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Case Reports

Malignant Peripheral Nerve Sheath Tumor in a Hamster

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An adult female golden hamster (*Mesocricetus auratus*) developed a firm subcutaneous mass on the lateral distal right forelimb that progressed to diffuse limb enlargement accompanied by extensive cutaneous ulceration and drainage and axillary lymph node metastasis. Touch imprint cytology revealed pleomorphic neoplastic mesenchymal cells. On histology, the invasive neoplasm merged with a large subcutaneous nerve and was composed of spindle cells with a high mitotic index, and lymph node metastasis was confirmed. Histologic morphology and positive immunohistochemical staining of neoplastic cells for vimentin, S100, and neuron-specific enolase were consistent with a malignant peripheral nerve sheath tumor. Although relatively common in dogs, peripheral nerve sheath tumors had not been reported previously in hamsters.

Abbreviations: GFAP, glial fibrillary acid protein; PNST, peripheral nerve sheath tumor; NSE, neuron specific enolase; STS, soft tissue sarcoma

Peripheral nerve sheath tumors (PNSTs) are a diverse group of neoplasms with variable histologic features. Although the origin of neoplastic cells is under debate, they are thought to be derived from cells comprising the nerve sheath (Schwann cells, fibroblasts, and perineural cells). These tumors generally are subclassified as benign (neurofibroma, schwannoma) and malignant (neurofibrosarcoma, malignant schwannoma).[3,4]

Both human and canine PNSTs exhibit highly variable morphology, which can confound accurate diagnosis.[3,4] Although human PNSTs have distinct morphologic patterns that aide in classification, patterns in canine PNSTs are not as clearly defined.[1,3,4] As a result, veterinary medicine relies heavily on the use of immunohistochemistry for further classification of PNSTs.[1,3,4]

Case Report

An approximately 3-y-old female golden hamster (*Mesocricetus auratus*) was presented for evaluation of a large, ulcerated mass involving the right forelimb. The growth was first noted approximately 1 mo prior to presentation and had rapidly enlarged to encompass most of the limb. The hamster was anesthetized, and the limb was amputated, along with excision of a smaller axillary mass presumed to be an enlarged lymph node. Touch imprints were collected from both masses for cytology. The remainder of the mass was immersed in 10% neutral-buffered formalin for fixation, routinely processed, and embedded in paraffin. Blocks were sectioned at 4 to 6 µm and stained with hematoxylin and eosin for routine histologic evaluation.

Evaluation of Wright–Giemsa-stained touch imprints identified a neoplastic mesenchymal population composed of fusiform to spindle cells, which exhibited moderate anisocytosis and anisokaryosis with a high nuclear-to-cytoplasmic ratio. Cells had variably distinct borders; low to moderate amounts of basophilic cytoplasm; and large, round, central nuclei with pale, finely stippled chromatin and 1 to 3 round, basophilic, variably sized nucleoli (Figure 1). Occasional binucleated cells and irregular mitoses were noted. Within the background, moderate numbers of degenerate neutrophils and mixed bacterial species, composed of many paired rods and occasional diplococci, were present.

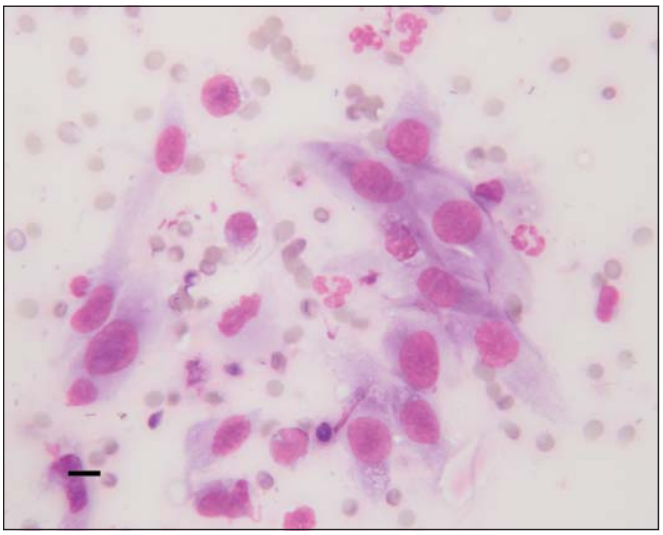

Figure 1. Touch imprint of tumor tissue from a hamster. This cytology specimen demonstrates the neoplastic mesenchymal population with many features of malignancy. Wright-Geimsa stain. Bar, 10 µm.

Histologically, the limb mass was composed of densely packed, large, neoplastic spindle cells arranged in poorly formed fascicles and occasionally Verocay-like bodies supported by vessel-poor collagenous stroma with alternating loosely and densely packed areas. Regionally, fine collagen bundles isolated individual or small clusters of the neoplastic cells. The

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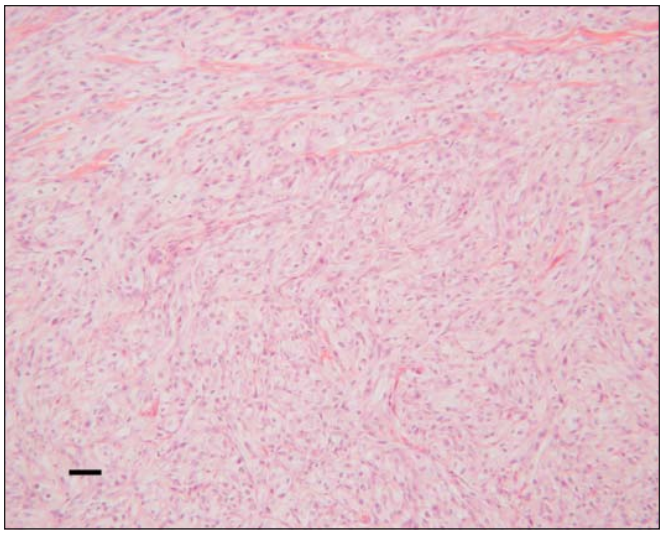

Figure 2. Tumor tissue from a hamster. This histologic specimen exhibits densely packed neoplastic spindle cells arranged in poorly formed fascicles supported by vessel-poor collagenous stroma. Hematoxylin and eosin stain. Bar, 50 µm.

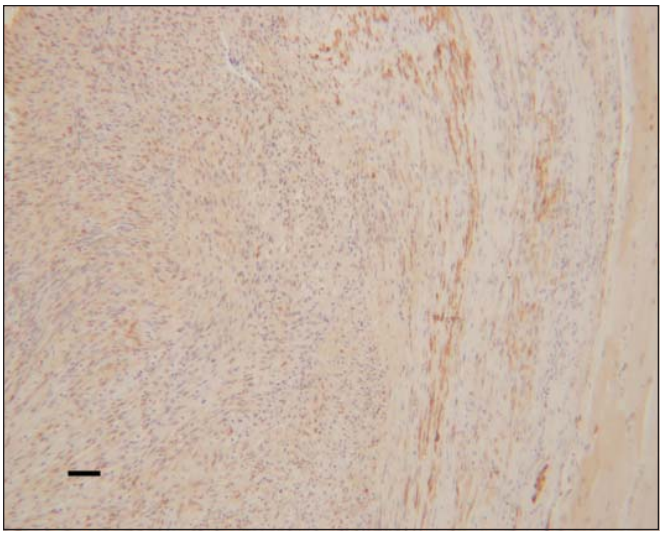

Figure 3. Tumor tissue from a hamster. Cells exhibit strongly positive cytoplasmic staining for S100 in a region where a peripheral nerve merges with the tumor mass. Bar, 50 µm.

neoplastic cells were characterized by a moderate amount of amphophilic cytoplasm, with indistinct cell borders and oval, occasionally vesiculate nuclei with moderate anisokaryosis, fine stippled chromatin, and 1 to 3 pale eosinophilic nucleoli (Figure 2). Mitotic activity was high, with 22 mitotic figures in 10 high-power (magnification, ×400) fields. A medium-sized subcutaneous nerve was found to merge with the periphery of the mass. In addition, multifocal areas of necrosis were present throughout the mass and were occasionally accompanied by degenerate neutrophils. The axillary nodule was identified as lymph node that had been effaced by similar population of neoplastic spindle cells.

Unstained, paraffin-embedded sections of the neoplasm, including the affected lymph node, were processed routinely for streptavidin–biotin peroxidase immunohistochemical evaluation for vimentin (VIM 3B4, diluted by the company; Ventana Medical Systems, Tucson, AZ), alpha smooth muscle actin (MU128-UC, diluted 1:100; BioGenex, San Ramon, CA), S100 (Z0311, diluted 1:300; Dako, Carpinteria, CA), and neuron-specific enolase (NSE; MU055-UC, diluted 1:20; BioGenex). Briefly, for staining vimentin and alpha smooth muscle actin, sections were processed on an automated staining machine (Ventana Medical Systems) with manufacturer-supplied biotinylated goat antimouse secondary antibody, streptavidin peroxidase, and 3,3′-diaminobenzidine as a chromagen. By use of similar methods, sections were stained manually for S100 by using a goat antirabbit secondary antibody (HK326-UR; BioGenex) and for NSE by using a goat antimouse secondary antibody (HK325-UM; BioGenex). Normal-appearing peripheral nerves, skeletal muscle, and arteries in the tissues adjacent to the neoplasm served as internal tissue controls and confirmed specific reactivity of antibodies to hamster tissue.

Immunohistochemical staining for S100 revealed moderate to intense, diffuse cytoplasmic positive staining of 70% to 80% of neoplastic cells in the primary and metastatic lymph node masses and intense staining of the nerve merging with the primary mass (Figure 3). NSE was associated with mild to moderate staining of the cytoplasm in 80% to 90% of the cells in the tumor and with normal dermal nerve staining. Most cells (80% to 90%) had moderate to intense cytoplasmic staining for vimentin (Figure 4). Staining for smooth muscle actin appropriately labeled the tunica media of vessels, and myoglobin staining labeled the panniculus carnosus, but neither agent stained neoplastic cells.

Discussion

This report describes a spontaneously occurring, appendicular, malignant PNST in a golden hamster. These tumors are relatively common in dogs and cattle but are rare in cats and humans.[3,4] Similar neoplasms, although relatively uncommon, have been reported to occur in the B6C3F1 strain of mice and historically have been induced in mice by injection of ^{90}Sr and in hamsters with injection of 1,1-dimethylhdrazine.[2,8] In addition, transplacental administration of N-ethyl-N-nitrosurea induced PNSTs in 75% of Syrian golden hamsters treated.[7]

Although used less frequently today, hamsters were once the species of choice for carcinogenesis studies, owing to an apparently low rate of spontaneously occurring neoplasms.[5,6,9] Many studies have outlined the frequency and spectrum of neoplastic lesions in colonies of research hamsters, with marked variation among laboratories and strains of hamsters. Early reports describe spontaneous tumor incidences of 0.5% to 17%.[5,6,9] One such study evaluated 2 hamster colonies raised under similar conditions and again found wide variation in the frequency and malignancy of neoplasms.[9] A later report described a 69% rate of spontaneously occurring neoplasms in control hamsters in carcinogenicity studies and noted that tumor-bearing animals had a longer life expectancy; 114 wk for tumor-bearing animals versus 102 wk for nontumor-bearing animals, thus suggesting that older hamsters are more likely to develop spontaneous neoplasms than are younger hamsters.[5]

Most reports of Syrian (golden) hamsters cite the adrenal cortex as having the highest frequency of spontaneously occurring neoplasia, followed by lymphoreticular tumors, endometrial and pancreatic islet cell neoplasms.[5,6,9] Cutaneous and subcutaneous neoplasms are uncommon in hamsters, representing fewer than 1% of all neoplasms. Of these tumors, trichoepitheliomas in older hamsters are the most common and are associated with polyomavirus infection.[5,6] Soft tissue sarcomas (STSs), including fibrosarcoma and rhabdomyosarcoma, have only rarely been identified in studies of large hamster colonies.[5,6,9]

A recent study of PNSTs and other STSs in dogs has described some of the variable morphologies and immunostaining pat-

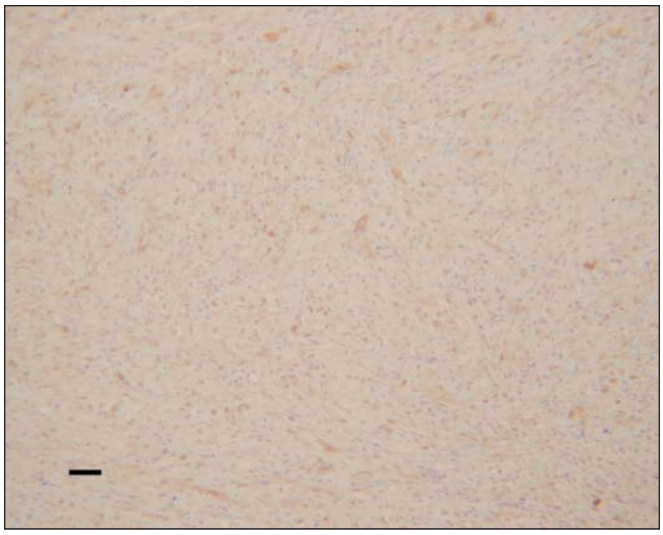

Figure 4. Tumor tissue from a hamster. Neoplastic cells exhibit strongly positive cytoplasmic staining for vimentin. Bar, 50 µm.

terns of PNST and has suggested criteria for identifying and differentiating malignant versus benign PNSTS. In that study, 76% of all PNSTs were diffusely positive for S100, whereas other STSs were less frequently and only focally positive (fewer than 20% of cells).[1] All PNSTs were negative for alpha smooth muscle actin, whereas other STSs, particularly hemangiopericytomas, were typically positive.[1] In addition, staining for nerve growth factor receptor and cytokeratin was positive in PNSTs more frequently than in other STSs.[1] Malignant PNSTs were characterized by a high mitotic index, necrotic foci, NGFR immunopositivity (71%), and myoglobin positivity (64%).[1] In addition to being locally invasive, malignant PNSTs have a tendency to metastasize to local lymph nodes and occasionally lung. All STSs evaluated in the cited study were strongly positive for vimentin.[1]

Like canine PNSTs, cells in the reported neoplasm were diffusely positive for S100 and negative for alpha smooth muscle actin. Unlike many canine malignant PNSTs, the described neoplasm was negative for myoglobin, but many other criteria of malignancy (including a high mitotic index, necrotic foci, and local metastasis) were present. Variable and atypical immunostaining in malignant PNSTs may be related to the embryonic origin of neural crest cells.[3,4] Interestingly, diethylstilbestrol-induced renal tumors in adult male Syrian hamsters may have a primordial relationship to malignant PNSTs, because the induced tumors exhibit immunoreactivity for S100, NSE, and GFAP.[10]

On the basis of histologic morphology, confluence with a peripheral nerve, high mitotic activity, lymph node metastasis, and positive S100, NSE, and vimentin immunostaining, the described lesion is consistent with a malignant neoplasm of peripheral nerve. To our knowledge, this report is the first description of a spontaneous malignant PNST in a hamster.

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