



**ORIGINAL RESEARCH PAPER**

**Pathology**

**EXTRAOSSEOUS GIANT CELL TUMOR ARISING IN BREAST TISSUE WITH FATAL OUTCOME: A CASE REPORT AND REVIEW OF LITERATURE.**

**KEY WORDS:** Pathology, Breast, Giant cell tumor.

<b>Rodolfo Franco-Márquez</b>	Anatomic pathology and cytopathology service, University Hospital "Dr. Jose E. Gonzalez", UANL. Av. Francisco I. Madero Pte. y Av. Gonzalitos Col. Mitras Centro, Monterrey, CP 64460
<b>Hersilia Aide Hernandez-Zamonnett*</b>	Anatomic pathology and cytopathology service, University Hospital "Dr. Jose E. Gonzalez", UANL. Av. Francisco I. Madero Pte. y Av. Gonzalitos Col. Mitras Centro, Monterrey, CP 64460 *Corresponding Author
<b>Luis Carlos Canales-Martínez</b>	School of medicine and University Hospital "Dr. Jose E. Gonzalez", UANL. Av. Francisco I. Madero Pte. y Av. Gonzalitos Col. Mitras Centro, Monterrey, CP 64460
<b>Marco Antonio Ponce-Camacho</b>	Anatomic pathology and cytopathology service, University Hospital "Dr. Jose E. Gonzalez", UANL. Av. Francisco I. Madero Pte. y Av. Gonzalitos Col. Mitras Centro, Monterrey, CP 64460
<b>Marcela Anahí Narro Martínez</b>	Surgery service, University Hospital "Dr. Jose E. Gonzalez", UANL. Av. Francisco I. Madero Pte. y Av. Gonzalitos Col. Mitras Centro, Monterrey, CP 64460
<b>Raquel Garza-Guajardo.</b>	Anatomic pathology and cytopathology service, University Hospital "Dr. Jose E. Gonzalez", UANL. Av. Francisco I. Madero Pte. y Av. Gonzalitos Col. Mitras Centro, Monterrey, CP 64460

**ABSTRACT**

Extra-osseous giant cell tumor (GCT) is a rare tumor that arises in superficial and deep soft tissue morphologically. Extra-osseous GCT arising in breast is exceedingly rare with only 5 reported cases. We report a case of a malignant GCT originating in breast from a 46-year-old patient. Imaging and needle biopsy couldn't exclude malignancy, excisional biopsy was performed, lesion showed a multinodular architecture, ovoid mononuclear cells and osteoclastic giant cells. Final diagnosis was malignant GCT, with deep surgical margin positive for neoplasia. A radical mastectomy was performed, with surgical bed marking and axillary dissection. 2 lymph nodes out of 20 showed metastatic disease. Resection margins were free of cancer. Extraosseous GCT is a rare neoplasm. Various localizations have been reported, including salivary glands, uterus, bladder. Four cases of malignant extra-osseous GCT arising in breast tissue have been reported, one with associated to aggressive behavior and a fatal outcome.

**Introduction**

Malignant stromal neoplasms of the breast are a rare entity, representing less than 1% of malignant breast tumors. Extra-osseous giant cell tumor (GCT) is a rare tumor that arises in superficial and deep soft tissue. Morphologically, resembles its bone counterpart, with the same histologic features as GCT of bone. Although generally benign, can develop an aggressive clinical course. Extra-osseous GCT arising in breast is exceedingly rare with only 5 reported cases in the literature. Histologically, it is composed of ovoid mononuclear cells, osteoclastic giant cells, and metaplastic bone formation.

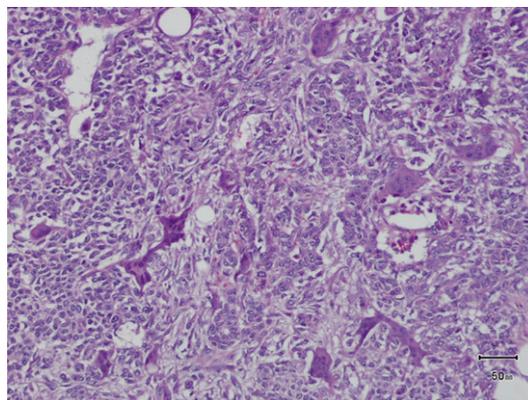
Extra-osseous GCT of breast usually present as a painless, growing mass; only one case has been reported with aggressive behavior and fatal outcome for the patient. Herein we report a case of a malignant GCT originating in the breast parenchyma of a 46-year-old patient, which ultimately led to our patient's death. This case is the second reported death from a malignant GCT arising in the breast.

**CASE REPORT**

A 46-year-old female presents with a breast mass located in the upper outer quadrant of the right breast which progressively grow and twice its size in 2 months. Mammography and ultrasonography revealed a lobulated, nodular mass, with architectural distortion and indistinct margins (BI-RADS 4C), without involvement of any other structure. A needle biopsy was performed, reporting a granulomatous inflammatory process, patient underwent antibiotic and anti-inflammatory treatment showing no clinical improvement. An excisional biopsy was

performed; cut surface appeared hemorrhagic with a purplish-brown color, with areas of necrosis. The tumor was clearly demarcated from the surrounding tissue.

Histologically, the lesion showed a multinodular architecture. These nodules were composed of ovoid mononuclear cells and osteoclastic giant cells. The mononuclear cells were round to oval, usually histiocytoid, some had a spindle-cell appearance, with vesicular chromatin and small nucleoli. The giant cells were osteoclastic type, with eosinophilic cytoplasm and 4-10 oval nuclei. (Image 1) These nodules are distributed in a cellular fibroblastic stroma showing prominent necrosis. The final diagnosis was malignant GCT, with positive deep surgical margin.



**Image 1**

Radical mastectomy was performed (Image 2), with surgical bed marking and axillary dissection. Macroscopic workup showed 3 yellowish tumor masses, measuring 3 cm in largest diameter. These were irregularly shaped and infiltrative, heterogeneous, with areas of hemorrhage and central necrosis. Histology showed the same cellular composition, and stromal background. 2 out of 20 dissected lymph nodes showed metastatic disease, as well as multiple tumor implants in the adipose tissue of the axilla. All surgical resection margins were free of cancer.



**Image 2**

The mononuclear fibrohistiocytic component was positive for vimentin, and focal staining for Calponin and smooth muscle actin; multinucleated giant cells were positive for CD68. Cytokeratin staining was negative.

The patient was treated with adjuvant chemotherapy. One month after surgery, multiple lesions were documented in both lungs, and left axillary adenopathy. Six later, the patient presented osteolytic skull lesions in the left parietal, occipital and frontal regions; radiation therapy was added to the treatment. The patient continued in poor general condition, without remission. Despite all efforts the patient died from this disease 9 months after diagnosis.

**DISCUSSION.**

Extrasosseous GCT is a rare neoplasm. Various localizations have been reported, including salivary glands, uterus, bladder and many others. 8-16 At least four cases of malignant extra-osseous giant cell tumor arising in breast have been reported, one associated to aggressive behavior and fatal outcome. Many lesions have been subsumed under the category of giant cell malignant fibrous histiocytoma (MFH). 1,17

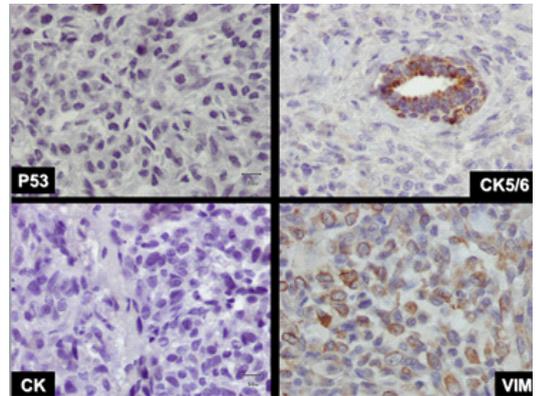
The origin of GCT in breast is uncertain; literature reports some association with history of apparent breast trauma. One case was associated with radiation in contralateral breast for ductal carcinoma. No definitive relationship has been observed between these entities. 6,17

Unlike its bone counterpart, most GCT of the soft tissues occur in older patients (Mean age at diagnosis 56 years). While the age range of patients in the reported cases was 50 -72 years, our patient is the youngest among the reported patients with breast GCT of the breast, at 46 years. 2

Most of the reported cases corresponded to nodular tumors, with diameters ranging from 3-10 cm, with infiltrating, hemorrhagic edges and necrotic areas.. Histologically, they are generally non-encapsulated solid tumors, composed of mononuclear cells of histiocytic characteristics, occasional atypia or moderate pleomorphism, and giant osteoclastic cells containing 3-10 vesicular nuclei with alternating areas of hemorrhage and ischemic necrosis. The aggressive histological characteristics are present in those patients with an aggressive clinical course.6 They usually show an increase in mitotic activity, similar to our case.

Immunohistochemistry shows positivity in mononuclear cells for vimentin, smooth muscle actin and calponin. In some cases S-100 protein and CD68 were also positive. The giant cells were positive

for CD68, alpha 1-antitrypsin and vimentin. Both components are negative for epithelial markers (image 3)



**Image3**

Differential diagnosis of these lesions includes epithelial or biphasic primary breast tumors that contain giant osteoclast-type cells. Generous sampling of the specimen should be carried to rule out this association. Giant cells of the osteoclast type have been reported in association with primary breast lesions such as ductal carcinoma, in situ carcinoma and malignant phyllodes tumor. 18 A study conducted on the osteoclast-like cells of ductal carcinoma found no differences at a morphological, functional or electron microscopy levels to its bone counterpart. 19

MFH with giant cells of the breast is another important differential diagnosis. Even though the GCT behaved aggressively in our case, it does not show the marked histiocytic pleomorphism observed in HFM. In most cases the giant cell component is frankly malignant. 1,17,20

Metastatic GCT to the mammary parenchyma should be discarded. This possibility has been reported in a 44-year-old patient diagnosed with GCT of the right distal radius, with a ten-year clinical course from the moment of the initial diagnosis to breast metastasis. 21

In our case, the absence of medical history and negative imaging prior to mastectomy ruled out a metastatic origin of this lesion. GCT originating in the rib anterior arch, which clinically present as mammary masses, have been reported, however in these cases the imaging studies show clear involvement of the anterior costal arch.22-24

Although the clinical course of extrasosseous GCT is uncertain, in our case, the clinical course was unfortunate, with disseminated disease and death within a year from date of diagnosis. This is the second reported case of GCT of the breast with fatal outcome. Unlike our patient, these neoplasms are usually curable with a wide resection of the tumor. So far, there are no clinical, radiological or histological criteria that can predict the behavior of these lesions.25 Tumor size, extension, infiltration to the adjacent parenchyma and high mitotic rate are factors that probably contributed to the aggressive behavior, which finally ended with patient's dead. In other cases reviewed in the literature with extra osseous GCT in other organs, the behavior has been benign in the majority of cases.

**CONCLUSIONS**

Primary GCT of the breast is an exceptionally rare neoplasm, reported at least in 4 occasions. The histological and immunohistochemical characteristics are identical to their bone counterpart. However, several factors, such as extensive tumor necrosis and adenopathies at the time of diagnosis seem to influence an aggressive clinical course.

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