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Case Report

Sebaceous gland epithelioma with potential malignancy in a dog

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ABSTRACT

Sebaceous gland tumors consist of neoplastic proliferations of sebaceous gland cells located around hair follicles in the dermis. These tumors are subclassified as sebaceous epithelioma, sebaceous adenoma, sebaceous adenocarcinoma and nodular hyperplasia. In this case report, a nodular growth in the sacral region of an eight-year-old male Belgian Malinois dog was presented. Macroscopically, the nodular mass had a slightly soft consistency, grayish-white, and dark red-black appearance. The mass was measured in the dimension of 2x1x1 cm. Histopathologically, the tumor was observed to have a multilobular structure shaped by neoplastic cell islands. The tumor consisted mainly of eosinophilic cells with small cytoplasm resembling epithelial basaloid cells and to a lesser extent differentiated sebocytes. The parenchyma of the tumor consisted of irregular islets containing a small number of mature sebocytes. Their nuclei are oval with one to three small nucleoli. Immunohistochemically, tumor cells for Ki67 antibody showed strongly positive immunoreactivity. Based on the histopathological and immunohistochemical features, the tumor was diagnosed as sebaceous epithelioma having, a potential malignancy. Since no case of sebaceous epithelioma with malignant potential has been reported in our country, we aimed to present the case with histopathological and immunohistochemical features.

INTRODUCTION

Sebaceous gland tumors are neoplastic proliferations of sebaceous gland cells around hair follicles in the dermis of the skin. These tumors are classified as sebaceous epithelioma, sebaceous adenoma, sebaceous adenocarcinoma, and nodular hyperplasia according to the degree of differentiation of the proliferating sebaceous gland cells (Hendrick 2016). These are dog's third most common skin tumors, accounting for 21-35% of all cutaneous epithelial tumors (Vail and Withrow, 2007). Sebaceous epitheliomas are primarly seen in dogs and account for approximately one-third of all sebaceous gland tumors and 2% to 3% of all skin tumors (Goldschmidt and Goldschmidt, 2017). Epitheliomas have typical macroscopic appearances ranging from a few millimeters to a few centimeters in diameter, with well-defined borders, hard consistency, ulcerated, nodular, and fungiform structures (Skelly and Franklin, 2002). Sebaceous epitheliomas are frequently seen on the head, ears, and dorsum in dogs between 8 and 13 years of age (Goldschmidt and Goldschmidt, 2017). It has been reported that sebaceous epithelioma is a common sebaceous tumor comprising 35.7% of all sebaceous tumors in dogs (Gross et al., 2005). A case of sebaceous epithelioma resulting in death due to metastases was reported by Bettini et al. (2009). Ki67, CK18, p63, CK14 and Bcl-2 antibodies were used to evaluate the potential malignancy of sebaceous epitheliomas in dogs (Yoon and Park, 2016). However, there are no reports on histopathological and immunohistochemical characterization of sebaceous epithelioma which has malignant potential and results in death in our country. In this study, histopathological and immunohistochemical features of sebaceous epithelioma were investigated using anti-Ki67 antibody.

MATERIALS and METHODS

An 8-year-old male Belgian Malinois dog was brought to the surgery clinic with the presentation of a mass. According to the history, the swelling had developed approximately 15 days prior at the level of sacral vertebrae. The patient was reported to have no loss of appetite but had experienced weight loss. During the clinical examination, the mass was firm, elastic in consistency, and ulcerative. For induction, 0.1 mg/butorphanol, 0.025 mg/kg medetomidine and, 5 mg/kg ketamine were administered intramuscularly. Anesthesia maintenance was achieved by continuous propofol infusion of 0.5 mg/kg/minute rate. The tumor, along with the surrounding macroscopically unaffected tissues, was excised entirely. The mass was sent to the pathology laboratory. The tumor mass was 2x1x1 cm in size and weighed 7.4 g. After routine tissue processing, the tissue samples were fixed in 10% buffered formalin and embedded in paraffin. Tissue sections of about 4 µm were stained with hematoxylin and eosin (H&E). Immunohistochemical analysis was performed using antibodies for Ki67 (MIB-1, Dako). Ki 67 immunoreactivity was determined according to the avidin-biotin complex procedure. Evaluation of the proliferation index by Ki67 immunolabelling was performed according to the method of Yoon and Park (2016).

FINDINGS

Macroscopically, the nodular mass appeared grayish-white

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and dark red-black, with a slightly soft consistency. The cut surface of the mass was multilobular in appearance separated by thin fibrous tissue, and hemorrhagic, and had a similar color to its outer surface (Figure 1 A, B).

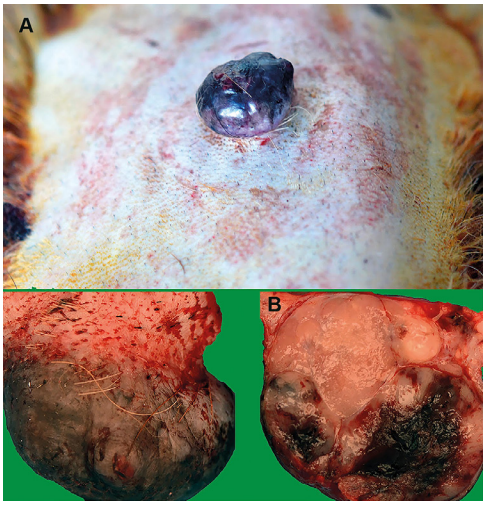

Figure 1. A) A tumoral nodular mass observed in the sacral region showing a grayish-white and dark red-black appearance. B) The cut surface was a multilobular structure separated by thin fibrous tissue, hemorrhagic, and had a similar color to its outer surface.

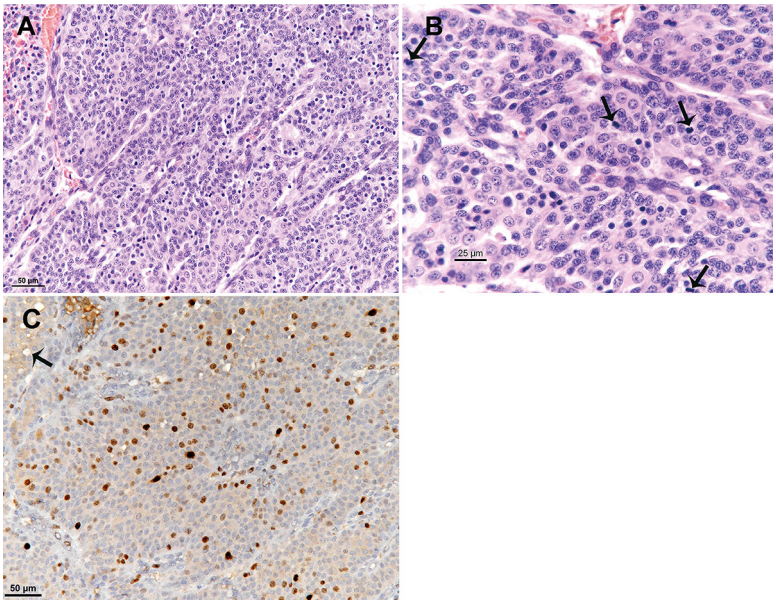

Figure 2. A) Tumor cells separated by a thin fibrovascular stroma consisted mainly of cells resembling epithelial basaloid cells with eosinophilic scant cytoplasm, round or oval nuclei, and one or three small nucleoli. HE, Scale bar = 50µm. B) Numerous mitotic figures (arrows) were observed in the parenchyma of the tumor. HE, Scale bar = 25µm. C) Immunohistochemical staining for Ki67 shows prominent immune expressions in the nuclei of many cells. The neoplastic cells have intracytoplasmic lipid vacuoles (arrow), Streptavidin Biotin Peroxidase method. Scale bar = 50µm.

Histopathological examination of the tumor mass revealed a multilobular structure consisting of tumor cell islets separated by an extensive fibrovascular connective tissue. Congestion, hemorrhage, and extensive areas of necrosis were observed in the tumor parenchyma. Tumor cells separated by an irregularly thin fibrovascular stroma reflected the characteristics of a sebaceous epithelioma pattern (Figure 2 A). The parenchyma of the tumor consisted mainly of cells resembling epithelial basaloid cells with eosinophilic scant cytoplasm, round or oval nuclei, one or three small nucleoli, and to a lesser extent of

differentiated sebocytes containing intracytoplasmic lipid vacuoles. Numerous mitotic figures, some of which were atypical in appearance, were observed in the parenchyma of the tumor (Figure 2 B). Mitoses were 4 to 6 per high power field (×400 magnification). However, mitoses are found only in the tumor cells resembling epithelial basaloid cells, not found in differentiated sebocytes. It was also observed that the foci of ductal differentiation were seen as small ducts lined by squamous epithelium and containing small amounts of keratin in some areas of the tumor parenchyma. Also, the local invasion of tumor cells was detected in peripheral lymphatics and blood vessels. To investigate the malignant potential of this case, immunohistochemistry for Ki67 was performed on sections of the tumor. Immune expressions were observed prominently in the nuclei of many cells for Ki-67. The proliferative activity index of tumor cells stained with Ki67 antibody was 35.7% (Figure 2 C). Based on these findings, the case presented here was diagnosed as sebaceous epithelioma with malignant potential.

DISCUSSION

Sebaceous glands are microscopic glands commonly found in all hairy skin areas and secrete an oily substance that lubricates the skin and hair. They also constitute the majority of hormonal metabolism in the skin (Chen and Zouboulis, 2009). The etiology of sebaceous gland tumors is not known for certain (Jakab, 2003). However, it has been emphasized that hormonal dysfunctions may play an essential role in their development (Rungsipipat et al., 2003). These tumors sometimes show locally aggressive behavior and metastasize to regional lymph nodes and other organs (Bettini et al., 2009). Although sebaceous gland tumors have been reported in all domestic animals, they are mostly reported in cats and dogs (Amaravathi et al., 2017; Goldschmidt and Goldschmidt, 2017). According to their histological characteristics and development, tumors are classified as nodular hyperplasia, epithelioma, glandular adenoma, ductal adenoma, and adenocarcinoma (Goldschmidt and Goldschmidt, 2017). Although adenomas have been widely reported in dogs, carcinomas (Amaravathi et al., 2017) have rarely been reported. Sebaceous carcinomas arise primarily on the head (39%), neck (11%) and thorax in dogs, and are similar on grossly to sebaceous adenoma and epithelioma. In carcinomas, a multilobular, solid, grey-whitish nodular mass and local invasion is the most common finding (Graham et al., 2004; Goldschmidt and Goldschmidt, 2017). Sebaceous epitheliomas typically appear as well-demarcated, firm, nodular, fungiform, or plaque-like masses in varying sizes, frequently with ulceration (Gross et al., 2005), and occur most often on the head, ears, and dorsum in dogs between 8 and 13 years of age (Goldschmidt and Goldschmidt, 2017). In the case presented here, the macroscopic appearance of the tumor mass was similar to those of sebaceous epithelioma described by Gross et al. (2005) and Goldschmidt and Goldschmidt (2017).

It has been reported that in sebaceous adenocarcinomas, histologically, the neoplastic cells have intracytoplasmic lipid vacuoles, but the degree of lipidisation varies from cell to cell and without significant amounts of well-differentiated small basaloid cells. The nuclei of tumor cells are reported to be large, chromatic, with prominent nucleoli and moderately pleomorphic. It was also reported that the number of mitotic figures was variable but atypical mitoses were also present. Mitotic figures will be found involving differentiated sebocytes as well as reserve cells, whereas in sebaceous epitheliomas mitoses are found only in the reserve cells (Goldschmidt and Goldschmidt, 2017). It has been reported that the histological pattern of sebaceous epitheliomas is very characteristic; the parenchyma of the tumor is mainly composed of a predominance of small basophilic reserve cells with fewer sebocytes. The reserve cells may show considerable mitotic activity. Also, there are foci of ductal differentiation lined with squamous epithelium and containing small amounts of keratin. The differentiation from sebaceous adenocarcinoma is based on the fact that the tumor cells have less cellular and nuclear pleomorphism and mitoses are not found in differentiated sebocytes (Bettini et al., 2009; Goldschmidt, 2017). In the case presented here, the parenchyma of the tumor was similar to those of sebaceous epitheliomas described by Bettini et al. (2009) and Goldschmidt and Goldschmidt (2017). In addition, the tumor was considered to have a potential malignancy due to the presence of numerous mitoses, some of which were atypical, in the reserve cells and local infiltration of peripheral lymphatics and blood vessels.

It has been reported that sebaceous epitheliomas are of low-grade malignancy and local infiltration frequently occurs. Therefore, recurrence occurs in incompletely excised neoplasms, but widespread metastases are rarely observed, and tumor cells spread to the mandibular lymph nodes and head region via lymphatics in metastasis cases (Gross et al., 2005; Bettini et al., 2009; Goldschmidt and Goldschmidt, 2017). The application of anti-CK14, CK18, p63, Ki67 and Bcl-2 antibodies in sebaceous epithelioma cases has been reported to be useful in the diagnosis and prognosis of these tumors (Yoon and Park. 2016). To differentiate between sebaceous carcinomas and benign sebaceous tumors in humans, proliferating cell nuclear antigen and Ki67 markers are used (Cabral et al., 2006). Bettini et al. (2009) recorded the proliferative activity index of Ki67 as 51.6% to 68% in a dog with metastatic (multiple lung and central nervous system metastases) sebaceous epithelioma. Yoon and Park (2016) recorded the proliferative activity index of Ki67 as 13.1% in a dog. In our case, the proliferative activity index of tumor cells stained with Ki67 was 35.7% and the tumor cells were histologically found to be locally invaded into the lymphatic and blood vessels. These findings indicate that the tumor might have a high metastatic potential. But in this case, the metastatic tumor foci were not observed in the other regions of the skin. Also, there was no information about the presence of metastases in the internal organs during the operation. However, although the tumor mass was completely incised with a successful surgical excision, the anamnesis taken six months later revealed that the general condition of the dog continuously deteriorated and the dog died.

CONCLUSION

As a result, in such cases, even if the animal is diagnosed with sebaceous epithelioma, a surgical intervention must be performed very carefully and the postoperative process must be managed very well due to the high metastatic potential of

these tumors.

DECLARATIONS

Ethics Approval

Not applicable.

Conflict of Interest

The authors declare that they have no conflict of interest.

Consent for Publication

Not applicable.

Author contribution

Idea, concept and design: ÖFK, CK.

Data collection and analysis: ÖFK, YK, CK.

Drafting of the manuscript: ÖFK, HAÇ.

Critical review: ÖFK, CK, HAÇ.

Data Availability

The data used to prepare this manuscript are available from the corresponding author when requested.

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