

A case of generalised cutaneous apocrine cystomatosis in a Pekingese dog

Marica Stazi  | Serenella Silvestri  | Luca Mechelli  | Chiara Brachelente 

Department of Veterinary Medicine,
Veterinary Pathology Service, University of
Perugia, Perugia, Italy

Correspondence

Serenella Silvestri, c/o Dipartimento di
Medicina e Chirurgia, Sezione di Ematolo-
gia ed Immunologia Clinica, Università degli
Studi di Perugia, Centro di Ricerche Emato-
Oncologiche (CREO), Piazzale Giorgio Mengh-
ini 9, 06132 Perugia, Italy.
Email: silvestri.serenell@gmail.com

Present address: Marica Stazi, USL Umbria 2,
Terni, Italy

Present address: Serenella Silvestri, Depart-
ment of Medicine and Surgery, Section of
Clinical Haematology and Immunology, Cen-
tre of Haemato-Oncologic Research (CREO),
University of Perugia, Perugia, Italy.

Abstract

Clinical, histological and immunohistochemical examination of a 13-year-old male client-owned Pekingese dog revealed an uncommon presentation of apocrine cutaneous cystomatosis. This is a rare non-neoplastic condition of uncertain cause, characterised by multiple cystically dilated apocrine sweat glands. We aimed to describe the features of this unusual case of generalised cutaneous apocrine cystomatosis in the dog, which can be useful to distinguish it from multifocal benign cystic apocrine tumours.

KEYWORDS

apocrine cystomatosis, cytokeratin, dogs, immunohistochemistry, Ki-67 antigen, smooth muscle actin

1 | INTRODUCTION

Apocrine cystomatosis, also called epitrichial sweat gland cystomatosis, is a rare non-neoplastic condition of middle-aged or older dogs characterised by single or multiple cystically dilated sweat glands. No sex or breed predispositions have been identified and the aetiology remains unknown, even if congenital conditions, gland duct obstruction, glandular hyperplasia with retention of the content of dilated glands or senile degenerative changes are proposed (Gross et al., 2005; López-Figueroa, 2020; Mauldin & Peters-Kennedy, 2016; Pulley & Stannard, 1990; Vilafranca et al., 1994). Macroscopically, skin lesions are often located on the head and neck and are characterised by numerous, solitary or grouped, tense to fluctuant bullae or vesicles with translucent and brownish appearance and a smooth surface. Cysts usually contain clear, watery and acellular fluid and measure up to 3 cm in diameter. Histologically, the cysts show the same morphology as normal apocrine glands, being lined by a double layer of cells composed of low cuboidal epithelial cells with apical blebbing (apocrine secretion), surrounded by myoepithelial cells (Scott et al., 2001).

We aimed to describe an uncommon case of severe cutaneous apocrine cystomatosis with a generalised distribution in a Pekingese dog. The clinical, cytological, histological and immunohistochemical findings described in this case report can be useful in differentiating this rare condition from benign apocrine tumours.

2 | CASE HISTORY

A 13-year-old male Pekingese dog was referred to the clinician with a 3-year history of multiple cutaneous nodules ranging from 0.2 to 1.5 cm in diameter, non-pruritic and indolent, involving the dorsal area of the trunk, the flank and partially extending to the neck; some solitary cysts were present on the cheeks. Benign multicentric apocrine cystadenoma was considered in the differential diagnoses (Gross et al., 2005).

Macroscopically, the lesions were single or multifocal to coalescent, had a dark brown to purple appearance and a soft elastic consistency (Figure 1).

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FIGURE 1 Skin, trunk. Bulla with translucent and brownish appearance, smooth surface with tense to fluctuant swellings

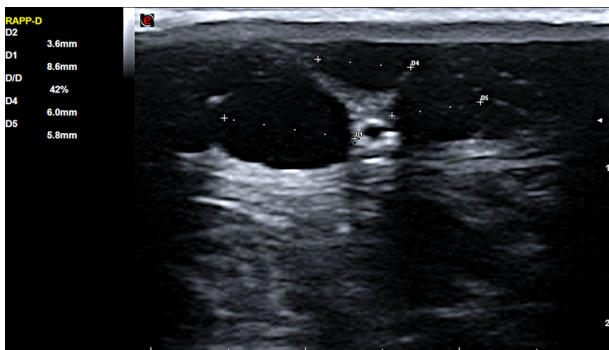


FIGURE 2 Skin. Multiple adjacent cystic formations varying in size, with a maximum diameter of 8.60 mm, are present involving different parts of dog's body. Ultrasonography.

Fine-needle aspiration from these lesions yielded about 0.3 ml of clear yellow-tinged liquid; cytological examination of the content revealed only a few macrophages and plasma cells with a pale blue amorphous proteinaceous fluid on the background.

Ultrasound examination revealed multiple cavitory round lesions, ranging from 0.1 to 0.5 cm in diameter, single or confluent, surrounded by a thin hyperechoic wall, filled with anechoic fluid and characterised by a posterior acoustic reinforcement (Figure 2).

Skin biopsies from trunk and neck were sampled, fixed in 10% neutral buffered formalin, and the serial sections of each biopsy were submitted for histological and immunohistochemical investigation.

Histological examination revealed multiple cysts, varying in size, lined by two layers of cells: an inner single layer of low cuboidal epithelium with dome-shaped apical blebbing (apocrine secretion) without morphological atypia, and an outer layer composed by myoepithelial cells that surrounded the wall. In the surrounding dermis, there was mild subepidermal fibrosis with lymphoplasmacellular inflammation (Figure 3).

Immunohistochemical staining with antibodies against pan-cytokeratin (epithelial cell marker), smooth muscle actin (α -SMA, smooth muscle marker) and Ki67 (cell proliferation marker) was performed. Briefly, after incubation with the primary antibody, a com-

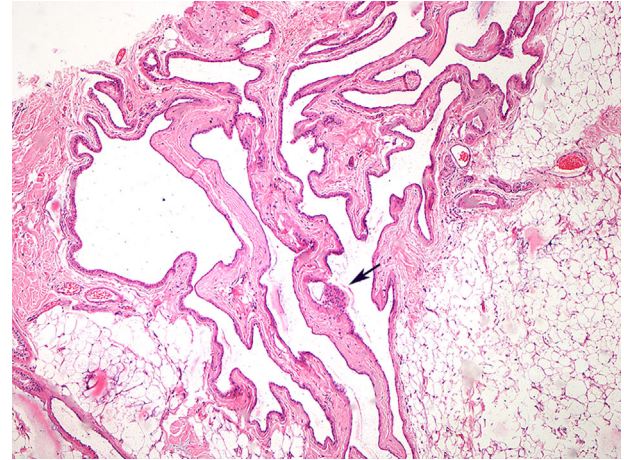


FIGURE 3 Skin, apocrine cysts. Multiple adjacent cystic lesions lined by a single layer cuboidal epithelium. Pseudopapillary projections protrude into the lumen of some cysts but show no fibrovascular core (arrow). H&E, $\times 2.5$

TABLE 1 The antibodies and protocols used for immunohistochemical evaluation

Antibody	Dilution	Incubation	Supplier
Pan-cytokeratin (AE1/AE3)	1:200	2 h RT	Dako; Golstrup, Denmark
α -SMA			
Ki67	1:150	ON 4°C	
Mouse and rabbit-specific HRP (ABC) detection IHC kit	Manufacturer instructions		Abcam; Cambridge, UK

RT, room temperature; ON, overnight.

mercially available HRP detection kit was used (Table 1); as a substrate we used the 3-amino-9-ethylcarbazole (AEC). Immunohistochemistry showed strong cytoplasmic positivity of apocrine secretory cells for pan-cytokeratin and marked cytoplasmic positivity of myoepithelial cells that surrounded the wall for α -SMA (Figure 4); the nuclei of apocrine cells were negative for Ki-67.

3 | DISCUSSION

Apocrine cutaneous cystomatosis, previously reported as apocrine cystic hyperplasia, is an uncommon cutaneous non-neoplastic condition reported in middle-aged or older dogs with no sex predilections or breed predisposition. The main differential diagnosis is multicentric apocrine cystadenoma, a true neoplasm (Gross et al., 2005). In the published literature, a single case of generalised apocrine cystomatosis was suspected in an Old English Sheepdog; however, based on histology, immunohistochemistry and biological behaviour, the authors concluded that the lesion was rather more consistent with a benign apocrine tumour (Vilafranca et al., 1994).

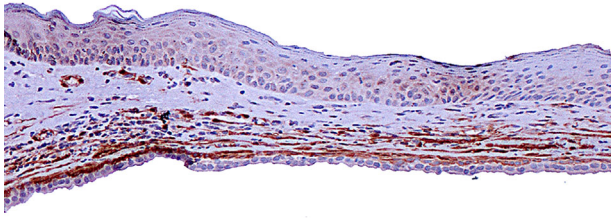


FIGURE 4 Skin, cyst wall. The outer layer is characterised by myoepithelial cells markedly positive for anti- α -SMA antibody, while the inner layer is lined by negative single-layered low cuboidal epithelial cells. Streptavidin-biotin-peroxidase complex method, Carazzi's haematoxylin counterstain, $\times 4$

A condition known as ceruminous cystomatosis is recognised in the cat and is characterised by similar lesions. A congenital condition, senile degenerative changes and obstruction of glandular ducts are suggested aetiologies also in the cat. However, differently from the canine species, the lesions are predominantly localised on the external ear canal and inner pinna, and a breed predisposition is recognised in Abyssinian and Persian cats. Additionally, otitis externa is often reported in the clinical history of cats with ceruminous cystomatosis and can be considered another possible aetiology (Gross et al., 2005; Goldschmidt & Goldschmidt, 2017). Similar lesions are also described in cats' eyelids (Giudice et al., 2009; Scott et al., 2001).

Furthermore, in a recent study apocrine cystomatosis in three young pig was described as an incidental finding at the slaughterhouse. The lesions were macroscopically and microscopically similar to those described in the dog, but the localisation was different, since the cysts were found within the subcutaneous fat of the dorsal region. Although in the swine the possible aetiologies are similar to the other species, due to the young age of the pigs, in this case senile degenerative changes were ruled out (López-Figueroa, 2020).

Similarly, in human beings, the histopathological examination of apocrine cystic lesions can occasionally pose diagnostic challenges in differentiating benign from malignant forms (Miyamoto et al., 2005). Furthermore, apocrine hidrocystoma, a retention type cyst, and apocrine cystadenoma, an adenomatous cystic tumour, uncommonly cystic lesions of apocrine glands usually found in the head and neck, are terms often used interchangeably by pathologists resulting in confusion about the nature of the disorders (Kikuchi et al., 2014; Miyamoto et al., 2005; Sugiyama et al., 2007). To facilitate the diagnosis, Sugiyama et al. (2007) classified apocrine cystic lesions in non-proliferative and proliferative types, based on the histological architecture of the cysts' wall. The non-proliferative group included lesions with a simple cystic architecture, where the wall is lined by flattened epithelium or pseudopapillary/papillary-like projections, with variable degrees of stratification and without fibrovascular core. The proliferative group included lesions characterised by cysts with true papillary projections into the cavity and composed by columnar cells with a well-established

fibrovascular core. Immunohistochemistry can be useful in distinguishing the two groups, since the non-neoplastic one shows a low proliferative index and strong positivity for α -SMA in the basal area of the lesion. Conversely, the neoplastic group shows usually a higher proliferative index, and a mild to absent positivity for α -SMA (Gross et al., 2005; Miyamoto et al., 2005; Sugiyama et al., 2007).

In our case, the cysts were lined by two populations of cells: an inner single layer of pan-cytokeratin positive, low cuboidal epithelium with apical blebbing, and an outer population of α -SMA positive myoepithelial cells. In both cell populations, no Ki-67 expression was observed as a consequence of the low proliferative activity. These results, together with the absence of a clinical progression over 3 years, would confirm the benign nature of the lesion and the diagnosis of apocrine cystomatosis. Due to the age of the dog, we may suspect that senile degenerative changes might be at the origin of the lesions in our case, but other aetiologies cannot be ruled out. Although in humans the presence of multiple apocrine hidrocystomas may be associated with inherited disorders (Vani et al., 2013), whether a genetic origin can be recognised also in the dog is unknown.

Over the years, the treatments of choice for apocrine cysts were considered surgical excision or observation without therapy (Scott et al., 2001). More recently other possible options were proposed such as chemical ablation with trichloroacetic acid, laser surgery, cauterisation and cryosurgery (Corriveau, 2012; Duclos, 2006; Loft et al., 2021; Yang et al., 2007). However, the continued formation of new lesions after removal is reported (Loft et al., 2021). In our case, due to the generalised distribution of the lesions, the dog was only monitored over time and no treatment was undertaken.

In conclusion, the clinical history, the architectural growth pattern of cysts' wall and the immunohistochemical results support the diagnosis of cutaneous generalised apocrine cystomatosis. To the best of the authors' knowledge, this is the first confirmed case in a dog. Morphological and immunohistochemical features of histologic lesions can help to distinguish hyperplastic from neoplastic apocrine lesions.

ACKNOWLEDGEMENTS

We would like to thank Dr Isabella Natalini and Dr Rita Moretti for their precious collaboration and availability.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as all the procedures were undertaken for diagnostic purposes with no original research data.

FUNDING STATEMENT

The authors received no financial support for the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Marica Stazi: conceptualisation; data curation; investigation; writing – original draft. Serenella Silvestri: data curation; investigation; visualisation; writing – review & editing. Luca Mechelli: supervision;

writing – review & editing. Chiara Brachelente: methodology; supervision; writing – review & editing.

CONFLICT OF INTEREST

No conflicts of interest have been declared.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the article.

ORCID

Marica Stazi  <https://orcid.org/0000-0002-9370-2428>

Serenella Silvestri  <https://orcid.org/0000-0002-2366-1210>

Luca Mechelli  <https://orcid.org/0000-0002-7711-700X>

Chiara Brachelente  <https://orcid.org/0000-0002-4812-3216>

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How to cite this article: Stazi, M., Silvestri, S., Mechelli, L., & Brachelente, C. (2022). A case of generalised cutaneous apocrine cystomatosis in a pekingese dog. *Veterinary Medicine and Science*, 8, 450–453. <https://doi.org/10.1002/vms3.711>