



## NOTE

Pathology

# Canine spindle cell tumor mimicking human classical hemangiopericytoma

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80(11): 1728–1732, 2018

doi: 10.1292/jvms.18-0382

Received: 4 July 2018

Accepted: 7 September 2018

Published online in J-STAGE:  
19 September 2018

**ABSTRACT.** The neoplastic mass developed in the left flank of a Border Collie dog. The tumor was resected surgically and evaluated histologically and immunohistochemically. Histologically a moderate number of spindle cells were proliferated with staghorn, placentoid, and myxoid growth patterns and a lack of perivascular whirling. Immunohistochemically, the tumor cells were positive to vimentin, laminin, S-100 protein, CD34 and CD117 antibodies. They were negative to cytokeratin AE1/3, desmin,  $\alpha$ -SMA and calponin antibodies. Endothelial cells of the staghorn channels were positive for vWF antibody. The present case was diagnosed as spindle cell tumor, but it was similar to human classical hemangiopericytoma (HEP) and canine HEP classified by Avallon and others.

**KEY WORDS:** dog, hemangiopericytoma, spindle cell tumor

The classification of hemangiopericytoma or perivascular wall tumor has been undergoing major changes in humans and dogs in recent years. Avallone and others [1] subclassified canine perivascular wall tumors (PWTs) into hemangiopericytoma (HEP), myopericytoma, angioleiomyoma, angioleiomyosarcoma, adventitial tumor, and angiofibroma based on a histologic and immunohistochemical features. Canine HEP in their classification is a tumor morphologically closer to a human counterpart and they conclude that HEP is less frequent than previously believed. Their report is reflected in the textbooks, and the title of canine HEP is shown together with the myopericytoma and PWT as a synonym [4]. Although the histological morphology of canine HEP is different from other PWTs, the classification name of HEP has remained, and the taxonomic positioning is still unclear.

In human, HEP was reported as a tumor of soft tissue presumably originated from pericyte by Stout and Murray [6]. Although staghorn branching vascular pattern was a diagnostic marker of the entity, a similar pattern was recognized in other soft tissue tumors over the years. By immunohistochemistry and genetically reclassification, HEP and a solitary fibrous tumor (SFT) is considered as a series of tumor groups having a common genetic abnormality caused by NGFI-A binding protein 2 (NAB2)-signal transducer and the activator of transcription 6 (STAT6) gene fusion [5]. And now, the immunoreactivity of STAT6 and progenitor cell marker CD34 is specific and reliable markers of SFTs [3, 5].

In this report, we present histological and immunohistochemical findings of the canine spindle cell tumor showing a morphological similarity to Avallone's HEP, and comparing with human HEP.

The animal in this report is a 13-year-old male Border Collie weighting 23 kg. The owner found a mass with a diameter of 8 cm in the left flank of the dog but was reluctant to his surgery for the elderly. The tumor was not stuck to the muscle and was movable. After 7 month, the mass increasing rapidly in a month caused the dog to have trouble carrying out daily activities and the tumor was resected surgically. After that, the health condition of the dog was good and no recurrence was observed.

The subcutaneous mass was slightly firm, 28 × 25 × 10 cm in size, and not adhered to muscle. Cross section revealed grayish white with a solid growth (Fig. 1). A part of the mass was fixed in 10% neutral buffered formalin and sectioned 5  $\mu$ m stained with hematoxylin and eosin. For immunohistochemical evaluation, formalin fixed paraffin embedding sections were stained using the universal immuno-enzyme polymer method (N-Histofine Simple Stain, Nichirei Biosciences Inc., Tokyo, Japan). Briefly, the sections were treated with high-temperature antigen retrieval solution (Target Retrieval Solution, Agilent Technologies Japan, Tokyo, Japan). Endogenous peroxidase activity was blocked by treatment with hydrogen peroxide and then non-specific binding was eliminated by incubating the sections with normal non-immune goat serum. The sections were incubated with the primary antibodies summarized in Table 1. These are briefly described as follows. CD34 represents a marker for hematopoietic stem and progenitor cells and immunoreactivity is observed in nearly 90% of SFT [3]. Desmin,  $\alpha$ -SMA and calponin are muscle related

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**Fig. 1.** A mass with a diameter of 8 cm in the left flank of a dog. The tumor moved to the dorsal side when laying down (arrow). Bar, 10 cm. Inset: cross section of the formalin fixed sample. Bar, 1 cm.

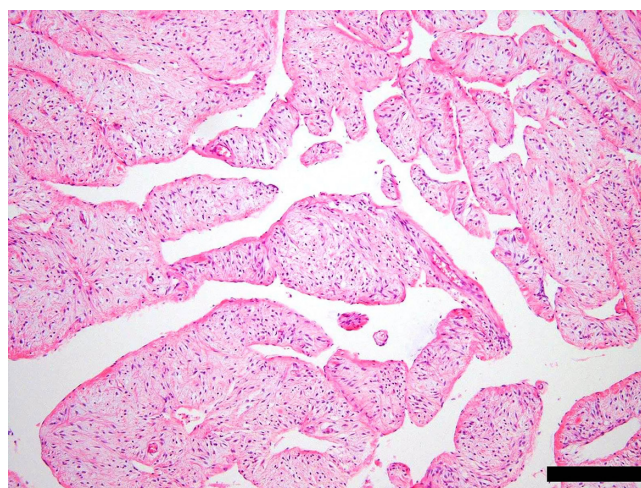
**Table 1.** The immunohistochemical markers used in this study

Antibody	Animal & Clonality	Dilution	Source
Cytokeratin AE1/3	Mouse monoclonal	Diluted	Nichirei
Vimentin	Mouse monoclonal	Diluted	Nichirei
Desmin	Mouse monoclonal	Diluted	Nichirei
CD34	Mouse monoclonal	Diluted	Nichirei
vWF	Rabbit polyclonal	1:200	Agilent
$\alpha$ -SMA	Mouse monoclonal	1:50	Agilent
Calponin	Mouse monoclonal	1:50	Agilent
Laminin	Rabbit polyclonal	1:25	Agilent
CD117	Rabbit polyclonal	1:400	Agilent
S-100	Mouse monoclonal	Diluted	Agilent

Nichirei: Nichirei Biosciences Inc., Tokyo, Japan. Agilent: Agilent Technologies Japan, Tokyo, Japan.



**Fig. 2.** Microscopical appearance of the tumor showing monotonous appearance with thin-walled branching staghorn channels (\*). The channels lined with endothelial cells (arrowhead) and thin fibrous bundles (arrow). Bar, 200  $\mu$ m.



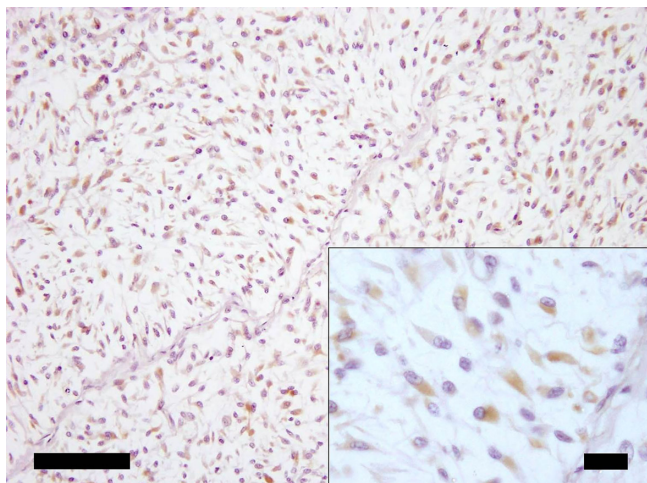
**Fig. 3.** Microscopical appearance of the tumor displaying placental growth pattern. Bar, 100  $\mu$ m.

protein identified on myoma and myopericytoma. S-100 and laminin referred to the differential diagnosis of peripheral nerve sheath tumor (PNST). CD117 is expressed in various tumors, especially GIST and mast cells, and seems to be an important indicator of tumor behavior and selection of therapeutic agents.

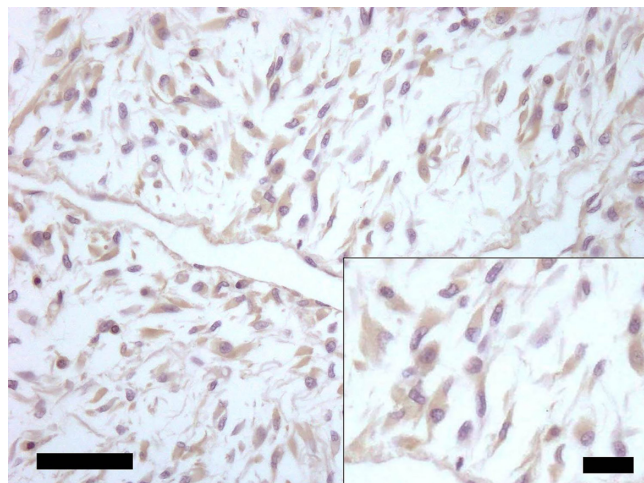
Subsequently, sections were reacted with labeled polymer with peroxidase and secondary antibody and counterstained with Mayer's haematoxylin.

Histologically a moderate number of spindle cells were proliferated with irregular admixing of thin collagen fiber. Growth patterns were mainly monotonous appearance with thin-walled branching staghorn channels, and there were also placental, and myxoid growth patterns (Figs. 2 and 3). Some blood cells were present in the staghorn channels lined with endothelial cells. There were also horny gaps without blood cells, which consisted of thin fibrous bundles. No perivascular whirling was observed. The tumor consisted of plump eosinophilic spindle cells with no atypia, and a few mitotic figures. There were large necrotic areas and scars diffusely.

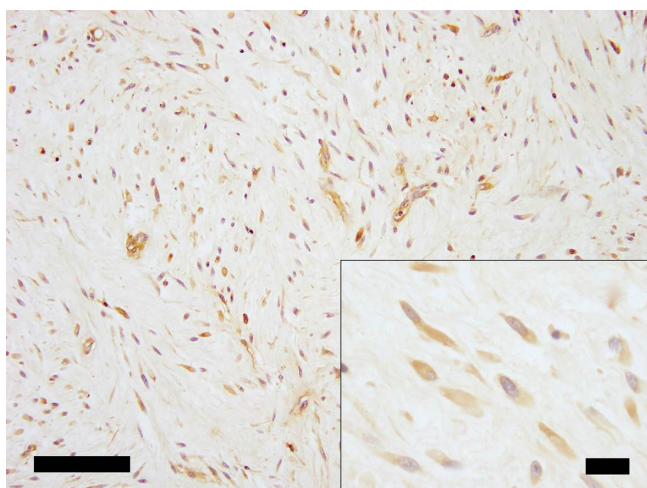
Immunohistochemically, the tumor cells were positive to vimentin (Fig. 4), CD34 (Fig. 5) and CD117 antibodies. The laminin and S-100 immunoreaction was weakly observed only in the cytoplasm (Figs. 6 and 7), and the outline of the cytoplasmic membrane did not stain with the laminin antibody. Endothelial cells of the staghorn vessels were positive for laminin and vWF antibody (Fig. 8). They were negative to cytokeratin AE1/3, desmin,  $\alpha$ -SMA (Fig. 9) and calponin antibodies (Fig. 10). Results of immunostaining compared with human SFT were shown in the Table 2 [3].



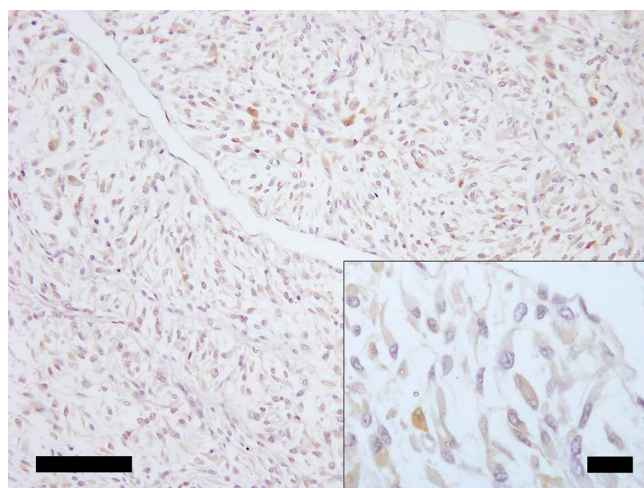
**Fig. 4.** Cytoplasmic expression of vimentin by the neoplastic cells. IHC, Bar, 100  $\mu\text{m}$ . Inset: high magnification. Bar, 20  $\mu\text{m}$ .



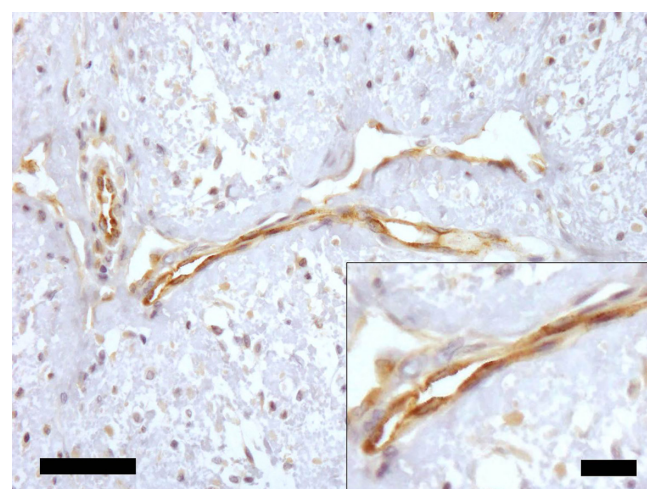
**Fig. 5.** Cytoplasmic expression of CD34 by the neoplastic cells. IHC, Bar, 50  $\mu\text{m}$ . Inset: high magnification. Bar, 20  $\mu\text{m}$ .



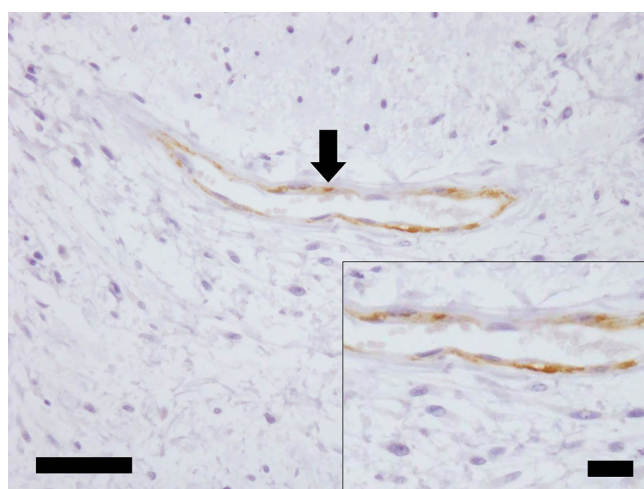
**Fig. 6.** The laminin expressed in the cytoplasm diffusely. IHC, Bar, 100  $\mu\text{m}$ . Inset: high magnification. Bar, 20  $\mu\text{m}$ .



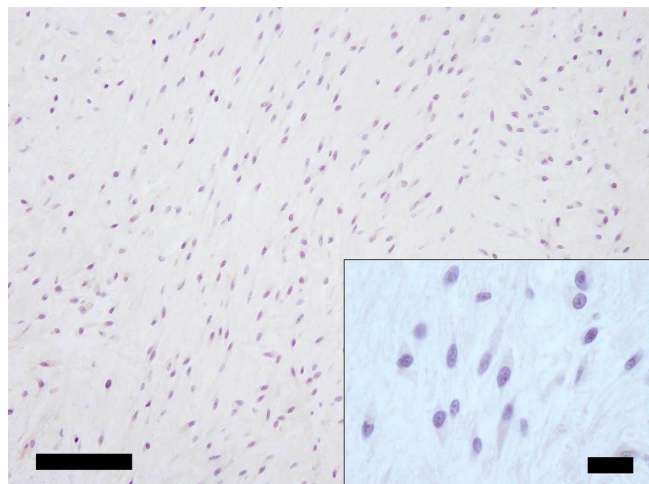
**Fig. 7.** The S-100 immunoreaction weakly observed in the cytoplasm. IHC, Bar, 100  $\mu\text{m}$ . Inset: high magnification. Bar, 20  $\mu\text{m}$ .



**Fig. 8.** Endothelial cells of staghorn vessels stained with vWF antibody. IHC, Bar, 50  $\mu\text{m}$ . Inset: high magnification. Bar, 20  $\mu\text{m}$ .



**Fig. 9.** Endothelial cells of the vessels were stained positively with  $\alpha$ -SMA (arrow), but the neoplastic spindle cells were negative. IHC, Bar, 50  $\mu\text{m}$ . Inset: high magnification. Bar, 20  $\mu\text{m}$ .



**Fig. 10.** The calponin antibody did not react with the neoplastic spindle cells. IHC, Bar, 100  $\mu$ m. Inset: high magnification. Bar, 20  $\mu$ m.

**Table 2.** Comparison of IHC results between this case and human SFT (HEP)

Antibody	This case	SFT (HEP)
Cytokeratin AE1/3	-	-
Vimentin	+	+
Desmin	-	-
CD34	+	+ (80–90% positive)
vWF	Vessels only positive	Vessels only positive
$\alpha$ -SMA	-	$\pm$ (focally positive)
Calponin	-	-
Laminin	$\pm$	NA
CD117	+	-
S-100	$\pm$ (weakly positive)	$\pm$ (focally positive)

As for canine HEP, the morphological characteristics that a spindle shape cell took concentric wholes-formed construction around capillaries have been classified in the main constituent. Avallone and others [1] subclassified canine PWTs into HEP, myopericytoma, angioleiomyoma, angioleiomyosarcoma, adventitial tumor, and angiofibroma based on histologic vascular pattern and the immunohistochemical expression. The growth pattern of perivascular whirling and bundles from media was evaluated as the PWTs having myocytic and fibroblastic feature. The tumor consistent with staghorn vascular pattern of human HEP was made a true canine HEP, and it was classified into another category from other PWTs. According to their criteria, this case was diagnosed as a rare HEP based on histological features, branching staghorn vessels and a lack of perivascular whirling.

For veterinary pathologists, the differentiation between HEP and PNST is sometimes annoying in the absence of typical morphological features, nuclear palisading and Verocay bodies. Immunostaining such as S-100, GFAP, and laminin is an important aid in such cases [7]. Although Avallone and others [1] excluded the S-100 positive tumor from their report, this case was weakly positive for S-100 immunostaining. However S-100 immunoreactivity is less consistent in canine schwannoma [2, 7]. In addition, some SFTs such as angiofibroma are S-100 positive [3], so S-100 should not necessarily be used as a standard for differential diagnosis from PNSTs. Immunoreactivity to laminin is reliable indication of canine schwannoma in which each cell is bordered by thin basal lamina. However, laminin expression in this case was found only the inside of cytoplasm weakly and no outlining membrane of each cell. Immunostaining with muscular markers, desmin,  $\alpha$ -SMA and calponin was all negative, suggesting that the likelihood of muscle related tumors such as myopericytoma and angioleiomyoma was less likely. From these immunostaining results, it was inferred that this case is close to fibrous tumor.

Human HEP has been diagnosed histologically for a long time since it was reported by Stout *et al.* [6] as a tumor of soft tissues characterized by vascular staghorn pattern. However, in recent years, attempts have been made to reclassify immunohistochemistry and genetics, and it is widely accepted that human SFT is present in a series of tumor groups having a wide spectrum of histological features, ranging from the fibrous form and the cellular form, which is previously called HEP. They consist of the same genetic abnormality, NAB2-STAT6 gene fusion and the expression of CD34, a marker of hematopoietic progenitor cell, is involved in their tissue morphology [3, 5]. As well as human HEP, CD34 is positive for canine endothelial cells and is widely expressed by most PWT including canine HEP [1]. Although the genetic abnormality was not demonstrated in this case, CD34 reactivity and the negative result of myocytic marker are important features together with histological findings. The present case was diagnosed as canine spindle cell tumor, but it should be classified into a category of fibrous tumor different from myopericytoma in canine PWT classified by Avallone and others [1].

**CONFLICT OF INTEREST.** The authors have no potential conflicts of interest to declare with respect to the research, authorship or publication of this article.

## REFERENCES

1. Avallone, G., Helmbold, P., Caniatti, M., Stefanello, D., Nayak, R. C. and Rocchbianca, P. 2007. The spectrum of canine cutaneous perivascular wall tumors: morphologic, phenotypic and clinical characterization. *Vet. Pathol.* **44**: 607–620. [Medline] [CrossRef]
2. Chijiwa, K., Uchida, K. and Tateyama, S. 2004. Immunohistochemical evaluation of canine peripheral nerve sheath tumors and other soft tissue sarcomas. *Vet. Pathol.* **41**: 307–318. [Medline] [CrossRef]

3. Gengler, C. and Guillou, L. 2006. Solitary fibrous tumour and haemangiopericytoma: evolution of a concept. *Histopathology* **48**: 63–74. [[Medline](#)] [[CrossRef](#)]
4. Hendrick, M. J. 2017. Mesenchymal tumors of the skin and soft tissues. pp. 142–175. *In: Tumors in Domestic Animals*, 5th ed. (Meuten, D. J. ed), Wiley-Blackwell, Hoboken.
5. Robinson, D. R., Wu, Y. M., Kalyana-Sundaram, S., Cao, X., Lonigro, R. J., Sung, Y. S., Chen, C. L., Zhang, L., Wang, R., Su, F., Iyer, M. K., Roychowdhury, S., Siddiqui, J., Pienta, K. J., Kunju, L. P., Talpaz, M., Mosquera, J. M., Singer, S., Schuetze, S. M., Antonescu, C. R. and Chinnaiyan, A. M. 2013. Identification of recurrent NAB2-STAT6 gene fusions in solitary fibrous tumor by integrative sequencing. *Nat. Genet.* **45**: 180–185. [[Medline](#)] [[CrossRef](#)]
6. Stout, A. P. and Murray, M. R. 1942. Hemangiopericytoma: a vascular tumor featuring Zimmermann's pericytes. *Ann. Surg.* **116**: 26–33. [[Medline](#)] [[CrossRef](#)]
7. Vandeveld, M. and Higgins, R. 2012. Neoplasia. pp. 129–156. *In: Veterinary Neuropathology: Essentials of Theory and Practice* (Overmann, A. ed), Wiley-Blackwell, Hoboken.