

Mammary comedocarcinoma in a rabbit

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Article Info	Abstract
Article history: Received: 19 January 2025 Accepted: 20 May 2025 Available online: 15 December 2025	A 4.5-year-old, nulliparous female New Zealand White Rabbit (<i>Oryctolagus cuniculus</i>) was presented for evaluation of a mammary mass located in right axillary mammary gland. The surgically excised mammary mass was submitted for histopathological and immunohistochemical evaluation. Histopathologically, neoplastic cells were arranged in sheets and nests of irregular sizes. The tissue was composed of amorphous eosinophilic material and necrotic cells. The neoplastic cells had round to oval nuclei with prominent nucleoli, scant basophilic cytoplasm and high mitotic activity. Cytokeratin and vimentin expressions of neoplastic cells were observed in immunohistochemical findings. Based on the microscopic characteristics and immunohistochemical staining, a diagnosis of a non-invasive comedocarcinoma was established. In this case, cytokeratin positivity confirmed the epithelial origin, whereas the vimentin positivity supported the presence of epithelial-mesenchymal transition and/or increased malignancy.
Keywords: Comedocarcinoma Mammary mass Neoplastic cell Rabbit	

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Introduction

Uterine carcinomas are the most common tumor in female rabbits, however, in recent years mammary cancer has also been increasingly recognized in pet rabbits.^{1,2} Studies have shown that affected rabbits range in age from 8 months to 14 years with mean ages between 4.90 to 5.50 years.^{3,4} The apparent rise in the incidence of mammary tumors in rabbits is likely attributable to the increased popularity of rabbits as pets combined with their relatively high life expectancy which is comparable to that of dogs.¹

Mammary carcinomas are subclassified into adenocarcinomas, solid carcinomas, spindle cell carcinomas, anaplastic carcinomas, squamous cell carcinomas and mucinous carcinomas.³ Among these, adenocarcinomas are the most frequently reported histological type which are further classified into solid, papillary, cystic, comedo, follicular, tubular and trabecular.^{3,5} Comedocarcinoma is a subtype of ductal carcinoma *in situ* (DCIS) which is considered a noninvasive breast cancer because it only affects cells in the milk ducts and has not spread to surrounding tissues. The frequent secretory activity observed in rabbit mammary tumors may suggest a role for prolactin in tumorigenesis.^{3,6}

The present study described the histopathological and immunohistochemical characteristics of a non-invasive

comedocarcinoma without evidence of metastasis in a female rabbit.

Case Description

A 4.5-year-old, nulliparous female New Zealand White Rabbit (*Oryctolagus cuniculus*) was presented to evaluate a mammary mass in the right axillary mammary gland. On clinical examination, the mass was firm in consistency with bloody and purulent discharges. Physical examination, complete blood count (Celltac Alpha VET MEK-6550K; Nihon Kohden, Tokyo, Japan), serum chemistry profile (Roche Hitachi 911 Chemistry Analyzer; Roche Diagnostics, Risch-Rotkreuz, Switzerland), radiography (Econet portable MeX+60; ECONET, Oberhausen, Germany) and ultrasonography (Esaote Mylab C30; Esaote, Genoa, Italy) were performed. Both the complete blood count and serum chemistry panel were within normal limits. Abdominal radiography and ultrasonography revealed no additional abnormalities.

The mass was surgically removed and fixed in a 10.00% buffered formalin solution and after embedding in paraffin, 5.00- μm sections were prepared and stained by Hematoxylin-Eosin (H & E).⁶

Also, immunohistochemical staining was performed for cytokeratin and vimentin with the Avidin-Biotin

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Peroxidase Complex method, similar to previous reports.^{7,8} Vimentin (1: 200 dilution, Clone Vim 3B4; Agilent-Dako, Santa Clara, USA) and cytokeratin (1:100 dilution, clone AE1-AE3; Agilent-Dako) were used as primary antibodies. The 3,3'-Diaminobenzidine (DAB; Agilent-Dako) was employed as chromogen, and Mayer's Hematoxylin (Agilent-Dako) was used for counterstaining.

Histopathologically, neoplastic cells were arranged in sheets and nests of irregular sizes. The tissue was composed of amorphous eosinophilic material and necrotic cells (Fig. 1). Sheets of packed cells were supported by dense connective tissue. These neoplastic cells had round to oval nuclei with prominent nucleoli, scant basophilic cytoplasm and high mitotic activity. Most cells were hyperchromatic with coarsely stippled chromatin. Some of the neoplastic cells had vacuolated cytoplasm (Fig. 2). Microscopic examination of immunohistochemically stained slides revealed cytokeratin expression in the

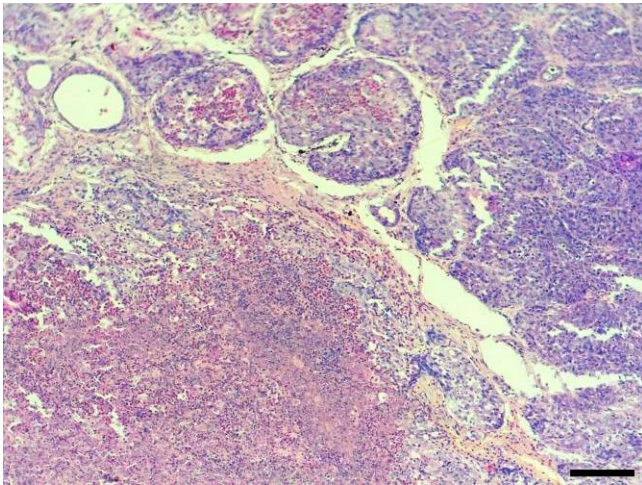


Fig. 1. Comedocarcinoma in a rabbit mammary gland. Neoplastic cells are arranged in nests. Note the presence of amorphous eosinophilic material and necrotic cells in dilated mammary ducts (H & E staining, bar = 75.00 μ m).

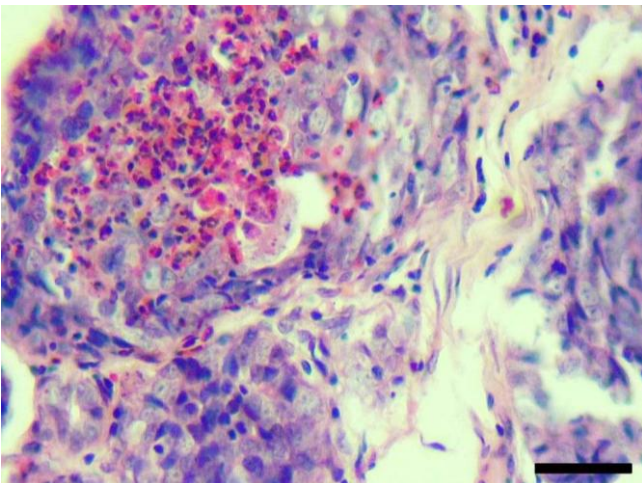


Fig. 2. The neoplastic cells with round to oval nuclei, basophilic and vacuolated cytoplasm (H & E staining, bar = 50.00 μ m).

neoplastic cells (Figs. 3 and 4). The stromal mesenchymal cells were positive for vimentin (Fig. 5).

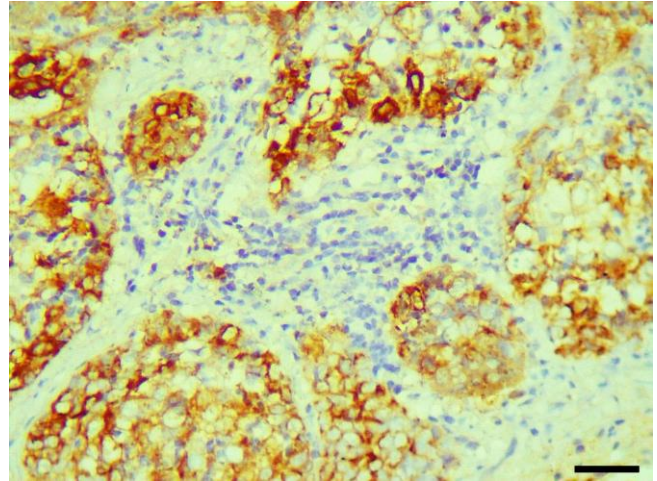


Fig. 3. Expression of cytokeratin in neoplastic cells (IHC, bar = 50.00 μ m).

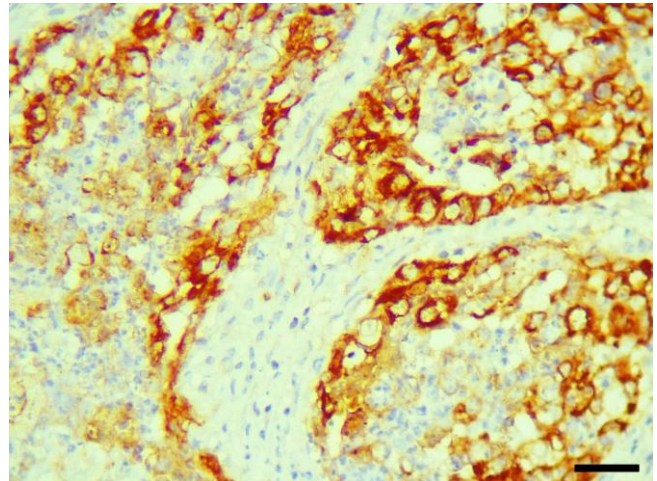


Fig. 4. Higher magnification of strong immunohisto-chemical staining for cytokeratin in neoplastic cells (IHC, bar = 50.00 μ m).

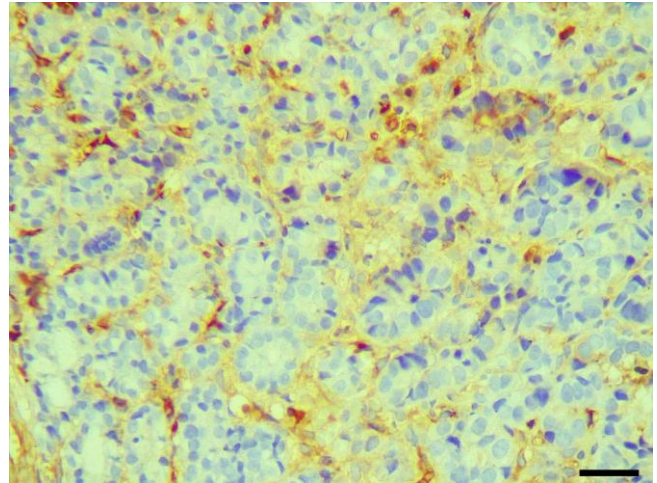


Fig. 5. Expression of vimentin in stromal mesenchymal cells (IHC, bar = 25.00 μ m).

According to the microscopic characteristics and immunohistochemical staining, a diagnosis of comedocarcinoma was established. Although the lymph nodes were large and follicles were active, there was no evidence of metastases to regional lymph nodes. Complete wound healing was observed within 4 weeks following the surgery. In addition, after 10 months, no evidence of tumor invasion was observed.

Discussion

Recent updates in the histological and clinical features of canine mammary gland tumors have led to the incorporation of several neoplastic subtypes-such as cribriform type of simple carcinoma, comedocarcinoma, ductal carcinoma and micropapillary carcinoma into the revised World Health Organization classification.⁹ Human breast comedocarcinoma is a DCIS with the poorest prognosis and the highest proliferation rate.^{6,10}

The majority of mammary tumors in rabbits are carcinomas,^{9,11} which can develop at any age ranging from 8 months to 14 years. Rabbit mammary carcinomas have a wide spectrum of mitotic activity, ranging from 0 - 36 mitotic figures at 100× high magnification.^{1,12} Common tumor growth patterns in rabbits include Simple adenoma/carcinoma, intraductal papillary adenoma/carcinoma and comedocarcinoma.^{3,13} There are two ways for the development of malignant mammary tumors in rabbits. In the more prevalent form, carcinomas arise in cystic mammary glands by stepwise progression from simple cysts over intra-cystic benign papillary tumors and non-invasive cancer to invasive carcinomas with possible metastases. In the other form, carcinomas develop in mammary tissue without pre-existing cystic lesions.¹ The present report described the macroscopic and histopathologic features of a mammary comedocarcinoma in a female rabbit. The term “comedo” was coined from the gross appearance of human comedocarcinoma, because the necrotic cellular debris oozed from the ducts when the excised tumor was squeezed, resembling comedones. Necrotic foci consist of amorphous eosinophilic material admixed with cell debris. The necrosis in comedo DCIS is felt to be of both apoptotic and oncotoc types. Apoptosis affects random individual cells and is characterized by pyknosis, karyorrhexis, cytoplasmic condensation and apoptotic bodies. The oncotoc type affects groups of cells and is characterized by karyolysis and cytoplasmic swelling.¹⁴ Ultrastructural analysis shows a relationship between the diameter of a duct and the presence of necrosis, such that ducts with DCIS and necrosis are larger with a reported mean diameter of 470 µm compared to ducts without necrosis that have a mean diameter of 192 µm. These findings suggest that central necrosis occurs because the central cells in a large duct are deprived of essential metabolites such as oxygen, possibly due to

limited diffusion in the non-vascularized ducts.¹⁴ Comedocarcinoma metastasis to regional lymph nodes has been reported but similar to the present case, despite the high grade of the tumor, no lymph node metastasis was detected.⁶ Patients with DCIS presented with a palpable mass, nipple discharge, or Paget’s disease of the nipple.⁷ In the present case, clinical examination revealed a firm mass accompanied by bloody and purulent discharges.

Immunohistochemistry is an important method for the diagnosis of neoplasms. The identification of various antibodies targeting cell-specific proteins has facilitated the diagnosis of neoplasms.³

There are a few reports on the immunohistochemical assessment of mammary tumors in rabbits.^{3,11} In the present report, immunohistochemical expressions were positive for cytokeratin and vimentin. The neoplastic cells were positive for cytokeratin and negative for vimentin. Cytokeratin positivity confirmed epithelial origin, while vimentin positivity supports the presence of epithelial-mesenchymal transition and/or increased malignancy.

In conclusion, this report described the clinical, macroscopic, histopathological and immunohistochemical characteristics of a non-invasive comedocarcinoma with no evidence of metastasis to the regional lymph nodes.

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Conflict of interest

The authors declared no conflict of interest.

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