

CUTANEOUS ANGIOLEIOMYOSARCOMA IN A DOG

ANGIOLEIOMIOSSARCOMA CUTÂNEO NUM CÃO

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Abstract: A 6 year-old male Labrador Retriever presented with a slow growing subcutaneous tumor in the elbow that mimetized a hygroma. Histologically the tumor consisted of a multinodular mass of spindle cells proliferating from the muscular layer of the subcutaneous vessels. Tumor cells stained positively for alpha-smooth muscle actin and vimentin but were negative for desmin and S-100. The diagnosis was cutaneous angioleiomyosarcoma.

Resumo: Um Labrador Retriever macho com 6 anos de idade foi submetido a uma cirurgia para extirpação de um nódulo localizado na região posterior do cotovelo, que mimetizava clinicamente um higroma.

Microscopicamente o nódulo caracteriza-se por apresentar uma neoformação multinodular não capsulada que apresenta uma proliferação de células fusiformes intimamente ligadas aos vasos sanguíneos e que dão a percepção de ter origem na camada muscular da túnica média. Foi feita a caracterização imunohistoquímica e houve imunomarcação positiva das células neoplásicas para a vimentina e α -actina e negativas para desmina e S100. A imagem microscópica e a imunohistoquímica são compatíveis com o diagnóstico de angioleiomiossarcoma cutâneo.

CASE REPORT

A 6 year old, male Labrador Retriever presented to a referring veterinary because of a large swelling in the right elbow that had been previously misdiagnosed as a hygroma. The subcutaneous tumor was removed by surgery and submitted for histopathology. Tissue samples were fixed in 10% neutral buffered formalin, processed routinely for paraffin embedding, sectioned at 5 μ m, and stained with hematoxylin and eosin. The histopathological examination revealed in the subcutaneous tissue, an irregular unencapsulated nodule composed of spindle cells arranged in bundles and whorls (fig. 1).

The tumor cells were closely connected with vascular structures and seemed to proliferate from the tunica media of the subcutaneous blood vessels.

In some of the vessels, the tumor cell proliferation protruded into the vascular lumen without, however, disrupting

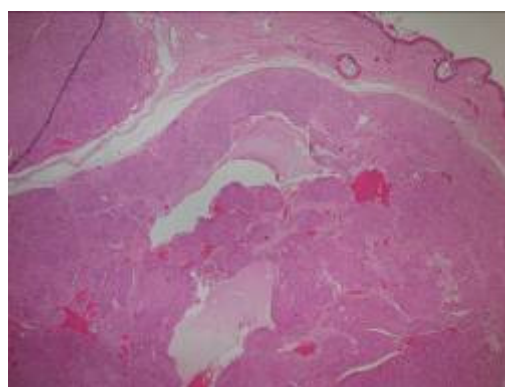


Figure 1- Cutaneous angioleiomyosarcoma. Irregular unencapsulated subcutaneous tumor composed of spindle cells proliferating from the muscular media of the subcutaneous blood vessels (H&E, 40X).

In some of the vessels, the tumor cell proliferation protruded into the vascular lumen without, however, disrupting the endothelium (fig 2).

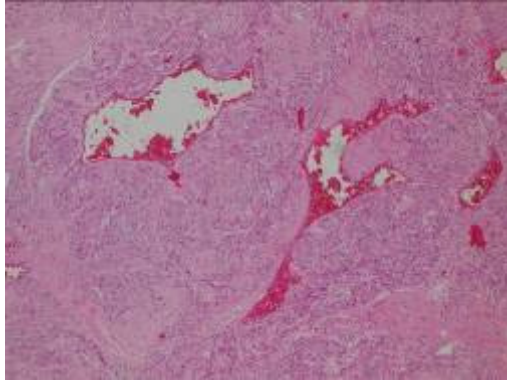


Figure 2- Cutaneous angioleiomyosarcoma. The spindle cells are arranged in bundles and whorls around blood vessels. In some of the vessels, the tumor cell proliferation protruded into the vascular lumen without, however, disrupting the endothelium (arrow). (H&E, 100x).

The neoplastic cells had eosinophilic cytoplasm that was sometimes vacuolated. The nuclei were of medium size, elongated and blunt-ended, with stippled chromatin and small nucleoli. The mitotic index was higher than 3 mitosis per 10 high power fields (400x) (fig 3).

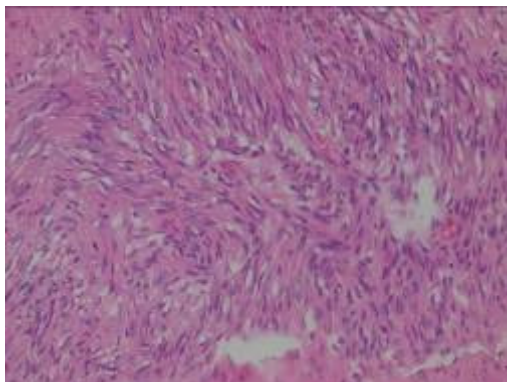


Figure 3- Cutaneous angioleiomyosarcoma. The neoplastic cells have eosinophilic cytoplasm, that is sometimes vacuolated. The nuclei is of medium size, elongated and blunt-ended. The chromatin is stippled and the nucleoli is small. The mitotic index is higher than 30 mitosis per 10 high power fields (400x).

Several thrombus and foci of hemorrhage were observed in the injured vessels and surrounding stroma, respectively.

Paraffin-embedded sections of the neoplasm were placed on positively charged slides and stained with antibodies against α -smooth-muscle actin (Dako Cytomation, N1584, clone 1/4; ready to use), vimentin (Novocastra, NCL-L-VIM-V9, clone V9; 1/100), desmin (Dako, IS606, clone D33; ready to use) and S-100 (Novocastra, RTU-S100P, polyclonal; ready to use). Immunohistochemical staining was performed using the Dako Envision detection system (Dako, Cambridge, UK) and the staining was completed by incubation with 3,3'diaminobenzidine chromogen solution (chromogen solution is part of the Envision kit). The neoplastic cells were strongly positive for α -smooth-muscle actin (fig. 4), and vimentin, but were negative for desmin and S-100.

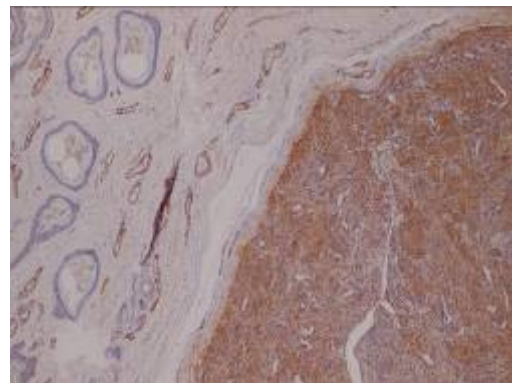


Figure 4- Cutaneous angioleiomyosarcoma. Immunohistochemistry staining for alpha-smooth muscle actin. Neoplastic cells react strongly as do smooth muscle of the tunica media of adjacent dermal vessels (positive internal control). Envision DAB. Mayer's hematoxylin counterstain (100x).

For electron microscopy, formalin-fixed tissues were placed in 2,5% glutaraldehyde solution in 0,1 M phosphate buffer, postfixed in 1% aqueous osmium tetroxide, embedded in Agar 100 (Agar Scientific Ltd, Essex England), sectioned at 80 nm and stained with uranyl acetate and lead citrate.

Ultrastructurally the neoplastic cells were fusiform with centrally located, elongated blunt-ended nuclei (fig. 5). In the cytoplasm, fine myofilaments in slightly undulated parallel bundles, along the longitudinal axis of the cell, were observed. And dense bodies that are very characteristic of smooth muscle cells were also present as numerous electron-dense structures, scattered in the cytoplasm (fig. 6).

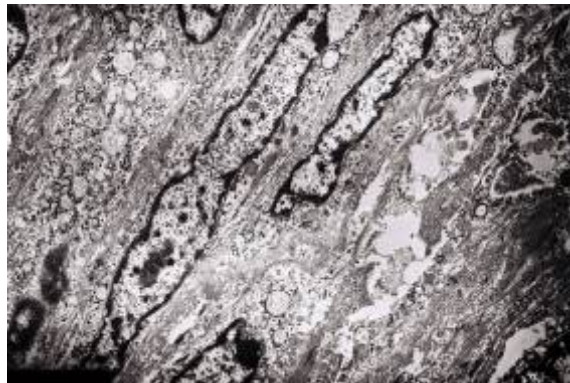


Figure 5- Transmission electron microscopy-subcutaneous tumor 5000x. Ultrastructurally the neoplastic cells were fusiform with centrally located, elongated blunt-ended nuclei.

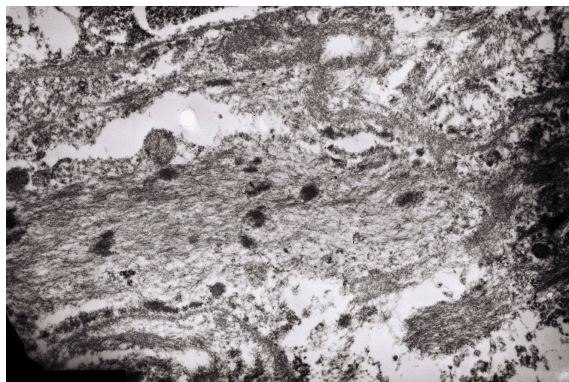


Figure 6- Transmission electron microscopy-subcutaneous tumor 10000x. In the cytoplasm of neoplastic cells, dense bodies and fine myofilaments in slightly undulated parallel bundles, along the longitudinal axis of the cell, were observed,

The histopathological findings, immunohistochemistry staining and ultrastructure are consistent with a diagnosis of angioleiomyosarcoma.

DISCUSSION

Smooth muscle tumors of the skin are very rare in dogs (Bevier & Goldschmidt, 1981), and they may originate from arrector pili muscles (piloleiomyosarcoma) or from vessel walls (angioleiomyosarcoma) (Liu & Mikaelian, 2003, Kheirandish et al., 2009). Cutaneous malignant smooth muscle tumors of dogs may however be under diagnosed due to their resemblance to far more common spindle-cell tumors such as fibrosarcomas, myofibroblastic fibrosarcomas, peripheral nerve sheath tumors and histiocytic sarcomas. Another differential diagnosis is the glomus tumors of spindle cell type, an uncommon subset of a rare tumor of the glomus body (a specialized arteriovenous anastomosis that serves in thermoregulation).

Fibrosarcoma and myofibroblastic fibrosarcoma contain variable amounts of collagen, and typically feature spindle cells with pointed nuclei, while smooth muscle tumors usually lack intercellular collagen, and are composed of spindle cells with oval blunt-ended nuclei.

Peripheral nerve sheath tumors are composed of smaller spindle cells with fusiform or serpentine nuclei, and the cellular arrangement in palisades and the mucinous-rich stroma is not observed in smooth muscle tumors.

In contrast to leiomyosarcomas, most histiocytic sarcomas contain some individualized round cells, admixed with the spindle cells.

Glomus tumor of spindle cell type is a subset of a rare tumor, derived from the smooth muscle cells of the glomus body (Enziger & Weiss, 1998). In this subset there is a gradual transition from round or polygonal cell of classical glomus tumor to fusiform cells resembling smooth muscle, which can be histologically very similar to angioleiomyosarcomas. However, in contrast to glomus tumor, angioleiomyosarcoma are composed of smooth muscle cells proliferating from the muscular layer of injured vessels, and no

small nerves are seen along the margin of this tumor.

Immunohistochemical studies of smooth-muscle tumors reveal that like other mesenchymal tumors they are positive for vimentin, and that the expression of desmin and alfa-smooth muscle actin identifies them with a smooth muscle origin (Andreasen & Mahaffey, 1987). In contrast, fibrosarcomas, peripheral nerve sheath tumors, and histocytic sarcomas lack expression of alfa-smooth-muscle actin and desmin. Myofibroblastic fibrosarcomas and glomus tumors on the contrary also retain the cytoplasmic expression of vimentin and alfa-smooth muscle actin and on rare occasions can even express desmin as well (Daugaard et. al., 1990, Shinya et. al., 1997). On those rare occasions, immunohistochemical differentiation from angioleiomyosarcomas may not be possible, however the absence of admixed neural elements is more consistent with a smooth muscle neoplasm than with glomus tumor, and the connection to the wall of pre-existing vessels is not a feature of a myofibroblastic fibrosarcoma.

The lack of desmin immunoreactivity in the present case is not inconsistent with a smooth muscle origin, because vascular smooth muscle may not express desmin (Miettinen et. al., 1983, Kheirandish et. al., 2009).

In the present tumor, we favor a diagnosis of angioleiomyosarcoma over angioleiomyoma because it showed an expansive and invasive growth, and had a mitotic index comparable with that observed in a study of human dermal leiomyosarcomas, in which two mitoses per 10 high-power fields warranted a malignant diagnosis (Fields & Helwig, 1981).

When last examined, 6 months after excision of the mass, the dog remained healthy with no evidence of recurrence or metastasis.

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