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Diagnosis of Mammary Carcinoma in a Castrated Male Maltese Dog

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Abstract : A 12-year-old castrated male Maltese dog was presented with a small-sized mass at the left fifth mammary gland. The dog had concurrent poorly responsive pruritus affecting the feet, pinnae, and trunk, a cystolith, and biliary sludge. Serum chemistry revealed elevated liver enzymes. The mammary gland mass was cytologically diagnosed as an early-stage mammary simple carcinoma and was surgically excised. Nine months after the diagnosis of the mammary carcinoma, hyperadrenocorticism was confirmed by adrenocorticotropic hormone stimulation test. This report describes the clinical signs, diagnostic imaging findings, and prognosis in a castrated male Maltese dog with mammary carcinoma.

Key words **:** mammary carcinoma, male, dog, hyperadrenocorticism.

Introduction

Mammary gland tumors (MGT) are the most common tumor in female dogs, constituting 70.5% of all tumors, 50% of which are malignant (10,12,18). However, MGT in male dogs are rare; one study reported the incidence from 1994 to 2004 as 4/100,000 (17). Unlike female MGT, malignancy in male MGT is low (2,11,17). Sex hormones are assumed to play an important role in the development of MGT, as ovariohysterectomy significantly reduces the risk of MGT in female dogs (21). The main risk factor of MGT in male dogs is hormonal abnormalities, especially testicular neoplasm that causes sex hormone imbalance (7,24). Diagnostic imaging modalities such as radiography, ultrasonography, and computed tomography (CT) are useful, non-invasive diagnostic tools for evaluating and staging canine MGT. Radiography and CT are used to evaluate pulmonary metastasis and calcification (10,16). Ultrasonography provides information about the size, shape, margins, internal structure, and vascularity of the MGT (1,13,15,18,23). Surgical removal of the affected mammary gland is the mainstay treatment (2,11,14,17). This report describes clinical signs, findings of diagnostic imaging, treatment, and prognosis in a castrated male Maltese dog with mammary carcinoma.

Case Report

A 3.8 kg, 12-year-old castrated male Maltese dog was presented with a subcutaneous mass on the left fifth mammary gland. The dog had concurrent pruritus affecting his feet, pinnae, and trunk, which had been poorly responsive to long-term therapy. A firm and small-sized mass on the left fifth mammary gland was identified. Serum chemistry profile revealed an elevated total protein level and increased liver enzyme levels including markedly high alkaline phosphatase (> 3,500 U/L, reference range 47-254 U/L), with moderately elevated alanine transaminase (151 U/L, reference range 17-78 U/L) and gamma-glutamyl transferase (32 U/L, reference range 5-14 U/L).

Right lateral and ventrodorsal radiographs of the thorax and abdomen were obtained. Abdominal radiography showed a subcutaneous, soft-tissue opacity, ovoid mass without calcification overlapping the os penis at the caudal abdomen (Fig 1). In addition, a small, mineral-opacity calculus was identified in the urinary bladder. There were no significant findings on thoracic radiography. Ultrasonography of the abdomen and mammary glands was performed using linear multifrequency transducer (Prosound F75, Hitachi; Tokyo, Japan). The subcutaneous mass at the left fifth mammary gland appeared as a well-demarcated, oval-shaped homogeneously

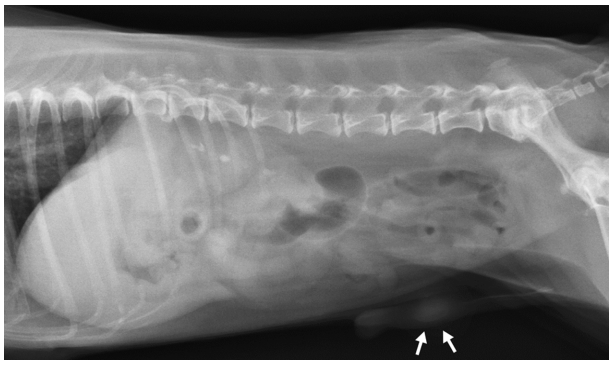

Fig 1. Right lateral radiograph of the abdomen in a male dog with a mammary gland mass. Ovoid mass with soft-tissue opacity in ventral subcutaneous layer is overlapping the os penis (arrows). Calcification of the nodule is not observed.

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hypoechoic mass. Furthermore, ultrasound examination revealed multiple hypoechoic, well-circumscribed, round nodules in the liver parenchyma, moderate amounts of echogenic sludge with intact gallbladder wall, and a hyperechoic cystolith showing acoustic shadowing with normal urinary bladder wall. Other abdominal organs including intestines, adrenal glands, and lymph nodes were normal.

A thoracoabdominal CT examination was performed using 32-Multislice CT (Alexion™, Toshiba; Otawara, Japan). The patient was scanned in dorsal recumbency under general anesthesia. The scanning parameters were as follows: 120 kV, 200 mA, 1.0 mm slice thickness, and 0.75 s rotation time. Contrast studies were performed after intravenous administration of 600 mgI/kg iohexol (Bonorex 300 Inj.; Daehan Pharm, Korea) injected for 20 s using an autoinjector (Medrad®, Bayer Healthcare LLC; Whippany, USA). Non-contrast CT image and post-contrast CT images of the arterial, portal-venous, and delayed phases were obtained. The CT images were evaluated in the soft-tissue window (window width, 450 HU; window level, 40 HU) and lung window (window width, 1600 HU; window level, −550 HU). Imaging by CT displayed a homogeneous, soft-tissue attenuating, smoothly marginated, round mass (5.9 × 7.2 × 10.6 mm) in the ventral subcutaneous region of left fifth mammary gland lateral to the os penis (Fig 2). The mass showed a progressive contrast enhancement pattern on contrast study. The mean attenuation value of the nodule was 45 HU in non-contrast and 95 HU in post-contrast delayed phase. There was no apparent metastasis to the lungs, lymph nodes, or other organs.

Subsequently, ultrasound-guided fine-needle aspiration samples were taken from the mammary gland mass and liver nodules. The mammary gland cytology was consistent with early-stage mammary simple carcinoma, and the hepatic nodules were diagnosed as hepatic nodular hyperplasia. Cytologically, the mammary gland mass showed clusters of neoplastic epithelial cells arranged in sheets or acinar forms. The neoplastic epithelial cells were characterized by moderate anisokaryosis, prominent nucleoli, high nuclear-cytoplasmic ratio with occasional mitotic figures (Fig 3). A simple mastectomy of the affected mammary gland was performed. Histopathological examination was not performed because of owner's refusal for financial reasons. No recurrence was noted during a follow-up one year later.

Nine months after the diagnosis, the dog was presented again with persistent, poorly responsive pruritus as the chief complaint. Ultrasonographically, the sizes of both adrenal glands were within the normal range. However, on adrenocorticotropic hormone (ACTH) stimulation test, the pre-ACTH cortisol level was 3.5 μg/dL (reference range, 2-6 μg/dL) and the post-ACTH cortisol level was 23.8 μg/dL (reference range, 6-18 μg/dL), as would be expected with hyperadrenocorticism. The dog was given 1 mg/kg of oral trilostane (Vetoryl®, Dechra Ltd; UK) twice daily, and the pruritus diminished after 3 months of treatment.

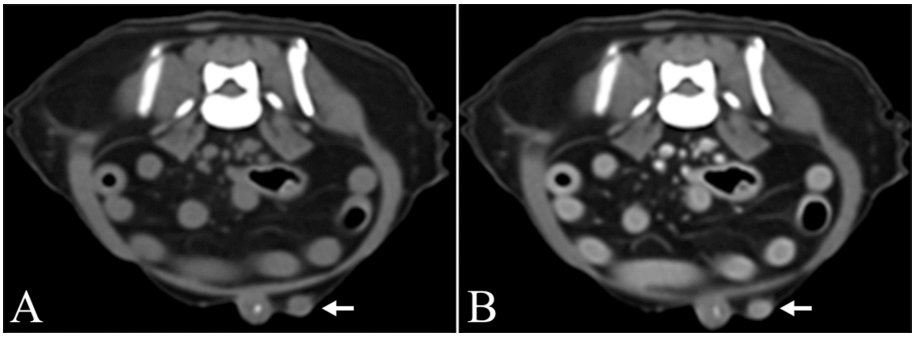

Fig 2. Non-contrast (A) and post-contrast (B) transverse CT images of a male dog with a mammary gland mass. The soft-tissue attenuating, homogeneous, smoothly marginated, round mass along the ventral subcutaneous region is homogeneously contrast enhanced (arrows). Maximal diameter of the mass is 7.4 mm.

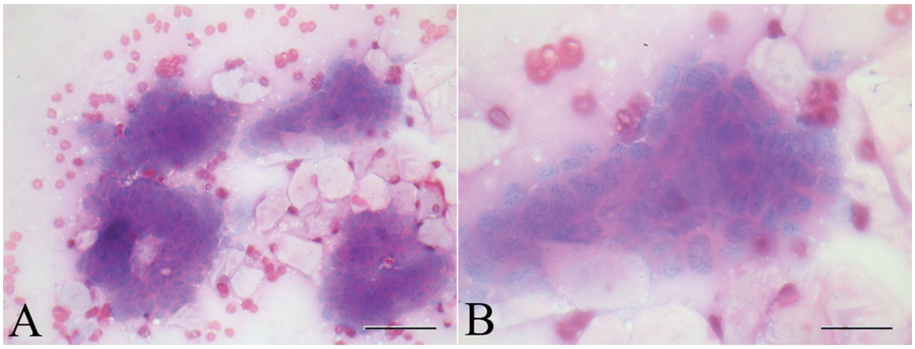

Fig 3. Cytology of the mammary gland mass (A, B). A cluster of neoplastic epithelial cells arranged in sheet form is seen. The cells are characterized by moderate anisokaryosis, prominent nucleoli, high nuclear-cytoplasmic ratio with occasional mitotic figures. Hematoxylin and eosin stain. Bar = 50 μm (A) and 25 μm (B).

Discussion

Although cases of MGT in male dogs are scarce, some common characteristics have been detected. In three recent studies investigating 42 MGT in 33 male dogs, only one tumor was histologically malignant. The average age at the time of diagnosis was between 9.2 and 11.5 years, and 30 of 33 patients were purebred dogs. Twenty-two of 33 dogs were castrated; however, no difference in the relative risk of MGT development between intact males and castrated males was found (2,11,17). In this report, the dog was a 12-year-old, castrated male purebred dog, consistent with previous reports. However, male Maltese dogs with MGT had not been previously reported, and this tumor was a malignant simple carcinoma. Age is reported to be a risk factor for malignancy of canine MGT, as the mean age of the dogs with malignant MGT is higher than that of dogs with benign tumors (2,10, 17,22,26). The age of the patient may have been associated with the malignancy of the tumor in this study. Although histology was not conducted in the present case, previous study reported 96.5% of diagnostic accuracy and 100% of positive predictive value for the diagnosis of malignancy by fine-needle aspiration of canine MGT (19).

On ultrasonography, benign MGT appears to be oval or round and homogeneous, with circumscribed margins. In contrast, malignant MGT appears to be irregularly shaped and heterogeneous, with spiculated or microlobulated margins, and the depth-to-width ratio is higher than 0.7 (1,23). In a single study describing CT features of canine MGT, the pattern of calcification according to the Breast Imaging Reporting and Data System classification can be used to distinguish malignant from benign MGT (10). Benign patterns include a distinct rim, dystrophic, punctate, and popcorn-like calcifications, while suspicious patterns include fine linear, amorphous, and coarse heterogeneous calcifications. In addition, the mean maximal diameter of the malignant tumors (4.59 ± 3.32 cm) is significantly larger than that of the benign tumors (1.68 ± 0.96 cm). Contrast enhancement, margins, surface, and morphology are not significantly different between benign and malignant tumors (10). In this study, the MGT showed benign characteristics on ultrasonography and CT, unlike the cytologic diagnosis, which showed features of simple carcinoma. This discrepancy may be a result of histopathologic shift of the small-sized, early-stage MGT, from benign to malignant. This hypothesis is based on previous canine MGT studies that proposed the possibility of histopathological progression from a benign tumor to malignancy as the size of the tumor increased (22). There has been one reported case of male MGT that transformed from a papillary cystadenoma to squamous cell carcinoma (17).

Malignant MGT metastasizes mainly to the lung and regional lymph nodes (4,20). The mean survival time of dogs without metastasis is higher than that of dogs with metastasis to other body systems (3,4,20,25). Using the TNM classification system, stage one dogs had a survival of 97.9% two years after a mastectomy (25). The survival rate of dogs with stage one MGT is significantly higher than that of dogs in other stages (8,25). In this case, the tumor was classified as $T_1N_0M_0$ or stage one based on radiography, ultrasonography, and CT findings. The dog survived to follow-up of one year after the mastectomy, and tumor recurrence had not occurred, consistent with previous survival reports. Presurgical staging of MGT by imaging modalities is imperative for predicting patient prognosis.

The development of MGT is associated with sex hormones in males as well as females (11,17,21). In a previous study of male dogs with MGT, strong estrogen receptor expression levels were detected by immunohistology in all MGT included, and another study also found high serum estrogen level in male dogs with MGT (11,17). Nevertheless, few studies have assessed risk factors of MGT in male dogs, such as hormonal abnormalities, particularly with testicular disorders (7,24). In this case, the dog was castrated at a young age, reducing the possibility of testicular disorders. At the time of the diagnosis, no hormonal disease had been identified; however, hyperadrenocorticism was diagnosed nine months later.

Hyperadrenocorticism that is associated with sex steroid excess lacks the typical clinical signs of hyperadrenocorticism, such as polyuria and polydipsia, and rather presents primarily as skin disease (6). Increased alkaline phosphatase, alanine transaminase, and gamma-glutamyl transferase are common findings in dogs with sex steroid excess. Uroliths and cholestatic diseases are also common in dogs with hyperadrenocorticism (5,9). In the present case, the dog had numerous findings consistent with hormonal imbalance described in previous studies, including poorly responsive pruritus, calculus in urinary bladder, sludge in gallbladder, and increased liver enzyme levels. This suggests the dog might have had undetected hyperadrenocorticism at the time of the MGT diagnosis. Undetected hyperadrenocorticism in this dog might have caused excessive sex steroid hormone levels and eventual development of MGT. In addition, there were two dogs with hyperadrenocorticism included in a previous study of MGT in male dogs (2). With such low incidence of MGT in male dogs, further investigations are needed to elucidate the relationship between hyperadrenocorticism and MGT.

Conclusions

This study described MGT in a castrated male Maltese dog. Unlike most MGT in male dogs, this tumor was malignant, identified as a mammary simple carcinoma without metastasis. Although findings on imaging examinations including radiography, ultrasonography, and CT were not consistent with the cytological diagnosis, they were useful in determining prognosis by ruling out metastasis and staging the neoplasm.

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