SOLID MAMMARY ADENOCARCINOMA IN A PET RABBIT *(Oryctolagus cuniculus)*

ADENOCARCINOMA MAMÁRIO SÓLIDO EM COELHO DOMÉSTICO (Oryctolagus cuniculus)

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ABSTRACT

Mammary gland tumors in domestic rabbits (Oryctolagus cuniculus) have been increasingly reported in clinical practice, and most cases exhibit malignant and biologically aggressive behavior. This report describes the clinicopathological features of solid mammary adenocarcinoma in an adult female rabbit presenting with a progressively enlarging and ulcerated mammary mass. The surgically excised nodule measured 6.2 × 5.0 × 3.0 cm and exhibited a white, multilobular appearance with friable areas upon sectioning. Histologically, the neoplasm was poorly demarcated, expansile, and infiltrative, composed of cuboidal to polygonal epithelial cells arranged in nests and compact solid sheets, showing marked pleomorphism, a high mitotic index (25 mitoses per 2.37 mm²), areas of necrosis, and pronounced anisocytosis, and anisokaryosis. Dilated mammary ducts and peritumoral inflammatory infiltrates were also noted. These findings support the diagnosis of solid mammary adenocarcinoma, a variant associated with aggressive biological behavior in rabbits. This case contributes to the growing body of knowledge regarding mammary neoplasia in pet lagomorphs and highlights the important diagnostic features for veterinary pathologists.

Keywords: Rabbit, *Oryctolagus cuniculus*. Mammary neoplasia. Solid adenocarcinoma. Veterinary pathology. Histopathology.

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RESUMO

Os tumores mamários em coelhos domésticos (*Oryctolagus cuniculus*) vêm sendo reconhecidos com maior frequência na prática clínica, e a maioria apresenta comportamento biológico agressivo. Este relato descreve as características clínico-patológicas de um adenocarcinoma mamário sólido em uma coelha adulta, atendida com aumento progressivo de massa mamária ulcerada. O nódulo removido cirurgicamente media 6,2 × 5,0 × 3,0 cm e apresentava coloração branca, arquitetura multilobular e áreas friáveis. Histologicamente, observou-se neoplasia epitelial mal delimitada, expansiva e infiltrativa, composta por células cuboides a poligonais dispostas em ninhos e massas sólidas, com pleomorfismo acentuado, alto índice mitótico (25 figuras em 2,37 mm²), necrose focal e intensa anisocitose e anisocariose. Ductos mamários ectásicos e infiltrado inflamatório peritumoral estavam presentes. Os achados são compatíveis com adenocarcinoma mamário sólido, variante tumoral associada a comportamento agressivo em coelhos. Este relato contribui para o entendimento clínico e diagnóstico das neoplasias mamárias em lagomorfos de companhia.

Palavras-chave: Coelho. *Oryctolagus cuniculus*. Neoplasia mamária. Adenocarcinoma sólido. Patologia veterinária. Histopatologia.

1 INTRODUCTION

Mammary tumors in domestic rabbits (*Oryctolagus cuniculus*) represent an increasingly recognized category of neoplasia in veterinary oncology, coinciding with the greater longevity and improved medical care of companion rabbits. Historically considered rare in laboratory populations, mammary tumors in pet rabbits have been reported with increasing frequency across multiple geographical regions, reflecting increased biopsy submissions to diagnostic laboratories (Baum; Hewicker-Trautwein, 2015; Hill *et al*., 2024). Epidemiological assessments have revealed a strong predilection for female rabbits, with mean affected ages ranging between 4.9 and 5.5 years (Schöniger *et al*., 2013; Silva *et al*., 2019). Unlike canine and feline mammary tumors, rabbit mammary neoplasms lack a standardized species-specific classification system, and their prognostic markers remain largely undefined (Schöniger *et al*., 2019).

Morphologically, rabbit mammary neoplasms encompass a wide spectrum of epithelial malignancies, including tubular, papillary, tubulopapillary, cribriform, solid, adenosquamous, matrix-producing carcinomas, and less common variants such as intraductal papillary carcinoma and malignant myoepithelioma (Shokrpoor; Ghaffari; Khanbabai, 2025; Silva *et al*., 2019). Studies involving immunohistochemistry have

consistently demonstrated partial retention of myoepithelial markers in invasive carcinomas, suggesting that rabbit mammary tumors may arise from a unique histogenetic pathway involving transitional stages from in situ to invasive lesions (Degner *et al*., 2019).

Recent molecular investigations have added complexity to the biological understanding of these tumors. The expression of indoleamine 2,3-dioxygenase (IDO) in rabbit mammary carcinomas provides evidence of immune modulatory mechanisms analogous to those observed in human breast cancer, highlighting the possible translational significance of lagomorph oncology (Schöniger *et al*., 2024). In addition to neoplastic proliferation, benign and reactive lesions, such as duct ectasia and cystic dilation, are frequently observed in rabbits, contributing to diagnostic challenges and emphasizing the need for precise clinical-pathological correlation (Okuyucu *et al*., 2022).

Given the diversity of histological subtypes, the absence of standardized prognostic indicators, and the limited therapeutic options, which are largely restricted to surgical excision, comprehensive documentation of individual cases is essential. This case report describes the clinicopathological features of solid mammary adenocarcinoma in a domestic rabbit (*Oryctolagus cuniculus*), integrating morphological, clinical, and comparative aspects within the context of the current literature.

2 CASE REPORT

We present the case of a 5-year-old, 2.60 kg, female mixed-breed rabbit (*Oryctolagus cuniculus*) that developed a mammary tumor. The lesion began as a small nodule measuring less than 1 cm but progressively enlarged over time. The patient frequently manipulated the area, resulting in ulceration of the tumor tissue. The rabbits were kept indoors and were fed a varied diet consisting primarily of commercial rabbit feed, minimal hay, cabbage, fruits, and treats. Given the progressive growth of the tumor, the patient underwent surgical excision of the nodule (Figure 1), which was subsequently submitted for histopathological evaluation. The tissue samples were fixed in 10% formalin for preservation.

Figure 1. Solid mammary adenocarcinoma in a pet rabbit.
Source: Authors, 2025

The patient was positioned on the surgical table, displaying a large mammary mass. The nodule was markedly ulcerated and hemorrhagic, with surface disruption and tissue loss.

On macroscopic examination, the surgical specimen represented the cranial right mammary gland and measured 6.2 × 5.0 × 3.0 cm. The lesion was ulcerated and expansile, with a white, multilobular appearance and friable areas upon sectioning. Fragments of mammary tissue were routinely processed, sectioned to a thickness of 4-5 µm thickness, and stained with Hematoxylin and Eosin (H&E).

Histologically, the neoplasm was ill-defined, expansive, and infiltrative, located within the dermis and hypodermis, extending to the margins of the examined specimen. It is characterized by dense cellularity, consisting of neoplastic epithelial cells arranged in solid nests and compact masses, supported by a sparse, collapsed fibrovascular stroma. The neoplastic cells were cuboidal to polygonal, with scant, eosinophilic, and homogeneous cytoplasm. The nuclei were vesicular to hyperchromatic, round to oval, with dense or reticulated chromatin, and had 1–2 prominent nucleoli. Marked pleomorphism was evident at both the cellular and nuclear levels, with significant anisocytosis and anisokaryosis. Mitotic activity was notably increased, with 25 mitotic figures observed per 2.37 mm². Focal areas of coagulative necrosis were observed, containing cellular debris and nuclear remnants. Additionally, superficial ulceration was observed, accompanied by crusting and a fibrinonecrotic exudate. The peritumoral stroma exhibited moderate inflammatory infiltrate composed of lymphocytes, plasma cells, and macrophages, associated with ectatic, dilated mammary ducts containing eosinophilic, amorphous material or cellular debris. The definitive histopathological diagnosis was mammary solid adenocarcinoma (Figure 2).

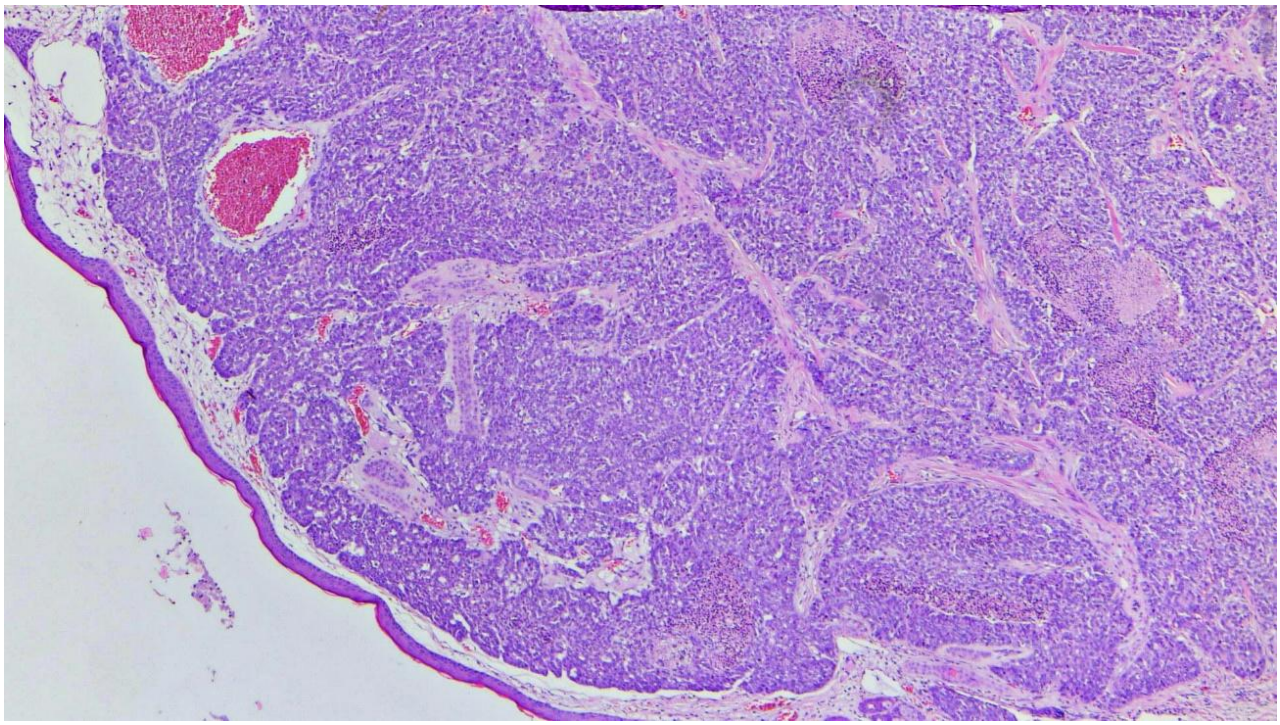

Figure 2: Solid mammary adenocarcinoma in a pet rabbit.
Note: Poorly demarcated, expansile, and infiltrative neoplasm extending to the margins, composed of densely packed epithelial cells arranged in solid nests and compact masses supported by scant, collapsed fibrovascular stroma (HE, 40x).
Source: Authors, 2025

3 DISCUSSION

Mammary gland tumors in domestic rabbits (*Oryctolagus cuniculus*) exhibit considerable histological and biological variabilities. The solid mammary adenocarcinoma described in this case closely aligns with the aggressive subset of epithelial mammary neoplasms reported in the literature. Epidemiological surveys have consistently demonstrated that mammary tumors occur almost exclusively in adult female rabbits, with mean ages ranging from 4.9 to 5.5 years (Schöniger *et al*., 2013; Silva *et al*., 2019), which is compatible with the age of the rabbit in this case. This demographic tendency reinforces the strong hormonal association observed in rabbits, as mammary and uterine neoplasms are major components of reproductive pathologies in this species (Baum; Hewicker-Trautwein, 2015; Bertram *et al*., 2020).

The microscopic features observed in the current case, including dense cellularity, compact solid architecture, marked pleomorphism, high mitotic index (25 mitoses/2.37 mm²), necrosis, and tissue infiltration, are hallmarks of solid mammary adenocarcinoma in dogs. This subtype is widely recognized as biologically aggressive, with rapid proliferation and extensive tissue destruction (Schöniger *et al*., 2013; Shokrpoor; Ghaffari; Khanbabai, 2025). Similar findings have been documented in cases reporting solid carcinoma with muscular invasion or concurrent tumor subtypes, further illustrating the malignant potential of this pattern (Shokrpoor; Ghaffari; Khanbabai, 2025; Shahbazfar *et al*., 2012).

Given the histological diversity of rabbit mammary tumors, an accurate diagnosis requires the careful exclusion of multiple differentials. For instance, tubular and tubulopapillary adenocarcinomas typically display lumina or papillary projections supported by fibrovascular cores, features that are absent in the present tumor (Schöniger *et al*., 2013). Similarly, intraductal papillary carcinoma retains a duct-centered growth pattern, characterized by papillary fronds. Although this subtype may coexist with solid carcinoma in the same individual (Shokrpoor; Ghaffari; Khanbabai, 2025), no such architectural arrangement was observed. Adenosquamous carcinoma can be excluded based on the absence of squamous differentiation or keratinization. Matrix-producing carcinoma, another rare subtype described in rabbits, is defined by the presence of a cartilage-like or osteoid matrix (Schöniger *et al*., 2013), which was not observed in our case. Malignant myoepithelioma, as reported by Silva *et al*. (2019),

predominantly presents spindle-shaped or polygonal myoepithelial cells with strong immunohistochemical staining for calponin and p63. However, the epithelial nature and solid growth pattern in the present case do not support this diagnosis. Carcinosarcoma, a rare mixed tumor described by Shahbazfar *et al*. (2012), is characterized by both epithelial and mesenchymal malignant components, neither of which were present in our case. Finally, duct ectasia, observed in this case, is recognized as a common secondary or pre-neoplastic finding in rabbit mammary glands, frequently coexisting with carcinomas but insufficient to account for the malignant features observed (Schöniger *et al*., 2013; *Okuyucu et al*., 2022).

An important aspect contributing to the diagnostic complexity of rabbit mammary tumors is the frequent retention of myoepithelial marker expression in invasive carcinomas. Degner *et al*. (2019) and Silva *et al*. (2019) report immunopositivity in up to 93% of cases, indicating that the presence of myoepithelial-like cells does not imply benign behavior. Although immunohistochemical analysis was not performed in this case, the invasive pattern, absence of glandular lumina, and architectural disruption strongly support the diagnosis of invasive carcinoma. These findings contribute to the ongoing discussion regarding the unique histogenetic pathways of lagomorph mammary tumors.

Additionally, recent molecular insights, such as the expression of indoleamine 2,3-dioxygenase (IDO) in rabbit mammary carcinomas, suggest potential mechanisms of immune evasion like those described in human breast cancer (Schöniger *et al*., 2024). This emphasizes both the translational relevance and the need for a refined understanding of tumor biology in rabbits.

The ulceration observed in the present case is likely attributable to a combination of rapid expansile growth and self-trauma, which is frequently reported in rabbits due to grooming or manipulation of painful masses (*Schöniger et al*., 2013; Shokrpoor; Ghaffari; Khanbabai, 2025). This clinical presentation, together with necrosis and an elevated mitotic index, underscores aggressive biological behavior.

As documented in numerous studies, surgical excision remains the only established treatment for mammary carcinomas in rabbits (Shokrpoor; Ghaffari; Khanbabai, 2025). Nevertheless, recurrence may occur in tumors with high proliferation indices or incomplete excision, which reinforces the importance of postsurgical monitoring (Schöniger *et al*., 2013). The findings of this case contribute

valuable information to the veterinary oncology literature by highlighting the aggressive histological features of solid adenocarcinoma and elucidating diagnostic differentials, prognostic considerations, and comparative aspects within the context of current knowledge.

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BIOETHICS AND BIOSECURITY COMMITTEE APPROVAL

We, the authors of the article entitled “Solid Mammary Adenocarcinoma In A Pet Rabbit *(Oryctolagus Cuniculus)*” for all intents and purposes, declare that the project that gave rise to its data was not submitted to the Ethics Committee for evaluation. However, we are aware of the provisions of the resolutions of the Conselho Nacional de Controle de Experimentação Animal - CONCEA (https://www.gov.br/mcti/pt-br/composicao/conselhos/concea) for projects involving animals. Therefore, the authors assume full responsibility for the data presented herein and are available to answer any questions that may be required by the competent authorities.

REFERENCES

BAUM, B.; HEWICKER-TRAUTWEIN, M. Mammary gland tumors in pet rabbits (Oryctolagus cuniculus): classification, epidemiology, and clinicopathological features. **Journal of Comparative Pathology,** London, v. 152, n. 4, p. 291–298, 2015. DOI: 10.1016/j.jcpa.2015.01.009.

BERTRAM, C. A. *et al*. Reproductive disorders and uterine neoplasms in female rabbits: a retrospective study of 80 cases. **Veterinary Pathology**, Thousand Oaks, v. 57, n. 4, p. 521–530, 2020. DOI: 10.1177/0300985820903531.

DEGNER, S. *et al*. Expression of myoepithelial markers in mammary carcinomas of pet rabbits: correlation with histological patterns and invasiveness. **Animals,** Basel, v. 9, n. 10, p. 740, 2019. DOI: 10.3390/ani9100740.

HILL, J. M. *et al*. Epidemiology of mammary tumors in domestic rabbits: a multicenter study. **Veterinary Sciences**, Basel, v. 11, n. 2, p. 66, 2024. DOI: 10.3390/vetsci11020066.

OKUYUCU, G.; ÖZYILDIZ, Z.; İPEK, V. A case of cystic mammary adenocarcinoma in a rabbit (Oryctolagus cuniculus). **Veterinary Journal of Kafkas University**, Kars, v. 28, n. 2, p. 25–31, 2022.

SCHÖNIGER, S. *et al*. Mammary carcinoma in pet rabbits: histological features and clinical outcome in 33 cases. **Journal of Comparative Pathology**, London, v. 148, n. 4, p. 344–353, 2013. DOI: 10.1016/j.jcpa.2012.09.006.

SCHÖNIGER, S. *et al*. A review on mammary tumors in rabbits: translation of pathology into medical care. **Animals,** Basel, v. 9, n. 10, p. 762, 2019. DOI: 10.3390/ani9100762.

SCHÖNIGER, S. *et al*. Indoleamine 2,3-dioxygenase (IDO) expression in rabbit mammary carcinomas and its immunomodulatory implications. **Veterinary Pathology,** Thousand Oaks, v. 61, n. 1, p. 22–30, 2024.

SHAHBAZFAR, A. A. *et al*. Carcinosarcoma of the mammary gland in a rabbit: case report. **Comparative Clinical Pathology**, Berlin, v. 21, n. 6, p. 1265–1268, 2012. DOI: 10.1007/s00580-011-1275-9.

SHOKRPOOR, S.; GHAFFARI, A.; KHANBABAI, M. Solid mammary carcinoma in rabbits: clinicopathological characterization and outcome**. Iranian Journal of Veterinary Pathology,** Tehran, v. 10, n. 2, p. 123–133, 2025.

SILVA, T. A. *et al*. Immunohistochemical and histopathological classification of rabbit mammary tumors. **Veterinary Sciences**, Basel, v. 6, n. 3, p. 45–56, 2019. DOI: 10.3390/vetsci6030045.