Microchip-Associated Sarcoma in a Shrew (Suncus murinus)

Leah K Schutt and Patricia V Turner*

A 16-mo-old female house musk shrew (Suncus murinus) with a 1-wk history of a rapidly growing subcutaneous mass in the interscapular region was euthanized and submitted for necropsy. Macroscopic examination identified an irregular, well-demarcated, solid, tan-white subcutaneous mass. A small cavity containing a microchip device was present at the center of the mass. In addition, massive splenomegaly was evident grossly. Histologically, the subcutaneous mass comprised spindle cells arranged in a storiform pattern of interweaving bundles, consistent with a high-grade soft tissue sarcoma with multifocal necrosis. Immunohistochemical investigation suggested that the neoplastic cells were positive for neuron-specific enolase and (rarely) α-smooth muscle actin and negative for cytokeratin, desmin, S100, and vimentin. In light of the mesenchymal histopathologic phenotype and the lack of specific immunoreactivity pattern, the mass was considered to be most consistent with a poorly differentiated sarcoma. To our knowledge, this is the first report of a microchip-associated soft tissue sarcoma in a shrew.

Case Report

A 26.5-g, 16-mo-old female house musk shrew (Suncus murinus) presented to the University of Guelph Laboratory Animal Diagnostic Service with a mass in the interscapular region. The shrew originated from a breeding and research colony maintained in accordance with the animal care policy and procedures at the University of Guelph. Shrews in this colony are singly housed in polycarbonate cages and fed a mixture of dry cat and ferret foods ad libitum, with continuous access to water. One week prior to presentation, a lump was noted in the interscapular region of the shrew. Because of the rapidly growing nature of the mass and its potential to interfere with the animal’s mobility, the shrew was euthanized and submitted for necropsy. At postmortem, the shrew was in good body condition, with adequate muscle and fat stores. There was a focal, moveable, 3 × 2 × 1.5-cm subcutaneous mass in the interscapular dorsum. Macroscopically, the mass was well-demarcated and expansile within the subcutaneous tissue. On cut surface, it was solid and diffusely white-tan, with a central area of caseous tan necrotic debris. A 2 × 11-mm cylindrical glass and metallic foreign body consistent with a microchip implant was present within a small cavity at the center of the mass (Figure 1). The spleen was enlarged to 3 × 1 × 0.4 cm and was diffusely pale tan and meaty. The liver was mildly enlarged, showing an enhanced lobular pattern on the capsular and cut surface, with alternating regions of tan and red-brown.

All tissues were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 4 μm, and stained with hematoxylin and eosin, with additional sections processed for immunohistochemistry. Immunohistochemical labeling for vimentin (diluted 1:2000; clone 3B4, Fisher Scientific, Pittsburgh, PA), pancytokeratin (diluted 1:100; AE1/AE3, Dako, Carpinteria, CA), α-smooth muscle actin (diluted 1:200; Dako), desmin (diluted 1:200; Dako), S100 (diluted 1:2000; Dako), neuron-specific enolase (clone BBS/NC/VH114, Dako) was used in an attempt to characterize the neoplastic cell of origin. All immunohistochemical stains except for S100 were processed by using the streptavidin–peroxidase method with 3,3′-diaminobenzidine as a substrate and hematoxylin counterstain. Sections immunolabeled with the antiS100 and vimentin primary antibodies were processed by using the EnVision detection system (Dako Canada, Mississauga, Canada). To confirm antibody cross-reactivity to shrew tissue, normal tissues containing epithelium, peripheral nerves, skeletal, and smooth muscle from the same animal were included as internal tissue controls.

Histologically, the mass was poorly demarcated, unencapsulated, infiltrative, and expansile, compressing adjacent dermal and subcutaneous tissues. It was composed of densely cellular bundles of spindle-shaped cells arranged in an interweaving storiform pattern (Figure 2 A). The neoplastic cells had indistinct cell borders, with variable amounts of eosinophilic cytoplasm and single central round-to-oval nuclei with vesicular chromatin and often one or more prominent nucleoli. There was moderate anisokaryosis and a high mitotic index, with an average of 6 mitoses per high-power (40×) field. Large areas of necrosis...
were scattered throughout the mass. No evidence of metastasis was observed.

Histologic examination of other organs revealed marked extramedullary hematopoiesis in the spleen, liver, adrenal glands, and left kidney. Splenic sinuses were massively distended with densely packed sheets of myeloid and erythroid precursor cells and numerous megakaryocytes at all stages of maturation (Figure 3A). In the liver, large numbers of myeloid precursor cells expanded portal tracts, and aggregates of hematopoietic cells were scattered throughout the parenchyma. In one adrenal gland, massive extramedullary hematopoiesis with sheets of myeloid precursors and scattered clusters of erythroid precursors and megakaryocytes expanded and replaced the adrenal medulla (Figure 3B). In addition, small clusters of extramedullary hematopoiesis were present within the renal cortical interstitium.

On immunohistochemical staining, the majority of neoplastic cells showed strong diffuse granular cytoplasmic labeling for neuron-specific enolase (Figure 2C). Approximately 5% of tumor cells were immunoreactive for α-smooth muscle actin, demonstrating variable cytoplasmic and membrane labeling (Figure 2B). Neoplastic cells were not immunoreactive with desmin (Figure 2D), S100 (Figure 2E), pancytokeratin (data not shown), or vimentin (Figure 2F).

Discussion

To our knowledge, this is the first report of a microchip-associated tumor in a house musk shrew. The histologic phenotype of the neoplastic cells associated with the implant was consistent with a foreign body-induced soft tissue sarcoma. We used immunohistochemical analysis with a variety of mesenchymal cell lineage markers to further characterize the neoplastic cell line of origin. The majority of tumor cells were immunoreactive for neuron-specific enolase, a homodimeric enzyme that is specific to neurons and neuroendocrine cells but that can be found as a heterodimeric subunit in a large number of nonneural tissues and tumors.10 As a result, the specificity of the neuron-specific enolase antibody is considered to be low. Despite strong immunolabeling for neuron-specific enolase, neoplastic cells did not react positively with S100, another marker specific for neural tissue, suggesting that the tumor cells were not neural in origin. Based on the lack of immunoreactivity with muscle-specific markers desmin and smooth muscle actin, we concluded that the neoplastic cells did not originate from smooth or striated muscle. Despite a strong mesenchymal phenotype on histopathologic evaluation, the tumor cells lacked immunoreactivity for vimentin, a universal mesenchymal cell marker. This finding was unexpected and may be attributed to a loss of vimentin expression by the tumor cells. A mesenchymal cell phenotype was supported further by the lack of immunoreactivity for pancytokeratin, an epithelial cell marker. In light of the mesenchymal histologic phenotype and the lack of a specific immunohistochemical profile, we concluded that the neoplasm was most likely fibroblastic or a poorly differentiated sarcoma, such as fibrosarcoma.

Implantable microchips are placed subcutaneously routinely in domestic and laboratory animals and are considered a rapid, safe, and durable method of identification. Microchips are hermetically sealed in an inert, biocompatible glass cylinder that is partially covered with a polypropylene antimigratory cap. They are implanted subcutaneously by using a sterile needle assembly in which the microchip is packaged.1,4,17

Foreign bodies are postulated to stimulate cell proliferation and inflammation in tissue, promoting neoplastic transformation in adjacent tissue.17 Because of their routine use for identification, tissue reaction to microchip implants have been studied extensively in a variety of species.6,8,11-13,17 Most studies report a connective tissue capsule of variable thickness surrounding the microchips. In a study of glass-sealed microchips with a polypropylene cap used in B6C3F1 mice,17 mild-to-moderate mixed inflammatory infiltrate was detected around the polypropylene cap, but no neoplastic changes were reported. Microchip-associated neoplasias have been reported in laboratory rodents, a dog (Canis familiaris), an Egyptian fruit bat (Rousettus aegyptiacus), a degu (Octogon degus), and a feather-tailed glider (Acrobates pygmaeus).5,16,18,20

Various strains of mice have developed microchip-associated tumors.2,9,14,19 Although the overall incidence is low, there appears to be variation in strain susceptibility, with incidence rates of 0% to 4.1% in B6C3F1 mice,9,14,17 1.2% in CBA/J female mice and 0.5% for CBA/J male mice,19 and no reported cases in CD1 mice.1,4,14 In one study using heterozygous p53+/– transgenic mice, 18 of 177 animals developed sarcomas at the site of microchip implantation.2 Tumor latency appears to be long, with a mean postimplantation time to diagnosis of 82 to 84 wk in B6C3F1 mice.9 Microchip-associated tumors in rats also, with an incidence of 1% in F344 rats used in chronic toxicity–carcinogenicity studies,4 and no cases reported in microchip-implanted Sprague–Dawley rats.1

Histologically, all reported microchip-associated tumors have been diagnosed as malignant and mesenchymal in origin. Fibrosarcomas, malignant fibrous histiocytomas, hemangioepicytomas, rhabdomyosarcomas, leiomyosarcomas, and sarcomas not-otherwise-specified have been diagnosed histologically at the sites of microchip implants in mice.9,14,19 In F344 rats, malignant schwannoma, fibrosarcoma, anaplastic...
Figure 2. Histopathology and immunohistochemical analysis of a microchip-associated sarcoma in the intrascapular subcutis of a house musk shrew; bar, 200 μm. (A) The mass comprised an interweaving storiform pattern of highly cellular bundles of spindle-shaped cells with indistinct cell borders, variable amounts of eosinophilic cytoplasm, and central round-to-oval nuclei with vesicular chromatin and often one or more prominent nucleoli. Mitoses averaged 6 per high-power field. Hematoxylin and eosin stain. (B) Approximately 5% of neoplastic cells were immunopositive for α-smooth muscle actin. (C) Approximately 95% of neoplastic cells exhibited strong diffuse granular cytoplasmic immunolabeling for neuron-specific enolase. However, neoplastic cells lacked immunoreactivity for (D) desmin and (E) S100, suggesting that they were less likely to derive from muscle or nerve tissue. (F) A diffuse lack of immunolabeling for vimentin was observed.

sarcoma, and histiocytic sarcoma were confirmed by immunohistochemistry.4

The long latency and malignant mesenchymal histopathologic phenotype of the microchip-associated tumor in this shrew are consistent with published reports in rodents. This shrew was implanted subcutaneously with a microchip transponder (BioMedic Data Systems, Seaford, DE) in the intrascapular
subcutis at 1 mo of age and a tumor was noted clinically at 16 mo, corresponding to a clinical tumor latency period of 15 mo. Marked extramedullary hematopoiesis was present in multiple organs of this shrew. The presence of erythroid and myeloid precursor cells and megakaryocytes in the red pulp of the spleen is a consistent finding in shrews from this colony and has been reported in the literature. Unlike other species of the class Mammalia in which hematopoietic functions transfer from the spleen to the bone marrow shortly before birth, splenic hematopoiesis in shrews is suspected to continue to supplement bone marrow hematopoiesis throughout life and thus has a physiologic function. The degree of multiorgan involvement with extramedullary myelopoiesis in this animal was remarkable and may be a physiologic response to the large nidus of necrotic tissue present within the tumor.

### References