Explor Anim Med Res.
Vol. 15, Issue 1, 2025
DOI: 10.52635/eamr/15.1.145-149

ISSN 2277-470X (Print), ISSN 2319-247X (Online)
Website: www.animalmedicalresearch.org

Short Communication

CASE STUDY: MALIGNANT MIXED MAMMARY TUMOR IN DOG

Dibyendu Biswas[1], Shib Shankar Saha[2], Mostafijur Rahman[2]

Received 24 July, 2024, revised 15 June 2025

ABSTRACT: A street bitch underwent surgery to remove a tissue mass that developed on the left thoracic mammary gland. The procedure was performed on an adult dog presenting with a growing mass in the mammary gland, tentatively diagnosed as a benign tumor. A surgical intervention was carried out to excise the tissue mass, and a sample was collected for pathological investigation of suspected mammary tumor tissues. Histopathological analysis of the affected tissue employed routine staining with hematoxylin and eosin, along with the routine paraffin embedding technique. In histopathology, the tissue exhibited significant pleomorphic, neoplastic proliferated lipid cells, myofibroblast, anastomosing blood vessel and smooth muscle cells scattered in the mucosa and submucosa. Morphologically, the cancerous tumor tissue was diagnosed as a case of malignant mixed mammary tumor (MMMT) in the mammary gland of the bitch. Following the successful surgical removal of the tumor mass, the patient experienced a complete recovery.

Keywords: Malignant mixed mammary tumor, Dog, Histopathology.

Malignant Mixed Mammary Tumors (MMMTs), alternatively referred to as carcinosarcomas, are highly aggressive and intricate neoplasms that manifest in the mammary glands of canines. These tumors exhibit the coexistence of both glandular (epithelial) and connective tissue (mesenchymal) components.

The prevalence of mammary neoplasms exhibits significant variability among different species, with dogs, particularly females, being highly susceptible. In canine populations, mammary tumors rank as the most frequently diagnosed neoplasms in female dogs, comprising approximately half of all tumors [1, 2, 3]. nicaThe incidence of these tumors is influenced by various factors, including breed predisposition, hormonal influences, and age.

Breed-specific conditions affect the mammary gland tumor incidence. Poodles and Boston terriers are more susceptible to mammary neoplasms, highlighting the role of genetic and breed variables in tumor formation [1, 2, 3]. The complicated interaction of endocrine variables in breast tumor development is highlighted by hormonal impacts, particularly estrogen [3, 4, 5]. Age is crucial to canine mammary tumor prevalence. Heifers over seven years old account for 80% of recorded cases (1–3). Age matters in canine mammary neoplasm dynamics, as this event shows. In 25%–50% of canine mammary tumors, malignant carcinoma is present [1, 2, 3]. Fawns also have mixed mammary tumors [2, 5, 6]. These findings demonstrate the histological variability of breast cancers and the necessity for sophisticated diagnosis and classification.

Histologically, the World Health Organization classifies canine mammary tumors into four distinct categories: malignant, benign, unclassified, and hyperplasia/dysplasia. This classification considers various factors, including the types of cells involved, the course of neoplastic growth, origin, and descriptive morphology [6, 7]. Further differentiation relies on parameters such as the histologic type, degree of invasiveness, cellular differentiation, and mitotic index [6, 7]. This comprehensive classification system aids in both diagnostic precision and understanding the behavior of different mammary tumors. These masses can vary widely in size and characteristics, encompassing solid, cystic, sessile, pedunculated, ulcerated, or skin and hair-covered presentations [1, 2,

[1]Department of Medicine, Surgery and Obstetrics, [2]Department of Pathology and Parasitology, Faculty of Animal Science and Veterinary Medicine, Patuakhali Science and Technology University, Bangladesh.
[*]Corresponding author, e-mail: sssaha@pstu.ac.bd

9]. Texture may range from soft to hard, and masses may appear as single or multiple entities, displaying a diverse array of colors, including crimson, purple, and off-white.

Myofibroblasts are specialized cells that share characteristics of both smooth muscle cells and fibroblasts. They play a significant role in wound healing and tissue repair by contributing to the formation of granulation tissue and ECM (extracellular matrix) remodeling. Myoid cells are a type of muscle-like cells that exhibit characteristics similar to smooth muscle cells. The term "myoid" is derived from "myo-" meaning muscle. These cells are typically associated with structures or tissues that have contractile properties similar to those of smooth muscle.

Understanding the intricacies of canine mammary tumors, including their prevalence, breed predispositions, hormonal influences, age-related dynamics, histological classifications, and diverse clinical presentations, is pivotal for advancing both veterinary oncology and comparative oncology research. This knowledge serves as a foundation for developing effective diagnostic, therapeutic, and preventive strategies to enhance the overall management of canine mammary tumors.

The study

An unclassified breed female street dog, aged seven years had pedunculated tumor like growth near to right cranial thoracic cavity, brought at the teaching veterinary clinic of the Faculty of Animal Science and Veterinary Medicine at Patuakhali Science and Technology University for correction this condition. It was confirmed that the tumor mass had clear neck and body. The dog was suffered for at least 1-year with this condition. After clinical examination it was considered for operation to excise the tumor part.

Before the surgical operation, a chest X-ray was performed, which revealed no pulmonary nodules, interstitial diffusion, or mediastinal lymphadenopathy. The CBC conducted as part of routine preoperative evaluation, it showed normal hematological parameters with a minor inflammatory reaction, likely due to the mixed mammary tumor, without evidence of systemic involvement or metastases. After 2 days, the pedunculated tumor mass was surgically excised using a standard surgical technique. Briefly, the dog was premedicated with atropine at 0.04 mg/kg body weight and then administered anesthetic drugs using combination of Ketamin HCL (G-Ketamin®, Gonosastho Pharmaceutical, Bangladesh) at 5 mg/kg body weight and Xyzaline HCL (Xyla®, Interchemie, Netherlands) at 1.1 mg/kg body weight. The maintenance of anaesthesia was maintained by half dose of initial dose of anaesthetic agents. During operation Hartmann's solution (Hartmann IV infusion, Opsonin Saline Limited, Dhaka, Bangladesh) was administered intravenously at 15 drop/min. The surgical area was clipped, shaved and washed with standard practices. The area was covered with sterilized window towel. The incision was made on skin of neck of the tumor mass. All types of bleeding were controlled by manual hemostat. The major blood vessels of the tumor mass were ligated by polyglycolide/L-Lactide (Mitsu™, Metril Endo Surgery Pvt. Ltd., Gujrat, India). The tumor mass was excised properly. The cutting edges of the skin were closed by a horizontal mattress suture with braided silk. The incision site was protected by povidone iodine-soaked gauze. The dimensions, mass, hue, texture, and other macroscopic characteristics of the tissue mass were meticulously documented. Representative surgical samples were fixed using a 10% neutral buffered formalin solution prior to being prepared for paraffin embedding. The suspicious tissue samples were prepared for histopathological investigation using a well-established standard process for light microscopy. The samples, which had been fixed in formalin, were cut into sections and then stained with hematoxylin and eosin, following an established technique [8, 9, 10].

Post-operative care and follow-up

After the operation, an antibiotic, gentamicin HCl (Inj. Genta-10®, Jason Pharmaceutical Limited, Bangladesh), was administered intramuscularly at a dose rate of 5 mg/kg for five consecutive days. An analgesic and antihistaminic, meloxicam and pheniramine maleate (Inj. Mel-vet®, 20 mg/ml, ACME Laboratories Ltd. Bangladesh and Inj. Antihista-vet®, 22.75mg/ml, Square PharmaceuticalLtd, Bangladesh, respectively), was injected intramuscularly at a dose rate of 0.5mg/kg and 0.4mg/kg body weight, respectively for five days. Skin sutures were removed after ten days of operation. The surgical wound was healed without any complications. After 7 days, the dog was released from the case. For the following year, the dog was monitored for any signs of recurrence and was confirmed to be in good health.

Results and discussion

The tissue mass has distinct characteristics that were discerned during a thorough medical examination. On gross examination, the dog revealed a big, firm pedunculated mass measuring 10 cm in diameter suspended from the right cranial thoracic mammary

gland (Fig. 1A). The majority had black speckles on its exterior and displayed a faint pink hue. Upon examination by touch, the item had dimensions of an elastic, solid texture without any apparent attachment to the nearby tissues (Fig. 1A). The tumor was fully excised with surgical intervention performed under general anesthesia. The weight of the lump was around 3 kilogrammes. Post-operatively, the patient was advised to undergo antibiotic and anti-inflammatory medication. Full recovery was reported.

The cut section of the mass displayed a multilobulated appearance, with a mixture of delicate fibrotic tissue. The color ranged from white to greyish, and the substance was viscous and greasy. (Fig. 1B). The internal masses exhibited a soft and yellowish appearance, accompanied by the secretion of a mucoid substance of a corresponding color. Additionally, there was a necrotic center surrounded by areas of hemorrhage (Fig. 1B).

Histopathological examination revealed a heterogeneous population of neoplastic cells, with a prominent population of lipoblasts and adipocytes in different phases of differentiation. These were admixed with highly cellular areas myofibroblast, dense collagen fibers (Fig. 1C), large anastomosing blood vessel and newly formed blood vessel (Fig. 1D). Scattered accumulation of myoid cells inside of the tumor are evident (Fig. 1F). In section, well-differentiated adipocytes containing lipid vacuoles of variable sizes in abundant cytoplasm, dislocating the nucleus to the periphery and intermingled in a prominent myxoid stroma (Fig. 1E). The analysis also showed the presence of lipoblasts, which are cells with a star-like or spindle-like structure with few lipid droplets, distributed throughout the tumor. This was accompanied by necrosis, indicating tissue death, and supported by a small amount of fibrovascular stroma (Fig. 1E). Histopathological findings were consistent with a well-differentiated canine malignant mixed mammary tumor. Likewise, there have been reports of dogs exhibiting a variety of mixed mammary cancer [11, 12, 13].

The aetiology of mammary gland tumors remains uncertain, although it is likely that hormones play a significant role in the hyperplasia and neoplasia of these tumors. Mammary gland tumor growth is regulated by multiple variables [2, 3, 14]. The elements encompassed in this list are inherited, hormonal, neuropsychological, age of neutering, reproductive data, age, lactation, inflammation, trauma, smoking, and various other aspects [15, 16]. The age of female dogs has a crucial role in the formation of mixed mammary tumors. Research has indicated that older dogs have a higher likelihood of developing these tumors, typically occurring between the ages of 8 and 13 years [1, 3, 14]. The dog undergoing investigation was likewise 9 years old.

In addition, changes in the regulation of developmental processes in the mammary gland and the presence of specific transcription factors, such as E2F5, have been linked to the formation of tumors in the mammary gland [17]. Additionally, research has demonstrated that the insulin-like growth factor 1 (IGF1) signaling pathway and persistent activation of the IGF1 receptor (IGF1R) contribute to the development of tumors in the mammary gland [18]. Deviation in the expression of TBX2 and TBX3, which are transcription factors implicated in the development of mammary glands, has also been linked to breast cancer [19]. Collectively, these factors lead to the formation of mammary gland tumors and underscore the intricate character of this ailment.

Canine mammary gland cancers have different prognoses and metastasis rates [20]. The dog that underwent surgery did not experience any recurrence and remained healthy for up to one year. Multiple studies have discovered predictive variables and biological indicators for metastatic gastrointestinal tumors (MGT). The study found that the mRNA levels of ICAM-1, PRR14, VEGF, hnRNP H, Oct4, Sox2, and Nanog were noticeably elevated in metastatic MGT compared to non-metastatic MGT [14]. A separate investigation revealed that histologic grade and clinical stage significantly impacted the prognosis of MGT. Specifically, high-grade tumors and the presence of metastatic lymph nodes were observed to have a notable influence on the course of the illness and overall survival [21].

In conclusion, dog Malignant Mixed Mammary Tumors (MMMTs) are complex, aggressive mammary gland neoplasia with epithelial and mesenchymal components. These tumors are more aggressive than basic carcinomas. A full MMMT diagnosis includes physical exam, imaging, and biopsy. Size, location, and surrounding tissue determine tumor therapy. Regular veterinarian examinations and meticulous owner attention to mammary gland abnormalities are crucial for early diagnosis of malignant mixed mammary tumors (MMMT). Performing a spaying procedure on female dogs before to their initial heat cycle effectively may reduce the development of mammary tumors, particularly malignant mixed mammary tumors (MMMTs).

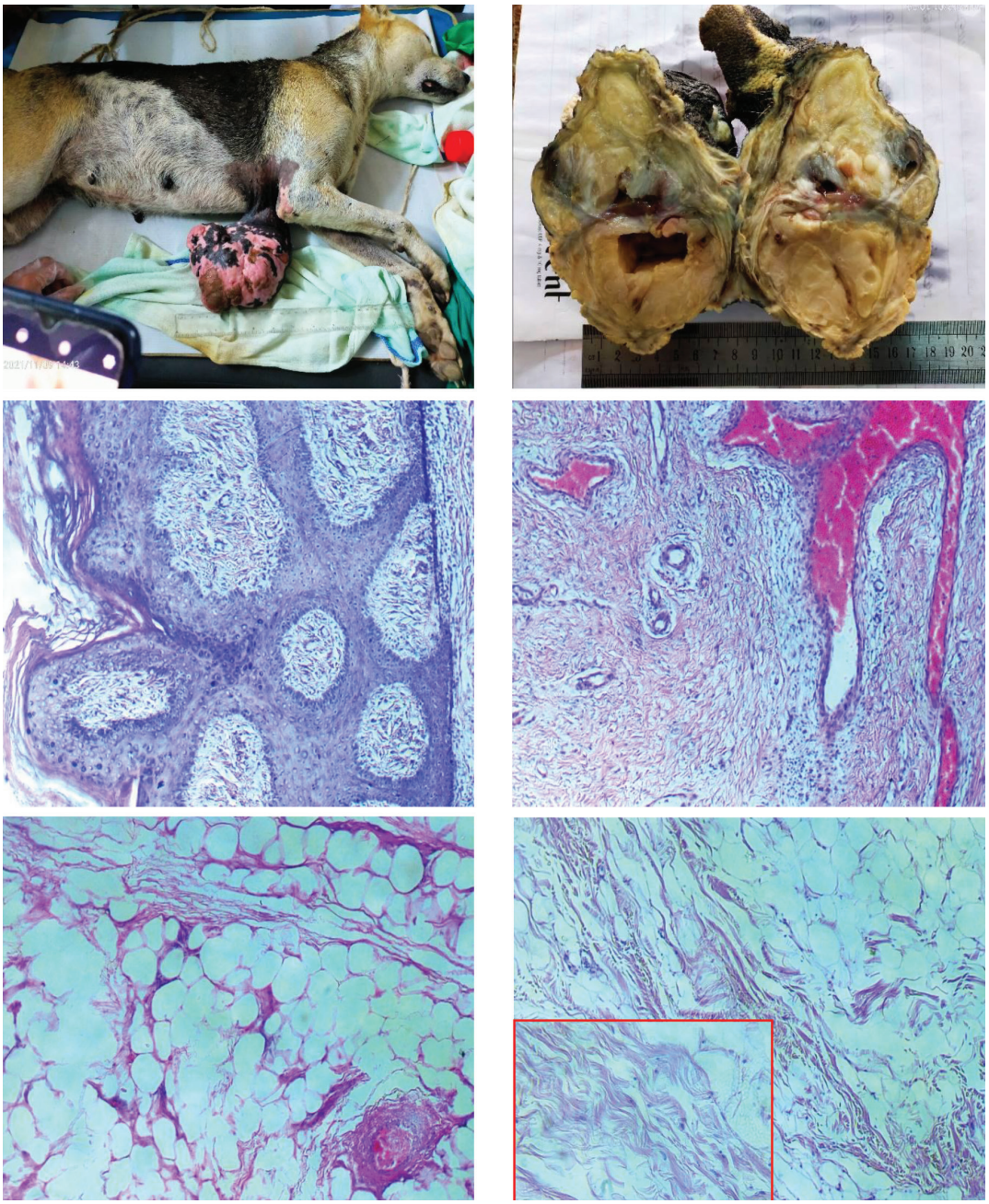

Fig. 1. Malignant Mixed Mammary Tumor. [A- Multilobulated lump originated from the left cranial thoracic mammary gland in a mongrel dog. B-Cut section of the mass demonstrating fatty substances. C- Thickening of the epidermis (parakeratosis) and proliferation of fibrous connective tissue (10x). D- Anastomosing large blood vessel, newly forming blood vessel and collagenous tissue matrix (10x). E- Extensive area of atypical lipoblasts admixed with well differentiated adipocytes (10x). F- Multinucleated giant cells with significantly pleomorphic (arrow) admixed adipocytes within a collagenous matrix (10x); Inset-myofibrils and myofibroblasts in the tumor microenvironment (40x)].

REFERENCES

1. Sorenmo KU, Kristiansen VM, Cofone MA, Shofer FS, Breen AM, *et al*. Canine mammary gland tumours; a histological continuum from benign to malignant; clinical and histopathological evidence. Vet Comp Oncol. 2009; 7(3):162–172.

2. Oliveira LC, dos Santos Lopes Fernandes ME, Peixoto AJR, da Camara Barros FFP, Coelho CMM, *et al.* Clinical, epidemiological, and histopathological aspects of breast cancer in female dogs at Federal Rural University of Rio de Janeiro Veterinary Hospital. Rev Bras Med Vet. 2022; 44.

3. Pastor N, Caballé NC, Santella M, Ezquerra LJ, Tarazona R, *et al*. Epidemiological study of canine mammary tumors: age, breed, size and malignancy. Austral J Vet Sci. 2018; 50(3): 143-147.

4. Nieto A, Pen L, Pé Rez-alenza MD, Sa MA, Flores JM, Castan M. Immunohistologic Detection of Estrogen Receptor Alpha in Canine Mammary Tumors: Clinical and Pathologic Associations and Prognostic Significance. Vet Pathol. 2000; 37(3): 239-247.

5. Misdorp W. Tumors of the mammary gland. Tumors in domestic animals, 4th edn. 2002; 575–606.

6. Goldschmidt MH, Peña L, Rasotto R, Zappulli V. Classification and grading of canine mammary tumors. Vet Pathol. 2011; 48(1):117–131.

7. Sbaraglia M, Bellan E, Dei Tos AP. The 2020 WHO Classification of Soft Tissue Tumours: News and perspectives. Vol. 113, Pathologica. Pacini Editore S.p.A./AU-CNS; 2021; 70–84.

8. Rani S, Alam KJ, Saha SS, Rahman MM, Alam MS. Seroprevalence, identification, and pathology of Salmonellosis in selected poultry farms at Barishal district of Bangladesh. Turkish J Agri-Food Sci Techno. 2022; 10(6):1158–1164.

9. Green KT, Regazoli É, da Silva EO, Hilst CLS, Di Santis GW. Case study: myxoid liposarcoma in a dog. Online J Vet Res. 2013; 17(5):218–226.

10. Kumar S, Tiwary R. Mammary gland fibroadenoma in a bitch. J Vet Sci Tech. 2015; 4(3):27–28.

11. Brunetti B, Muscatello LV, DeTolla LJ, Avallone G. Unusual myoid differentiation in a canine benign mixed mammary tumour. Case Rep Vet Med. 2021; 6615256.

12. Tkaczyk-Wlizło A, Śmiech A, Kowal K, Różańska D, Ślaska B. Histopathological evaluation of canine mammary gland tumours: A study of 92 cases. Med Weter. 2023; 79(6): 356-363.

13. Tunc AS, Taşdemir A, Rocchigiani G, Karaman H, Güneş V, *et al*. The histological and immunohistochemical features of a metastatic mammary carcinosarcoma in a dog-a case report. Vet Arh. 2022; 92(1):109–117.

14. Marconato L, Stefanello D, Solari Basano F, Faroni E, Dacasto M, *et al*. Subcutaneous mast cell tumours: a prospective multi-institutional clinicopathological and prognostic study of 43 dogs. Vet Record. 2023; 193(1): 2991.

15. Guray M, Sahin AA. Benign breast diseases: Classification, diagnosis, and management. Oncologist. 2006; 11(5): 435–449.

16. Beauvais W, Cardwell JM, Brodbelt DC. The effect of neutering on the risk of mammary tumours in dogs–a systematic review. J Small Anim Pract. 2012; 53(6):314-322.

17. To B, Broeker C, Jhan JR, Rempel R, Rennhack JP, *et al*. Insight into mammary gland development and tumor prevention in a newly developed metastatic mouse model of breast cancer. Available from: https://doi.org/10.1101/2021.09.24.461727.

18. Werner LR, Gibson KA, Goodman ML, Helm DE, Walter KR, *et al*. Progesterone promotes immunomodulation and tumor development in the murine mammary gland. J Immunother Cancer. 2021; 9(5): e001710.

19. ter Braak B, Siezen CL, Lee JS, Rao P, Voorhoeve C, *et al*. Insulin-like growth factor 1 receptor activation promotes mammary gland tumor development by increasing glycolysis and promoting biomass production. Breast Cancer Res. 2017; 19(1):14

20. Cassali GD, Lavalle GE, De Nardi AB, Ferreira E, Bertagnolli AC, *et al*. Consensus for the diagnosis, prognosis and treatment of canine mammary tumors. Braz J Vet Pathol. 2011; 4(2): 153-180.

21. Kim S, Bok E, Lee S, Lee HJ, Choe Y, *et al*. Metastasis prognostic factors and cancer stem cell-related transcription factors associated with metastasis induction in canine metastatic mammary gland tumors. J Vet Sci. 2021; 22(5): e62.

Cite this article as: Biswas D, Saha SS , Rahman M. Case study: Malignant mixed mammary tumor in dog. Explor Anim Med Res. 2025; 15(1), DOI: 10.52635/eamr/15.1.145-149.