

## Mammary Gland Carcinosarcoma in a New Zealand White Rabbit (*Oryctolagus cuniculus*)

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### ABSTRACT

**Background:** Carcinosarcoma of the breast (metaplastic, biphasic metaplastic, metaplastic sarcomatoid carcinoma, sarcomatoid carcinoma) is an aggressive, rare neoplasm that has been reported to account for 0.08-0.2% of all breast malignancies. Mammary carcinosarcoma is rare in rabbits. Carcinosarcoma is a neoplasia composed of cells morphologically resembling malignant epithelial components and cells resembling malignant connective tissue elements. In spite of the rarity in rabbits, carcinosarcoma should always be considered in the different diagnoses of the mammary neoplasias, especially those of undifferentiated neoplasias.

**Case:** An eight-month-old, female New Zealand white rabbit (*Oryctolagus cuniculus*) weighing 1.9 kg was referred to Tabriz university veterinary hospital for acute swelling on the abdomen and history of mammary mass. The complete blood count was within the reference ranges. The rabbit had been slightly depressed and anorectic. At clinical examination, the patient presented a huge lobulated mass in the mammary gland area. Clinical signs were included: emaciation and hardness in moving. Due to unfavorable prognosis the rabbit was euthanized and afterward complete mastectomy was performed. At necropsy, a non-infiltrative multilobulated mass were observed in the chirurgic area. The mass didn't infiltrate into the skin, subcutaneously and adjacent to the musculature and it was moved easily. The neoplasia was solid, firm, and yellow-brownish. Tissue samples of the tumor were fixed in 10% neutral buffered formalin, embedded in paraffin, cut at 5 µm, and stained with hematoxylin and eosin and masson trichrome. Microscopically, the neoplasm had a solid pattern and was composed of a heterogeneous cell population, mainly pleomorphics. Polyhedral cells showing ovoid or vesicular nuclei with prominent nucleoli and abundant lightly acidophilic cytoplasm resembling epithelial cells were observed. Cells with scant cytoplasm and elongated or oval nuclei containing inconspicuous nucleoli resembling mesenchymal cell were also observed. There were also neoplastic areas with a myxoid matrix. Some young cartilage pieces were observed in the tumor. In some parts of the tumor a very dense fibrous connective tissue was observed. Based on the histological findings, the diagnosis of mammary carcinosarcoma was confirmed. Other organs showed normal histological characteristics.

**Discussion:** The carcinosarcoma is a neoplasia characterized as containing a mixed cell population with malignant proliferation of both mesenchymal and epithelial-like cells. Although the carcinosarcoma is rare in the domestic species, their origin has been discussed in two theories: 1) multiclonal theory suggests that the epithelial and the mesenchymal components originated from two or more stem cells; 2) the monoclonal theory suggests that the epithelial and the mesenchymal components originated from totipotential neoplastic cells play multiple potential pathways of terminal differentiation. Abnormal level of growth and Prolactin hormones is one cause to breast tumors. Recent evidence supports the speculation that prolonged hyperprolactinemia leads to malignancy, given the case of ductal carcinoma in one woman who, after incomplete pituitary adenomectomy, was hyperprolactinemic for 15 years. This physiologic relationship and disease progression are important to consider in clinical diagnosis and management of these cases in rabbits. Although some studies were not showed any difference in level of mentioned hormones. In spite of being rare in rabbit, the carcinosarcoma should always be considered in the different diagnoses of the mammary neoplasias, mainly of those undifferentiated neoplasias.

**Keywords:** carcinosarcoma, rabbit, *Oryctolagus cuniculus*, mammary gland, histopathology.

## INTRODUCTION

Mammary carcinosarcoma is rare in rabbits, and also occurs with low frequency in dogs, rats and mice [4,8,9]. Carcinosarcoma is a neoplasia composed of cells morphologically resembling malignant epithelial components and cells resembling malignant connective tissue elements [4]. In spite of the rarity in rabbits, carcinosarcoma should always be considered in the different diagnoses of the mammary neoplasias, especially those of undifferentiated neoplasias. To correctly recognize these tumor types, their histological and immunohistochemical characteristics are important. Several cases of cutaneous neoplasms have been reported in rabbits, including basal cell carcinoma, squamous cell carcinoma, sebaceous carcinoma, trichoepithelioma and lymphoma [6]. Also some cases of cystic mammary, uterine and apocrine adenocarcinoma were reported in rabbits previously [3,6,10]. Though, to the authors' knowledge, no mammary gland carcinosarcoma cases have been reported previously. The objective of this paper is to describe a case of mammary carcinosarcoma in a rabbit.

## CASE REPORT

An eight-month-old, female New Zealand white rabbit (*Oryctolagus cuniculus*) weighing 1.9 kg was referred to Tabriz university veterinary hospital for acute swelling on the abdomen and history of mammary mass. The complete blood count was within the reference ranges. The rabbit had been slightly depressed and anorectic. At clinical examination, the patient

presented a huge lobulated mass in the mammary gland area. Clinical signs were included: emaciation and hardness in moving. Due to unfavorable prognosis rabbit was euthanized and afterward complete mastectomy was performed.

At necropsy, a non-infiltrative multilobulated mass were observed in the chirurgic area (Figures 1 and 2). The mass didn't infiltrate into the skin, subcutaneously and adjacent to the musculature and it was moved easily. The neoplasia was solid, firm, and yellow-brownish. Tissue samples were collected from some organs (lung, heart, kidney, liver, spleen, and brain), embedded in paraffin, sectioned and then stained with haematoxylin and eosin.

Tissue samples of the tumor were fixed in 10% neutral buffered formalin, embedded in paraffin, cut at 5 µm, and stained with hematoxylin and eosin and masson trichrome. Microscopically, the neoplasm had a solid pattern and was composed of a heterogeneous cell population, mainly pleomorphic. Polyhedral cells showing ovoid or vesicular nuclei with prominent nucleoli and abundant lightly acidophilic cytoplasm resembling epithelial cells were observed. Cells with scant cytoplasm and elongated or oval nuclei containing inconspicuous nucleoli resembling mesenchymal cell were also observed. There were also neoplastic areas with a myxoid matrix. Some pieces of young cartilage (Figure 3) and some areas of dense fibrous connective tissue were observed too (Figures 4 and 5). Based on the histological findings, the diagnosis of mammary carcinosarcoma was confirmed. All other organs showed normal histological characteristics.



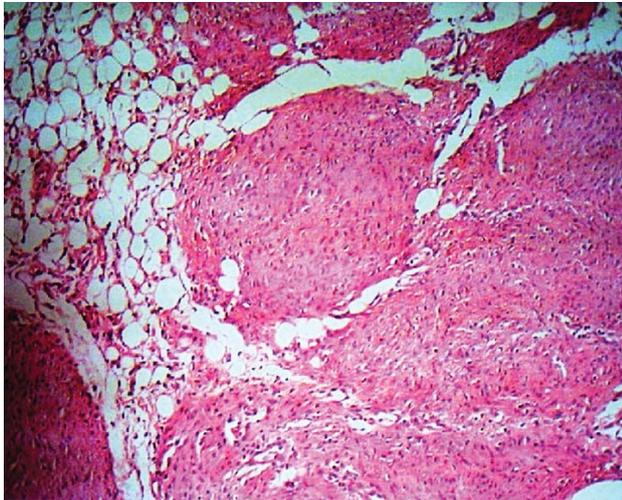
Figure 1. Multilobulated tumor mass after removal.



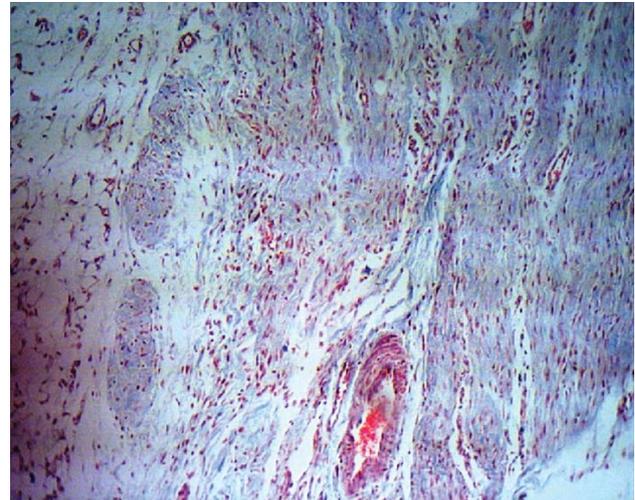
Figure 2. The tumor showed two distinct parts after cross section. A firmer (lighter) and a looser (darker) part.



**Figure 3.** Pieces of young cartilage with high chondrocyte population. H&E staining (Obj. 10x).



**Figure 4.** Dense collagenous connective tissue with some fat storing cells. H&E staining (Obj. 10x).



**Figure 5.** Dense collagenous and loose connective tissue. Masson trichrome staining (Obj. 10x).

## DISCUSSION

Carcinosarcoma of the breast (metaplastic, biphasic metaplastic, metaplastic sarcomatoid carcinoma, sarcomatoid carcinoma) is an aggressive, rare neoplasm that has been reported to account for 0.08–0.2% of all breast malignancies [2]. Carcinosarcomas have been observed in various organs throughout the body, including the ovary and uterus.

The true definition of metaplastic carcinoma of the breast is a tumor of malignant epithelial tissue (carcinoma) mixed with malignant cells of mesenchymal origin (sarcoma) with apparent histologic and cytologic features present on light microscopy [1]. The carcinosarcoma is a neoplasia characterized as containing a mixed cell population with malignant proliferation of both mesenchymal and epithelial-like cells [9].

Although the carcinosarcoma is rare in the domestic species, their origin has been discussed in two theories: 1) multiclonal theory suggests that the

epithelial and the mesenchymal components originated from two or more stem cells; 2) the monoclonal theory suggests that the epithelial and the mesenchymal components originated from totipotent neoplastic cells play multiple potential pathways of terminal differentiation [7].

Abnormal level of growth and Prolactin hormones is one cause to breast tumors. Recent evidence supports the speculation that prolonged hyperprolactinemia leads to malignancy, given the case of ductal carcinoma in one woman who, after incomplete pituitary adenomectomy, was hyperprolactinemic for 15 years. This physiologic relationship and disease progression are important to consider in clinical diagnosis and management of these cases in rabbits. Although some studies were not showed any difference in level of mentioned hormones [10]. In spite of being rare in rabbit, the carcinosarcoma should always be considered in the different diagnoses of the mammary neoplasias, mainly of those undifferentiated neoplasias.

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