacuoles and eosinophilic, glassy cytoplasm. Occasionally, signet ring cells were noted. The tumor cells were characterized by marked anisocytosis and anisokaryosis with a few multinucleated forms noted (Figure 2B). The nuclear chromatin was vesicular with large, prominent, single or multiple nucleoli, and occasionally, mitotic figures were seen. Necrosis, hemorrhage, and perivascular to interstitial suppurative inflammation were noted. All margins of the section were free of tumor. The diagnosis was sebaceous adenocarcinoma with complete excision.

To document the epithelial origin of the cells in this pleomorphic tumor and to rule out anaplastic sarcoma and balloon cell melanoma with certainty, given the differences in the cytologic and histologic features, sections were stained for the presence of pancytokeratin (mouse antihuman pancytokeratin, 1:50 dilution, DakoCytomation Inc, Carpinteria, CA, USA), Melan-A (mouse antihuman, DakoCytomation, 1:20 dilution), S100 (rabbit antibovine, DakoCytomation, 1:200 dilution), and vimentin (mouse antiswine, DakoCytomation, 1:20 dilution) using the horseradish peroxidase-streptavidin technique. Positive and negative controls for each antibody were performed. The tumor cells were positive for pancytokeratin (Figure 3) and negative for Melan-A, S100, and vimentin, confirming the epithelial origin of this tumor.[1,2]

There was no evidence of metastasis on thoracic radiographs taken at the time of presentation and, again, 1 month later. Other than surgical excision, the dog received no additional therapy.

Discussion

Sebaceous gland tumors are common skin tumors in the dog, accounting for 7.9% of all skin tumors according to one retrospective analysis.[3] Sebaceous gland tumors can be subclassified according to their histologic appearance and clinical behavior into 5 main types: nodular sebaceous hyperplasia, sebaceous adenoma, sebaceous ductal adenoma, sebaceous epithelioma, and sebaceous adenocarcinoma.[1] Sebaceous hyperplasia and sebaceous epithelioma are the most commonly diagnosed types (53.5% and 37.2%, respectively, of 172 sebaceous tumors) according to the retrospective analysis noted previously.[3] Sebaceous hyperplasia is characterized histologically by circumscribed, nodular proliferations of mature sebaceous gland lobules around a central duct in the superficial dermis.[1,3] The lobules are surrounded by a single layer of basal reserve cells.[3] Sebaceous epitheliomas are irregular masses consisting predominantly of relatively uniform basal reserve cells that may have many mitotic figures.[1,3] In addition, smaller numbers of intermediate and mature sebaceous cells are found throughout the mass.[1,3] Sebaceous adenomas are diagnosed less frequently (7.5% of sebaceous tumors), with sebaceous adenocarcinomas accounting for rare cases (1.7% of 172 sebaceous tumors).[3] Sebaceous adenomas are typically well-circumscribed, nodular proliferations of incompletely differentiated sebaceous lobules with few reserve basal cells.[1,3] Sebaceous ductal adenomas consist mainly of ducts with few sebaceous cells or reserve basal cells.[1] Sebaceous adenocarcinomas are typically poorly circumscribed, irregular, multilobulated masses with irregular proliferations of pleomorphic and atypical sebaceous cells and basal reserve cells.[1,3] In a retrospective study of 9 sebaceous tumors in cats, 2 were diagnosed as sebaceous carcinomas, and there are rare reports of this tumor in 1 horse, 1 rabbit, and humans.[4–8] On histologic examination, true sebaceous adenocarcinomas are described as irregular, poorly circumscribed, multilobular, cutaneous lesions comprising sheets of pleomorphic polygonal cells and lacking significant numbers of well-differentiated basal cells.[9] Individual tumor cells can have highly vacuolated cytoplasm. However, the degree of sebaceous differentiation is variable based on the lipid and sebum content of the cells. Nuclei are large and contain prominent nucleoli. Cytologic and histologic features of malignancy have been described, including anisocytosis, anisokaryosis, variable nucleolar morphology, multinuclearity, and mitotic figures.[10,11] Sebaceous adenocarcinomas are slow to metastasize; however, metastasis to regional lymph nodes can occur,[11] and metastasis to the femur has been reported in a dog that had a sebaceous carcinoma removed from behind the left ear 3 years earlier.[12] Complete excision, which requires aggressive surgical technique, is typically associated with a low rate of recurrence and a good prognosis.[13] In intact male dogs, perianal sebaceous adenocarcinomas have a tendency to recur locally, and additional surgeries may be required.[13]

Several other cutaneous and subcutaneous tumors, including balloon cell melanoma, liposarcoma, and, infrequently, clear-cell basal cell carcinoma, share some histologic features with sebaceous adenocarcinoma.[14] Balloon cell melanoma and liposarcoma were ruled out in this case based on negative staining for Melan-A and vimentin, respectively, and positive staining for pancytokeratin.[15] The histopathologic sections of the tumor revealed sheets of cells that stained positive for pancytokeratin adjacent to sheets of nonneoplastic cells that were negative for pancytokeratin. In the tumor cells, the positive staining was noted in the peripheral cytoplasm whereas the perinuclear region remained unstained. This pattern may be due to the accumulation of secretory material in the perinuclear region that prevents focal positive staining. Oil-Red-O can be used to detect intracytoplasmic lipid in frozen sections of sebaceous adenocarcinomas[16] but would also stain lipid in a liposarcoma and was not done in this case. Clear-cell basal cell carcinomas are reported rarely in dogs and can be differentiated histologically from sebaceous adenocarcinoma by the observation of epidermal contiguity of the tumor, which is lacking in sebaceous adenocarcinoma.[14]

The unique and previously unreported cytologic features of this small, sebaceous adenocarcinoma were the extreme pleomorphism, including marked anisocytosis, anisokaryosis, and multinuclearity, and the paucity of epithelial features.

Tumor cells were individualized and polygonal, features that generally characterize connective tissue tumors. Although rare acinar-like arrangements of tumor cells were identified, this designation is subjective and may not correspond to the presence of true acini noted on histologic sections. The definitive diagnosis required histologic evaluation of the mass, whereby the tissue architecture of the tumor could be assessed, revealing the intact primary hair adjacent to lobules of neoplastic epithelial cells. Although the cytologic and histologic specimens had different appearances in this case, both contained markedly pleomorphic and bizarre, multinucleated tumor cells, which are not characteristic of sebaceous adenocarcinoma. Only 1 slide was received for cytologic evaluation before excision of the mass. Additional cytologic samples might have been more representative of the lesion and had more similarities with the histologic appearance.

Acknowledgment
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Abstract: A 3-year-old, neutered, male Golden Retriever was presented for evaluation of a 10 × 9 × 5 mm, firm, red, raised, cutaneous mass located over the left cranial thorax and noted incidentally by the owner. On cytologic evaluation of a fine-needle aspirate of the mass, the interpretation was a malignant tumor with predominantly mesenchymal features. Differentials included liposarcoma, atypical amelanotic melanoma, anaplastic sarcoma, and anaplastic carcinoma. Following complete excision of the mass, a diagnosis of sebaceous adenocarcinoma was made based on histologic features, positive immunostaining for pancytokeratin, and negative staining for vimentin, Melan-A, and S-100. There was no evidence of metastasis on physical examination or thoracic radiographs, and the prognosis was good. The unique and previously unreported cytologic features of this small, sebaceous adenocarcinoma were the extreme pleomorphism, including marked anisocytosis, anisokaryosis, and multinuclearity, and the paucity of epithelial features. (*Vet Clin Pathol.* 2005;34:421–424)

Key Words: Canine, cutaneous, gland, sebaceous adenocarcinoma, skin

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