

<Case report>

Metastatic lipid-rich mammary carcinoma in a dog

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Abstract : An adult female dog was presented for evaluation of mammary gland masses. Complete blood count and serum chemistry data were within normal limits. Fine-needle aspiration cytology of the mammary masses revealed clusters of malignant epithelial cells with clear cytoplasmic vacuoles. Based on histopathological findings, a diagnosis of lipid-rich mammary carcinoma was made. Approximately 5 weeks after surgical removal, the tumor recurred at the surgery site and metastasis to the tibia was detected. Due to the poor prognosis and deterioration of the condition, the dog was euthanized.

Keywords : dogs, lipid-rich carcinoma, mammary, metastasis

Mammary gland tumor is one of the most common neoplasms in female dogs, accounting for 25 to 42 % of canine neoplasms [6]. Annual incidence rate of canine mammary tumors has been estimated at 205/100,000 [4]. In dogs, the ratio of malignant to benign mammary gland tumor is approximately 1 : 1 [1]. Simple carcinoma predominates in malignant mammary tumors, and both complex adenomas and benign mixed tumors are the most common among benign counterparts [7, 10]. Other histological subtypes of carcinomas in mammary gland are uncommon, and lipid-rich carcinomas are relatively rare in veterinary literature [5, 10]. Despite the small number of clinical cases, the prognosis of the lipid-rich carcinomas is known to be extremely poor [5]. The present report describes a canine lipid-rich carcinoma with tibial metastasis in an adult dog.

An intact, adult, female German shepherd dog was presented to the Veterinary Medical Teaching Hospital, Seoul National University (VMTH-SNU), for the evaluation of two masses in mammary glands. Upon physical examination, the larger mass was 12.5 × 6.0 × 12.2 cm in size, affecting both left and right 5th mammary glands. The tumor was solid, and margins were indistinct with adhesion to the surrounding tissues. The skin overlaying the tumor was erosive. The smaller mass, approximately 0.5 cm in diameter, was present in the left 3rd mammary gland. Upon palpation, the mass was solid, mobile, and well-circumscribed, but located deep within

underlying subcutaneous tissues. The sizes of the regional lymph nodes were within normal limits. Complete blood count and serum chemistry were within normal limits except mild thrombocytosis. Thoracic radiographs revealed no significant abnormalities.

For cytological examination, fine-needle aspiration (FNA) was performed from the mass in the right 5th mammary gland. The FNA revealed a high cellularity of epithelial cells mainly arranged in aggregates and clusters (Fig. 1A). The neoplastic cells were characterized by small to moderate amount of basophilic cytoplasm with variably-sized vacuoles that peripheralized the nucleus (Fig. 1B). The nuclei were round to oval and had clumped to coarse chromatin, and single to multiple nucleoli with occasional macronucleoli. Anisocytosis and anisokaryosis were moderate to marked. Bi- and multinucleated cells and aberrant mitotic figures were occasionally observed. Abundant lipid droplets were scattered in the background. Based on the FNA cytology features, the mammary aspirates were interpreted as mammary carcinoma with moderate to marked malignancy.

Both left and right 5th and left 3rd mammary gland masses were removed by radical excisional mastectomy. Grossly, the former was solitary, round to oval, and 13 × 6.5 × 14 cm in size, extending to the underlying dermis and subcutaneous tissues (Fig. 2A). The tumor consisted of variably sized, gray-colored, multiple nodules on cut surface (Fig. 2B). The

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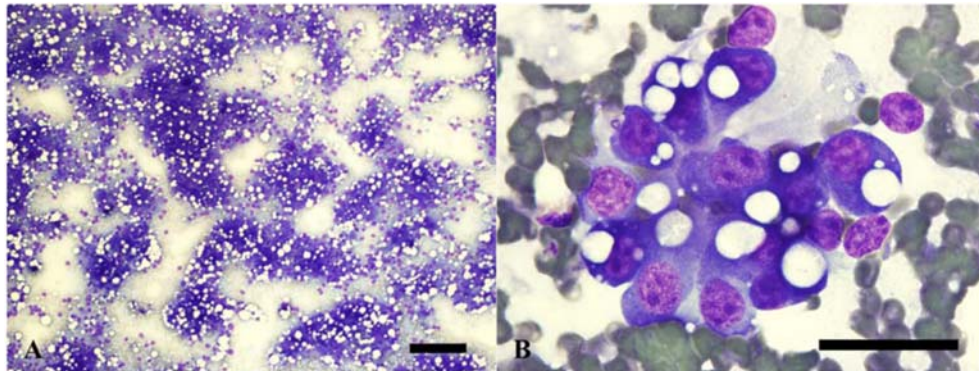


Fig. 1. Fine-needle aspirates of the 5th mammary gland mass in a dog. (A) Note the high cellularity and epithelial cells in small to large clusters with abundant lipid droplets in the background. (B) The cohesive cluster of neoplastic cells containing large clear vacuole and peripheralized nucleus is present. Aqueous-based Wright; HP oil, A: $\times 100$, B: $\times 1,000$. Scale bars = 200 μm (A), 50 μm (B, enlarged).

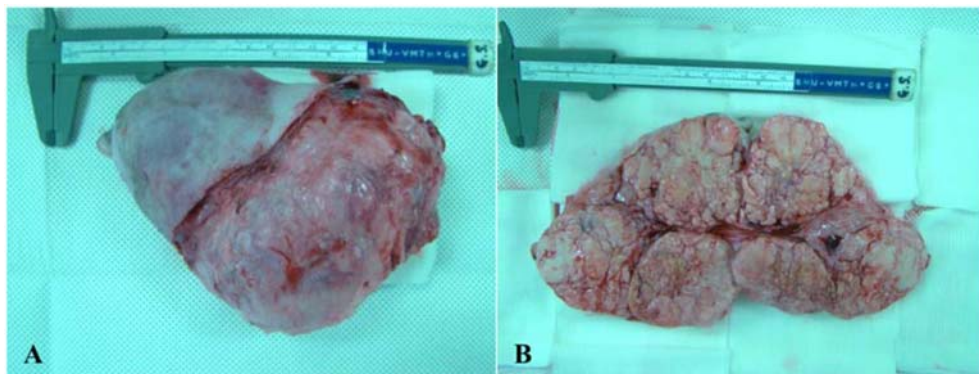


Fig. 2. Gross morphology of the right 5th mammary gland tumor in a dog. (A) The tumor is 13 \times 6.5 \times 14 cm in size, and exhibits sessile growth with nodular lesions. (B) On the cut surface, the tumor is subdivided into grayish white multiple nodules with well-demarcated borders.

latter was found to be solitary, round, and slightly firm on palpation. The masses were fixed in 10% neutral-buffered formalin, routinely processed and embedded in paraffin wax. Four μm sections were prepared and stained with hematoxylin and eosin (H&E).

Microscopically, the neoplastic tissue of the right 5th mammary gland consisted of small to medium nests which were separated by delicate fibrovascular stroma (Fig. 3A). The majority of the neoplastic cells contained multiple small lipid droplets and/or single, large lipid vacuoles in the cytoplasm, displacing the nucleus peripherally (Fig. 3B). The neoplastic cells exhibited moderate to marked anisocytosis and anisokaryosis. Frequent nuclear atypia and occasional mitotic figures were observed. Invasion of neoplastic cells into blood or lymphatic vessels was occasionally observed (Fig. 3B, insert). Additionally, the Sudan III method and Oil-red O staining were performed to the paraffin-embedded tumor tissue sections in order to illustrate the presence of lipid deposition, but the results of the staining were negative possibly due to loss of the lipid contents during the tissue processing. Nevertheless, the morphological feature of intracytoplasmic vacuole was highly consistent with lipid droplet, but not with glyco-

gen deposition. Based on the microscopic findings, the right 5th mammary gland mass was diagnosed as lipid-rich carcinomas with tumor emboli. Meanwhile, the left 3rd mammary gland mass was diagnosed as mammary gland lobular hyperplasia.

The dog was discharged without major postsurgical complications. Approximately 5 weeks after the surgery, the patient revisited the VMTH-SNU for the evaluation of the lameness affecting left hind limb. Upon physical examination, multiple masses with various sizes, ranging from 0.5 cm to 4 cm, were detected in both right 4th and 5th, and left 3rd mammary glands. Orthopedic examination revealed moderate atrophy of left femoral muscle and bilateral hip dysplasia with crepitus. Radiographic examination of hind limbs showed cortical bone lysis in the left proximal tibia (Fig. 4A). Thoracic radiographs were within normal limits. Pelvic radiographs revealed an oval mass with soft tissue opacity ventral to 6th and 7th lumbar vertebrae. FNA was prepared from the proximal left tibia. Cytology findings were similar to those of the aspirates from the 5th mammary gland mass which had been surgically removed (Fig. 4B). Based on the patient's history, clinical findings, radiographs, and cytology evalua-

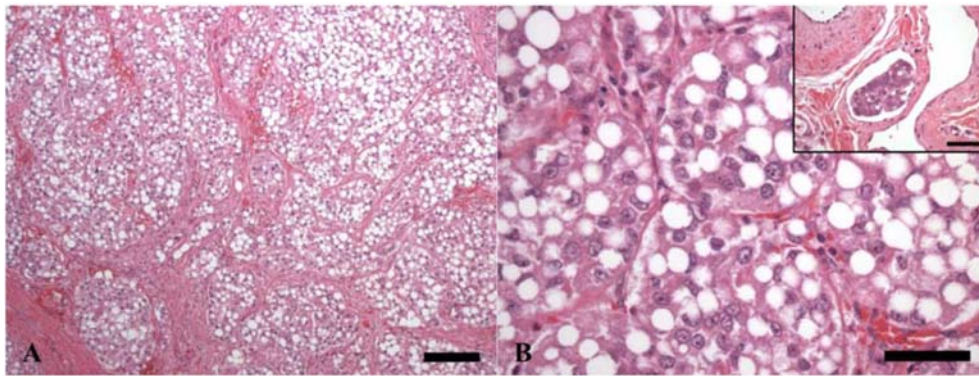


Fig. 3. Histological section of the lipid-rich mammary carcinomas in a dog. (A) Note the area of solid nests of neoplastic epithelial cells separated by fine to moderate fibrovascular stroma. (B) Individual neoplastic cells contain single, large lipid vacuole and a peripheralized nucleus. (insert; tumor cell emboli within a lymphatic). H&E stain, A: $\times 100$, B: $\times 400$, insert: $\times 400$. Scale bars = 200 μm (A), 40 μm (B), 40 μm (Insert, enlarged).

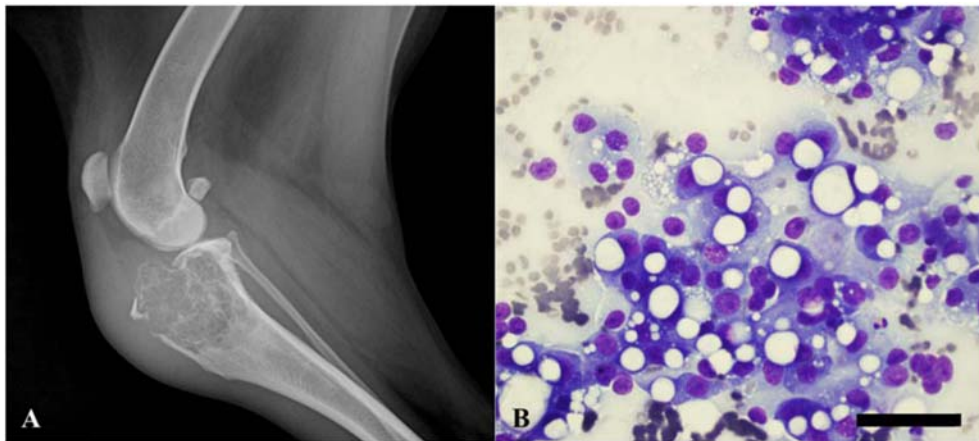


Fig. 4. (A) Mediolateral radiographic view of left stifle joint in a dog. Geographic and permeative bone lysis with partial cortex destruction is present in the left proximal tibia. (B) Fine-needle aspirates of the affecting osteolytic lesion in the left proximal tibia. Neoplastic cells revealed moderate to marked anisocytosis, anisokaryosis, and prominent nucleoli. Note the abundant intracytoplasmic lipid vacuoles and peripheralized nucleus. Aqueous-based Wright; HP oil, B: $\times 400$. Scale Bar = 40 μm , enlarged.

tions, diagnosis of metastatic lipid-rich mammary carcinoma was made. Approximately 11 weeks after the mastectomy, the patient was euthanized due to devastating clinical condition and poor prognosis.

Mammary carcinomas in dogs are classified into non-infiltrating carcinomas, complex carcinomas, simple carcinomas, and other variant types of carcinomas based on histological structures and cell types arising from mammary gland [10]. Lipid-rich carcinoma has been considered a rare variant of ductal carcinomas and morphologically characterized by neoplastic cells that contain a large amount of lipid in the cytoplasm [10, 14]. To date, lipid-rich carcinoma of the mammary gland has been reported in only 15 dogs [5, 9, 11-13, 15]. Biological behavior of lipid-rich carcinoma is reportedly aggressive and prognosis is poor [11, 12, 15]. A retrospective study encompassing seven dogs with lipid-rich carcinomas revealed that 5 out of 7 tumors recurred, and metastases to local and distant organs were determined [5]. Consistent

with published reports, the present case was characterized by recurrence and distant metastasis. Underlying mechanisms driving the malignant behavior of the lipid-rich carcinomas remain uncovered. Le *et al.* [8] noted that lipid droplets in the tumor cells might play an important role in the clinical aggressiveness. The lipid droplet has been considered a secretory product synthesized by apocrine tumor cells rather than the results of cellular degeneration changes [12]. It has been suggested that intracellular accumulation of lipids permits the survival of the circulating cancer cells in the blood by inducing membrane phase separation, which reduces cell to cell contact and promotes tissue invasion [8].

Many organs including regional lymph nodes, lung, brain and bone have been associated with the spread of tumor in canine mammary carcinomas [2]. Among these organs, regional lymph nodes and lungs are common destinations of metastatic cancer cells, and bone marrow involvement of canine mammary tumors is infrequent [3, 10]. After the euthanasia,

the postmortem examination was not performed to evaluate potential metastasis in distant organs. Although radiographs did not reveal suspected metastatic lesions, it was still possible that clinically undetectable micrometastasis could exist in various organs, particularly sublumbar lymph node. Approximately 40-60% of dogs with the mammary carcinoma have an evidence of micrometastasis at their first presentation [10]. High resolution imaging techniques and histopathological examination of the regional lymph nodes might be necessary for the detection of micrometastatic spreads.

In summary, the present report describes clinical, cytological and histopathological findings of a metastatic lipid-rich carcinoma in an adult dog. To the best of our knowledge, this is the first report of lipid-rich mammary carcinoma with metastasis to the tibia. The present case could make a valuable contribution to expand the knowledge about the rare subtype of canine mammary tumor.

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