Subcutaneous Leiomyosarcoma in a Common Squirrel Monkey (*Saimiri sciureus*)

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**ABSTRACT.** Leiomyosarcoma in soft tissue has only been reported in humans or animals. We performed pathological examination of a 3-years-old male squirrel monkey which had a large mass in the right axilla. The mass in the right axilla was surgically resected but it soon reoccurred. This tumor was diagnosed as a leiomyosarcoma based on histopathology and immunohistochemistry using the expression of α-smooth muscle actin and desmin. Leiomyosarcoma in squirrel monkey has been reported in one case, there was no reoccurrence or metastasis. Most of the reported tumors in nonhuman primates have occurred in aged monkeys. This case was a rare tumor considering the young age of the animal.

Key words: leiomyosarcoma, soft tissue tumor, squirrel monkey.

Leiomyosarcoma is a malignant tumor arising from smooth muscle cells, and is characterized by broad interlacing fascicles of spindle-shaped or ovoid neoplastic cells that retain many features of normal smooth muscle cells with elongate nuclei and eosinophilic cytoplasm. Leiomyosarcomas are nonencapsulated but frequently invasive tumors which show malignant phenotypes such as pleomorphic spindle-shaped or ovoid to round cells, a high mitotic index, necrosis, hemorrhage, and metastasis [6]. In humans and most other animals, leiomyosarcomas are relatively common in the visceral organs, especially the gastrointestinal tract and female genital tract, and in the spleen in dogs [5, 6]. Leiomyosarcoma rarely occurs in other organs; only a few cases in the oral cavity, esophagus, and urinary bladder have been reported in humans and animals [5, 6]. Subcutaneous leiomyosarcoma is extremely rare in animals. Although it has been reported in a cow, a squirrel monkey, and a hamster, metastasis is uncommon [4, 7, 15].

A large number of squirrel monkeys are kept in zoos and experimental facilities, but there are few reports of tumors in this species such as malignant lymphoma [1], hepatocellular carcinoma [3, 11], osteosarcoma [8], adenocarcinoma of the cecum [9], squamous cell carcinoma of the oral cavity [12], and mammary adenocarcinoma [14]. In the present study, we describe a case of subcutaneous leiomyosarcoma in the right axilla with pulmonary metastasis in a squirrel monkey.

A 3-year-old, 664 g, male common squirrel monkey (*Saimiri sciureus*) kept in a zoo was found to have an abnormal shoulder. A mass formed in the right axillary region and gradually increased. The mass was surgically resected, but reoccurred after 3 months. The tumor was resected again, but the monkey died shortly afterwards. A complete necropsy was performed in the Laboratory of Veterinary Pathology of Azabu University, and the various tissues were fixed in 10% phosphate-buffered formalin for histological and immunohistochemical analysis. Tissue was embedded in paraffin, and sectioned at approximately 4 μm for hematoxylin-eosin stain, Masson’s trichrome stain, van Gieson’s stain, silver stain (Watanabe method), periodic acid-Schiff reaction, and immunohistochemical staining. Immunohistochemistry was done using primary mouse monoclonal antibodies to vimentin (vimentin, v9; DakoCytomation Denmark A/S, Glostrup, Denmark), human smooth muscle actin (α-SMA, 1A4; DakoCytomation Denmark A/S), human desmin (desmin, D33; DakoCytomation Denmark A/S), cytokeratin AE1/3 (cytokeratin, AE1, AE3; Boehringer Mannheim Biochemica, Basel, Switzerland), and S-100 protein (S-100; JIMRO, Takasaki, Japan). Secondary antibody reaction was done using a peroxidase-conjugated Histofine-Simplestain kit (Simplestain MAX-PO, Nichirei, Tokyo, Japan). 3’3-diaminobenzidine was used to visualize the reaction products. The slides were counterstained with Mayer’s hematoxylin.

The size of the primary mass in the subcutaneous tissue of the right axilla was 5.0 × 2.2 × 1.5 cm (Fig. 1). The cut surface of the mass was solid and grayish white or white with central necrosis and hemorrhage (Fig. 2). At necropsy, the subcutaneous mass in the right axilla was found to be almost the same size as the initial mass. The tumor had extensively invaded skeletal muscle on the inside of the upper arm. In other findings, there were found several variably sized (2 mm to 1 cm diameter) white masses in the lung, and there was also pulmonary edema. No metastasis to lymph nodes or other organs was observed. Histologically, the subcutaneous mass was composed of interlaced, proliferating spindle cells (Fig. 3). The tumor was highly cellular. Neoplastic cells interwove in various directions were also observed, and they sometimes formed a herringbone or palisaded pattern. The nuclei of these cells were usually centrally located, long and elliptic, and blunt-ended, and contained 1–2 indistinct nucleoli. There were sixteen to seventeen mitoses per 10 high power fields. The nuclei of neoplastic cells
Fig. 1. Solid subcutaneous, primary mass in the right upper arm after formalin fixation. Bar, 1 cm.

Fig. 2. Cut surface of Fig. 1. The tissue is grayish white or white with central necrosis (asterisk) and hemorrhage (arrows). Bar, 1 cm.

Fig. 3. Subcutaneous, primary mass in the right axilla. Neoplastic spindle cells interweaving in various directions are also seen. Hematoxylin and eosin. ×100.

Fig. 4. Subcutaneous mass in the right axilla. Strongly positive immunoperoxidase staining for α-smooth muscle actin. ×200.

Fig. 5. Subcutaneous mass in the right axilla. Weakly positive immunoperoxidase staining for desmin. ×200.

Fig. 6. Lung, metastatic mass of leiomyosarcoma. There were scattered multinucleated giant cells (arrowheads). Hematoxylin and eosin. ×200.
showed slight to moderate pleomorphism. The neoplastic cells extensively invaded the adjacent skeletal muscle layer, and hemorrhages and necrosis were scattered in the tumors. The cytoplasm was eosinophilic, and stained red with Masson’s trichrome stain and yellow with van Gieson’s stain. Mild proliferation of collagen fibers was observed between neoplastic cells, and in better differentiated tumors a delicate reticulin network was present between cells. Periodic acid-Schiff stain showed fine glycogen deposits within the cytoplasm of some neoplastic cells. Neoplastic cells were intensely positive for vimentin (data not shown), α-SMA (Fig. 4), and desmin (Fig. 5), and negative for cytokeratin and S-100 protein (data not shown). Positive controls were positive for each antibody. No immunostaining for any of the antibodies was detected in negative controls. The morphology and staining in the initial mass, the reoccurred mass, and the pulmonary metastasis were similar, but in the pulmonary metastasis, there were scattered multinucleated giant cells and some pleomorphic neoplastic cells with more round to ovoid, hyperchromatic, and irregularly shaped nuclei than in the subcutaneous mass (Fig. 6). There were eighteen to nineteen mitoses per 10 high power fields in the lung mass.

Histologically, this tumor was composed of interlaced, proliferating spindle cell streams, and was in accord with the leiomyosarcomas which have been hitherto reported. Tumors with many mitotic figures invading the skeletal muscle and having multiple metastases to the lungs are considered highly malignant. This tumor was considered to have spread hematogenously to the lungs, since the same morphology, staining, and metastasis were not observed in other organs including regional lymph nodes. Immunohistochemical demonstration of α-SMA and desmin are useful markers for both human and animal smooth muscle tumors [5, 6]. This tumor was positive for both α-SMA and desmin, the same as in humans and dogs. Cutaneous leiomyosarcoma originates from the arrector pili muscle in hair follicles and has few vascular components, whereas subcutaneous leiomyosarcoma usually originates from the smooth muscle constituting the walls of small or medium veins in subcutaneous tissue. In the present case, the tumors had well-developed vascular components and invaded the adjacent skeletal muscle layer. Although it is important to differentiate leiomyosarcomas from fibrosarcomas, rhabdomyosarcomas, malignant fibrous histiocytomas, nerve sheath tumors, and synovial sarcomas, some special stains and positive reactions for α-SMA and desmin were useful in identifying the smooth muscle origin. Malignant myopericytoma is a recently described perivascular tumor which in humans arises in subcutaneous or deep soft tissue [10] and in Fischer rats in the mesentery of the rectum [13]. It is characterized histologically by concentric perivascular proliferation of ovoid to spindle-shaped cells showing apparent differentiation toward perivascular myoid cells or myopericytes. It is thought that myopericytes have intermediate features between pericytes and vascular smooth muscle cells. Both malignant myopericytoma and leiomyosarcoma are composed of cells that show myoid differentiation and generally stain for smooth muscle actin. However, true smooth muscle neoplasms generally show more brighter eosinophilic cytoplasm and plump, cigar-shaped nuclei. Perivascular concentric growth is not a feature of leiomyosarcomas. Leiomyosarcomas very often show positive staining with desmin, but only one case of five cases in malignant myopericytoma in humans showed positive staining for desmin in a dot-like pattern [10]. In this squirrel monkey case, tumor cells showed cigar-shaped nuclei, and weakly positive staining for desmin. There was no perivascular concentric growth in our case. On the basis of these findings, we diagnosed this case as recurrence of subcutaneous leiomyosarcoma of the right axilla with multiple pulmonary metastases. Currently, malignant myopericytoma also may be confused leiomyosarcoma, monophasic synovial sarcoma, or malignant peripheral nerve sheath tumor. Myopericytoma is recognized as a tumor derived from myopericytes and shares features with other perivascular myoid tumors, such as myofibroma, glomus tumors, and smooth muscle tumors. Recently, Avallone et al. described the spectrum of canine cutaneous perivascular wall tumors including myopericytoma, hemangioepericytoma, and angioleiomyoma/sarcoma [2]. In the future, it is necessary to distinguish malignant myopericytoma from perivascular myoid tumors such as subcutaneous leiomyosarcoma not only in humans but also in animals.

In squirrel monkeys, there are a few reports of spontaneous tumors, most of them in adults or in monkeys of advanced age (over the age of 10), but in this case, the animal was a still young, 3-year-old. On the other hand, in a subcutaneous leiomyosarcoma case in a squirrel monkey previously reported, the monkey was 15 years old, and metastasis and reoccurrence were not seen. Subcutaneous leiomyosarcoma is a rare condition of soft tissue tumor in humans and animals [5, 6]. In humans, such tumors occur generally at middle-to-advanced age (50 to 70 years) but there are sporadic reports of young patients [6]. On the other hand, in animal cases, although there are few reports, subcutaneous leiomyosarcoma occurs at a relatively young age such as a 4-year-old cow [7], a 10-month-old hamster [15], and this 3-year-old squirrel monkey case. This case was rare because of the young age, animal species, and site of tumor formation.

REFERENCES