



## Concurrence of solid carcinoma and intraductal papillary carcinoma in a rabbit

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### Abstract

In recent years mammary gland neoplasm has been recognized in pet and laboratory rabbits. The present study describes the concurrence of two malignant mammary gland neoplasms in a six-year-old intact female domestic rabbit. On clinical examination, the masses were observed in the left inguinal and right thoracic mammary glands. Based on owner information, the inguinal mammary gland mass within the previous 3-month period, and the thoracic mammary gland mass within the previous 6-month period, had become evident. Finally, complete surgical removal of the masses was selected. Tissue samples of the masses were fixed in 10% neutral buffered formalin and stained with H&E. In addition, immunohistochemical studies on masses sections were performed using primary antibodies against cytokeratins AE1/AE3. Microscopically, the left mass was diagnosed as solid carcinoma, and the right mass was diagnosed as intraductal papillary carcinoma. Immunohistochemistry showed diffuse positive cytoplasmic staining of the neoplastic cells in both of masses with primary antibodies against cytokeratins AE1/AE3. The best treatment option for mammary masses in pet rabbits is surgical excision, that is performed under general anesthesia. In this case, no new growth of the masses was observed 4 months following surgical procedures.

**Keywords:** Rabbit, Neoplasia, Mammary gland, Carcinoma, Histopathology

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## Introduction

Rabbits belong to the family of Leporidae in the order Lagomorpha (Percy and Barthold, 2013). In recent years, rabbits are kept by humans as companion animals (DeMello, 2016). The numbers of biopsy submissions from rabbits to diagnostic pathology laboratories are increasing (Baum and Hewicker-Trautwein, 2015). Neoplastic diseases are important causes of morbidity and mortality in pet rabbits. There is an increasing recognition of mammary tumors in pet rabbits (Degner *et al.*, 2018). Studies showed that affected rabbits have a wide age range between 8 months and 14 years with mean ages between 4.9 to 5.5 years and are nearly exclusively female or female spayed (do Carmo Silva *et al.*, 2019; Schöniger *et al.*, 2019). Most mammary tumors are carcinomas together with non-neoplastic lesions or benign neoplasms. A standardized tumor classification for rabbits is not available, prognostic factors are unknown, and the only treatment option is surgical excision (Schöniger *et al.*, 2019). The present study, describes history, clinical signs, histopathological findings of the concurrence of solid carcinoma and intraductal papillary carcinoma in the mammary glands of a rabbit.

## Material and methods

In December 2023, a Six-year-old intact female domestic rabbit (*Oryctolagus cuniculus*) was referred to the veterinary hospital. On clinical examination, two mammary gland masses were observed in the left inguinal and right thoracic

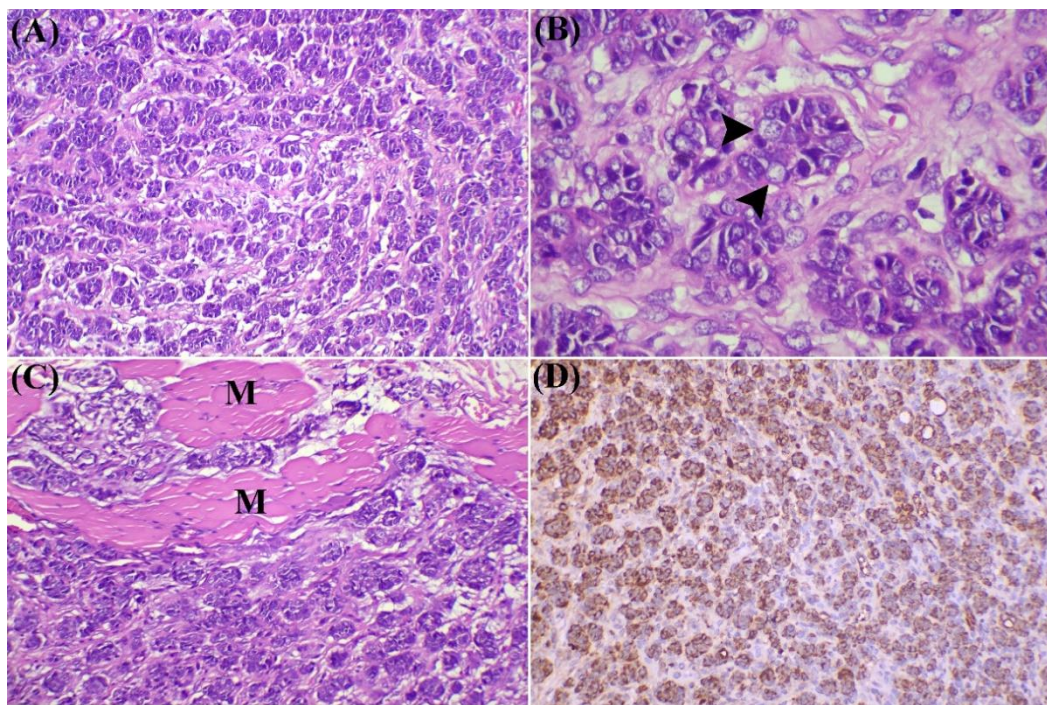
gland. Based on owner information, the inguinal mammary gland mass within the previous 3-month period, and the thoracic mammary gland mass within the previous 6-month period, had become evident and grew larger. On gross examination, the cranial thoracic gland mass was approximately  $1.2 \times 1.5 \times 1$  cm in size, and the size of the inguinal region mass was  $3 \times 2.5 \times 1.7$  cm. Finally, complete surgical removal of the masses was selected. On section, the cranial thoracic mammary gland mass was firm and white to gray with scattered areas of hemorrhage. The inguinal mammary gland mass was circumscribed, dense, white to yellow and divided by fine connective tissue trabeculae into small lobules. Tissue samples of the masses were fixed in 10 % neutral buffered formalin, routinely processed, dehydrated, embedded in paraffin wax, sectioned at 5  $\mu$ m in thickness (Rotary Microtome RM2 145; Leica, Wetzlar, Germany) and stained with Haematoxylin and Eosin. In addition, immunohistochemical studies on masses sections were performed using primary antibodies against cytokeratins AE1/AE3. Sections were examined using a light microscope (Motic, BA310 Epi-LED FL) and representative images were taken.

## Results

In histopathological investigations, the left inguinal mammary gland mass was composed of the cells arranged in solid sheets without lumina and irregularly sized lobules that were supported by a fine fibrovascular stroma. The cells were

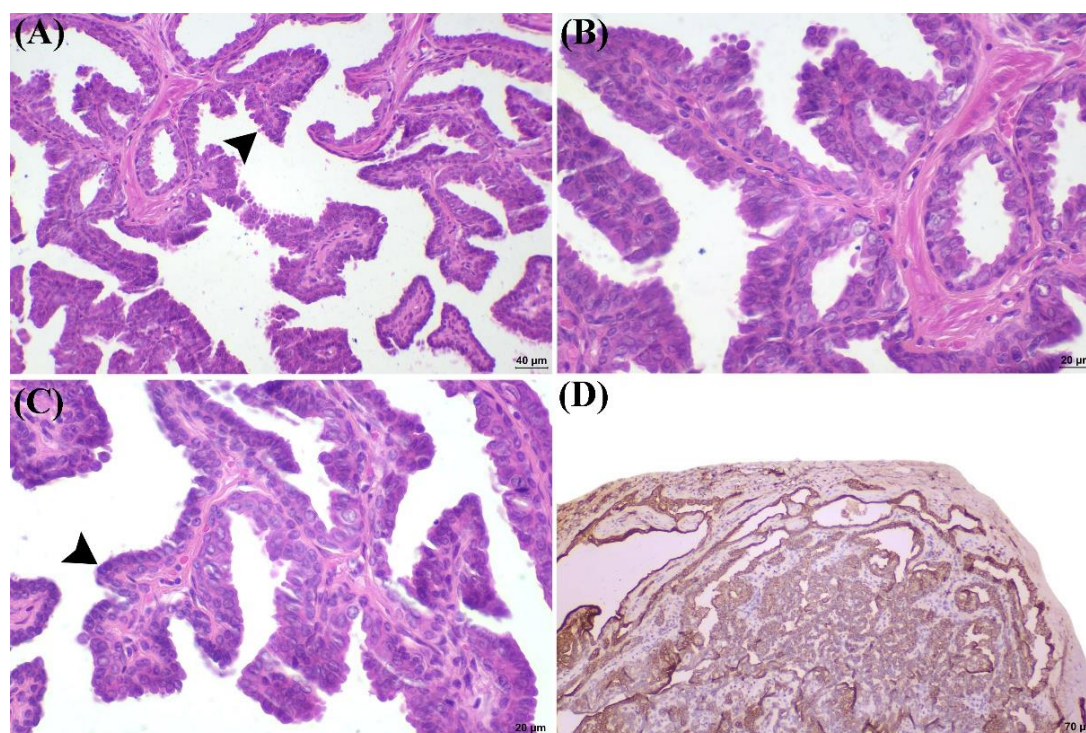
polygonal to oval, had poorly demarcated cell margins and scant lightly eosinophilic to basophilic cytoplasm. Nuclei were oval and hyperchromatic with stippled chromatin and a single central basophilic nucleolus. Anisokaryosis and anisocytosis were moderate. The muscle was also infiltrated by neoplastic cells. The mass was diagnosed solid carcinoma (Fig. 1A-C). The right thoracic mammary gland mass was composed of proliferation of a multilayered population of epithelial cells with characteristics of malignancy such as a higher nuclear to cytoplasmic

ratio, nuclear and cellular pleomorphism, and increased numbers of mitotic figures. The fibrovascular tissue was supported papillae. The neoplasm was diagnosed intraductal papillary carcinoma (Fig. 2A-C). Immunohistochemistry showed diffuse positive cytoplasmic staining of the neoplastic cells in both of masses with primary antibodies against cytokeratins AE1/AE3 (Fig. 1D & 2D). Based on owner information, no new growth of the masses was observed 4 months following the surgical procedures.



**Figure 1 (A-D):** Histopathological findings of solid carcinoma in the left inguinal mammary gland. (A): solid sheets of neoplastic cells without lumina and irregularly sized lobules. (B): Anisokaryosis (arrowheads). (C): Neoplastic cells invaded to the muscle (M), H&E. (D): Positive cytoplasmic staining of the neoplastic cells with primary antibodies against cytokeratins AE1/AE3, IHC.





**Figure 2(A-D):** Histopathological findings of intraductal papillary carcinoma in the right thoracic mammary gland. (A): invagination of the lining epithelial cells to form papillae (arrowhead). (B-C): High magnification of papilla (arrowhead), H&E. (D): Positive cytoplasmic staining of the neoplastic cells with primary antibodies against cytokeratins AE1/AE3, IHC.

## Discussion

With the increase in the number of domestic rabbits, rabbit oncology has become very important (Baum, 2021). In a study, mammary tumors in pet rabbits were classified according to the World Health Organization's histological classification for canine and feline mammary neoplasms (Baum and Hewicker-Trautwein, 2015). The uterine adenocarcinoma is the most common tumor in rabbit, whereas mammary neoplasms are reported in pet and laboratory rabbits (Percy and Barthold, 2013; Baum and Hewicker-Trautwein, 2015). Histopathological findings of neoplastic (cystic adenocarcinoma) and nonneoplastic mass of the mammary gland in laboratory rabbits are described in a few publications (Greene, 1939;

Schöniger *et al.*, 2014). In a study of tumors and tumor-like lesions in the mammary gland of 24 pet rabbits, 7 cystadenoma, 2 intraductal papilloma, 1 intraductal papillary carcinoma, 14 adenocarcinoma, 2 adenosquamous carcinoma, and 1 matrix-producing carcinoma were reported. Some rabbits had two to three neoplasms. In histopathological investigations, in mammary gland mass of one rabbit, the intraductal carcinoma had a papillary growth pattern, but unlike the present study, it was an in-situ carcinoma (Schöniger *et al.*, 2014). Like the present study, all observed tumors were epithelial neoplasms (Greene, 1939; Schöniger *et al.*, 2014). Like present case, based on semiquantitative evaluation, 80% of the epithelial

neoplasms showed positive cytoplasmic staining with primary antibodies against cytokeratins AE1/AE3 (Schöniger *et al.*, 2014). Mastectomy is the standard treatment for canine mammary gland tumors (Meuten, 2020; Nunes *et al.*, 2018; Kluthcovsky *et al.*, 2024). So far, the only treatment option for mammary masses in pet rabbits is surgical excision, that is performed under general anesthesia (Tan *et al.*, 2020). In this case, no new growth of the masses was observed 4 months following the surgical procedures

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### References

- Baum, B. and Hewicker-Trautwein, M., 2015.** Classification and epidemiology of mammary tumours in pet rabbits (*Oryctolagus cuniculus*). *Journal of Comparative Pathology*, 152(4), pp.291-298. <https://doi.org/10.1016/j.jcpa.2015.01.009>
- Baum, B., 2021.** Not just uterine adenocarcinoma—neoplastic and non-neoplastic masses in domestic pet rabbits (*Oryctolagus cuniculus*): a review. *Veterinary Pathology*, 58(5), pp.890-900. <https://doi.org/10.1177/03009858211002190>
- Degner, S., Schoon, H.A., Laik-Schandelmaier, C., Aupperle-Lellbach, H. and Schöniger, S., 2018.** Estrogen receptor- $\alpha$  and progesterone receptor expression in mammary proliferative lesions of female pet rabbits. *Veterinary Pathology*, 55(6), pp.838-848. <https://doi.org/10.1177/0300985818788611>
- DeMello, M., 2016.** Rabbits multiplying like rabbits: The rise in the worldwide popularity of rabbits as pets. *Companion Animals in Everyday Life: Situating Human-Animal Engagement within Cultures*, pp. 91-107.
- do Carmo Silva, H., de Oliveira, A.R., dos Santos Horta, R., Moereira, B.S., Silveira, T.L., Cassali, G.D. and Dantas, M.C., 2019.** Mammary gland malignant myoepithelioma in a domestic rabbit (*Oryctolagus cuniculus*). *Acta Scientiae Veterinariae*, 47. <https://doi.org/10.22456/1679-9216.92568>
- Greene, H.S., 1939.** Familial mammary tumors in the rabbit: I. Clinical history. *The Journal of Experimental Medicine*, 70(2), pp.147-158. <https://doi.org/10.1084/jem.70.2.147>
- Kluthcovsky, L.C., Jennifer, M., Merisio, T.M., Castro, J.L.C. and Filho, J.R.E., 2024.** Treatment of mammary gland tumors in bitches: effects of sodium dichloroacetate as neoadjuvant therapy. *The Journal of veterinary medical science*, 86(6), 677–683. <https://doi.org/10.1292/jvms.23-0393>
- Meuten, D.J. ed., 2020.** *Tumors in domestic animals*. John Wiley & Sons.

- Nunes, F.C., Campos, C.B., Teixeira, S.V., Bertagnolli, A.C., Lavalle, G.E. and Cassali, G.D., 2018.** Epidemiological, clinical and pathological evaluation of overall survival in canines with mammary neoplasms. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, 70, pp.1714-1722. <https://doi.org/10.1590/1678-4162-10217>
- Percy, D.H. and Barthold, S.W., 2013.** *Pathology of laboratory rodents and rabbits*. John Wiley & Sons.
- Schöniger, S., Horn, L.C. and Schoon, H.A., 2014.** Tumors and tumor-like lesions in the mammary gland of 24 pet rabbits: A histomorphological and immunohistochemical characterization. *Veterinary Pathology*, 51(3), pp. 569-580. <https://doi.org/10.1177/0300985813497486>
- Schöniger, S., Degner, S., Jasani, B. and Schoon, H.A., 2019.** A review on mammary tumors in rabbits: translation of pathology into medical care. *Animals*, 9(10), p.762. <https://doi.org/10.3390/ani9100762>
- Tan, P.H., Ellis, I., Allison, K., Brogi, E., Fox, S.B., Lakhani, S., Lazar, A.J., Morris, E.A., Sahin, A., Salgado, R. and Sapino, A., 2020.** The 2019 WHO classification of tumours of the breast. *Histopathology*, 77(2). <https://doi.org/10.1111/his.14091>