Case Report

Smooth Muscle Hamartoma of the Nipple in a Beagle Dog

Hiro Eda¹, Atsuko Ichikawa¹, Yoshiki Tate¹, and Yoshihiko Kobayashi¹

¹Kobuchisawa Research Laboratories, Fuji Biomedix Co., Ltd., 10221 Kobuchisawa-cho, Hokuto-shi, Yamanashi 408–0044, Japan

Abstract: A smooth muscle hamartoma of the nipple was found in a 9-month-old beagle dog. No abnormalities were observed on necropsy. Histopathologically, there was a solitary lesion measuring 3 × 1 mm in size in the dermis of the nipple. The lesion was unencapsulated but well demarcated and was composed of numerous intersecting fascicles, with the nuclei of the some of the cells being round or oval-shaped, and those of others being fusiform with blunt edges. These fascicles, associated with the nipple smooth muscle, were surrounded by a large amount of mature collagen. There was no evidence of cytologic atypia or mitotic figures. Immunohistochemistry showed positive staining for alpha-smooth muscle actin (α SMA), but negative staining for S-100 protein, cytokeratin and p63, suggesting that the lesion was derived from the smooth muscle of the nipple. Therefore, a diagnosis of smooth muscle hamartoma of the nipple was made. (*J Toxicol Pathol* 2007; **20**: 175–177)

Key words: smooth muscle hamartoma, beagle, nipple

Smooth muscle hamartoma is a rare benign skin tumor characterized by the proliferation of randomly oriented smooth muscle bundles. It is usually congenital, but may also arise later in life. In humans, it usually takes the form of a congenital skin lesion presenting as an indurated macular or plaque lesion, typically on the trunk, extremity or mammary region^{1,2}. Histologically, it is characterized by the presence of numerous well-defined, randomly oriented, thick bundles of smooth muscle fibres scattered throughout the dermis, sometimes extending into the subcutaneous tissue^{3,4}. Smooth muscle hamartomas, whether congenital or acquired, show no evidence of malignant transformation and do not appear to be associated with other congenital abnormalities. In this report, we describe a case of a smooth muscle hamartoma of the nipple in a beagle dog, with a description of its morphological characteristics.

The female beagle dog was a 9-month-old dog and was an individual in the vehicle control group of a 4-week oral repeated-dose toxicity study. At the scheduled necropsy, no abnormalities were observed in the mammary glands in the abdominal region. The mammary glands were routinely fixed in 10% phosphate-buffered formalin and embedded in paraffin. Paraffin sections were stained with hematoxylin and eosin (HE), van Gieson and Luxol fast blue stain. Immunohistochemical staining for alpha-smooth muscle

actin (α SMA), S-100 protein, cytokeratin 18 and p63 was performed by the streptavidin-biotin complex method.

Histopathologically, a solitary lesion measuring 3 × 1 mm in size was found in the dermis of the nipple. The lesion was unencapsulated but well demarcated, and was composed of numerous intersecting fascicles, with the nuclei of some of the cells being round or oval-shaped, while others were fusiform with blunt edges (Fig. 1). The cells in the fascicles contained many small to large vacuoles and scanty eosinophilic cytoplasm around the nuclei. The fascicles, associated with the nipple smooth muscle, extended in different directions and were surrounded by a large amount of mature collagen. There was no evidence of cytologic atypia or mitotic figures (Fig. 2). The cytoplasm of the cells in the fascicles were stained yellow by van Gieson stain, but were negative for Luxol fast blue. Immunohistochemistry showed positive staining for α SMA (Fig. 3), but negative staining for S-100 protein, cytokeratin and p63.

A hamartoma, which literally means a mass of tissues gone wrong, is a circumscribed malformation characterized by an abnormal mixture of non-neoplastic tissue elements, with excess or deficiency of one or more of the tissue elements in a given organ. In the skin, hamartomas may occur in the epidermis, skin appendages, dermis and/or subcutaneous tissue¹.

Cutaneous smooth muscle hamartomas have been infrequently described in humans and dogs. In humans, a smooth muscle hamartoma was first described by Stokes in 1923. Initially, these hamartomas were known as congenital smooth muscle neoplasms, however, later, a few cases of the acquired variant were also described^{5,6}. In dogs, smooth

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Mailing address: Hiro Eda, Kobuchisawa Research Laboratories, Fuji Biomedix Co., Ltd., 10221 Kobuchisawa-cho, Hokuto-shi, Yamanashi 408–0044, Japan

TEL: 81-551-36-2455 FAX: 81-551-36-3895

E-mail: jiang@fbm.co.jp

Fig. 1. Lesion in the dermis of the nipple which is unencapsulated but well demarcated and composed of numerous intersecting fascicles. H.E.stain, ×10.

Fig. 2. Fascicles composed of cells with round or oval nuclei and eosinophilic cytoplasm, are surrounded by a large amount of mature collagen. H.E.stain, ×200.

Fig. 3. Immunostaining for alpha-smooth muscle actin. The cells in the fascicles show a positive reaction for alpha-smooth muscle actin, ×200.

muscle hamartoma is usually encountered in the dorsal lumbar region. Histopathologically, it is a solitary dermal lesion, arising directly from the arrector pili muscle. The lesion is unencapsulated but well demarcated, and composed of abnormally large or thick but well-differentiated smooth muscle bundles separated by a small to moderate amount of mature collagen⁷.

Smooth muscle hamartoma is histologically different from piloleiomyoma, which is characterized by large aggregates of poorly marked, ill-defined, interlacing bundles of smooth muscle interspersed with collagen, and may compress adjacent tissue and encompass or displace follicles, with loss of the distinct perifollicular orientation of muscle cells. In contrast, smooth muscle hamartoma is characterized by well-defined distinct smooth muscle bundles surrounded by ample amounts of collagen and a normally maintained anatomic relationship between the muscle cells and hair follicles⁷. Smooth muscle lineage is evidenced by cells staining yellow with van Gieson stain and showing positive immunohistochemical staining for alpha smooth muscle actin and desmin. The features in the present case were consistent with the histopathological features of smooth muscle hamartoma associated with the nipple smooth muscle. Immunohistochemistry showed positive staining of the cells for alpha-smooth muscle actin, suggesting that the lesion was of smooth muscle origin. Based on the findings, the dog was diagnosed as having smooth muscle hamartoma of the nipple.

The cells in the fascicles were distinctly vacuolated and differentiation from peripheral nerve origin was necessary. We therefore stained the specimens with Luxol fast blue stain and also performed immunohistochemical staining for the S-100 protein. The fascicles were negative for Luxol fast blue and showed negative immunostaining for the S-100 protein; therefore, the lesion was concluded to be not of peripheral nerve origin. The lesion was located in the dermis of the nipple, therefore, it was necessary to differentiate it from a tumor arising from the mammary gland myoepithelial cells. P63 is a specific marker of myoepithelial cells in the canine mammary tissue. In the normal canine mammary glands and in mammary hyperplasia, the p63 antibody reacts exclusively with myoepithelial cell nuclei, and the labeling patterns within the benign mammary tumors are, to a large extent, consistent with those seen in normal tissues⁸. The lesion in the present study showed negative staining for both p63 and cytokeratin, indicating that it was not of myoepithelial cell origin.

In humans, smooth muscle hamartomas have been divided into two types, congenital and acquired. Until now, in all the cases of congenital smooth muscle hamartoma described, the lesion has developed from the arrector pili muscles¹⁻⁴, whereas in the cases with acquired smooth muscle hamartoma, lesions have been reported to originate from either the arrector pili or dartos muscles^{5,6}. In animals, on the other hand, there is no classification into congenital and acquired hamartomas. Cutaneous smooth muscle hamartoma in dogs has been reported to occur between 4-9

years of age and to arise from the arrector pili muscles⁷. In our case, the dog was very much younger (9 months old) than the above range, and the lesion arose from the nipple smooth muscle, leading us to make the diagnosis of congenital smooth muscle hamartoma.

References

1. Slifman NR, Harrist TJ, and Rhodes AR. Congenital arrector pili hamartoma. A case report and review of the spectrum of Becker's melanosis and pilar smooth-muscle hamartoma. *Arch Dermatol*. **121**: 1034–1037. 1985.
2. Viglizzo G, Nemelka O, Nozza P, Occella C, and Rongioletti F. Congenital smooth muscle hamartoma presenting with an unusual pseudo-Darier's sign. *Clin Exp Dermatol*. **31**: 148–149. 2006.
3. Johnson MD and Jacobs AH. Congenital smooth muscle hamartoma. A report of 6 cases and a review of the literature. *Arch Dermatol*. **125**: 820–822. 1989.
4. Holst VA, Junkins-Hopkins JM, and Elenitsas R. Cutaneous smooth muscle neoplasms: Clinical features, histologic findings and treatment options. *J Am Acad Dermatol*. **46**: 477–490. 2002.
5. Hsiao GH and Chen JS. Acquired genital smooth-muscle hamartoma. A case report. *Am J Dermatopathol*. **17**: 67–70. 1995.
6. ul Bari A and Rahman SB. Acquired smooth muscle hamartoma. *Indian J Dermatol Venereol Leprol*. **72**: 178–180. 2006.
7. Liu SM and Mikaelian I. Cutaneous smooth muscle tumors in the dog and cat. *Vet Pathol*. **40**: 685–692. 2003.
8. Gama A, Alves A, Gartner F, and Schmitt F. p63: a novel myoepithelial cell marker in canine mammary tissues. *Vet Pathol*. **40**: 412–420. 2003.