# Breast Granular Cells Tumor Presenting as a BI-RADS 5 Nodule on Ultrasonography: Case Report

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*Tumor de Células Granulares em Mama Apresentando-se como Nódulo BI-RADS 5 à Ultrassonografia: Relato de Caso*

Tumor de Células Granulares de Mama que se Presenta como Nódulo BI-RADS 5 en Ecografía: Informe de Caso

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## ABSTRACT

**Introduction:** Granular cell tumor (GCT) is a rare and predominantly benign neoplasm that can be found in various parts of the body, frequently found in the neck and head region. It typically occurs in adults aged 40 to 60 years, with a higher incidence in females. Granular Cell Tumor of the breast represents 5% to 15% of all GCTs, and due to clinical and radiological characteristics that may resemble breast malignancies, histopathological diagnosis is essential. It typically manifests as a solitary, palpable mass, although multicentricity is possible in up to 20% of cases, whether in breast tumors or other sites. **Case report:** 43-year-old patient with a hypoechoic nodule classified as BI-RADS 5 on ultrasound, located in the superolateral quadrant of the left breast, at 2 o'clock, with an irregular shape, measuring 7.0 x 6.0 mm in the longest axis and 50 mm from the papilla. As it was radiologically suspicious, a breast core biopsy was performed, which microscopically was categorized as a lesion of uncertain malignancy potential. Immunohistochemical analysis revealed positivity for S100 and CD68, indicating Schwann cell origin, associated with negativity for cytokeratins and hormone receptors, disfavoring the epithelial origin of the carcinomas. The therapeutic approach was complete surgical excision of the nodule, and histopathological analysis confirmed it was GCT. **Conclusion**: Reporting this case is important due to its rarity and potential to mimic breast cancers.

**Key words:** Breast Neoplasms/epidemiology; Granular Cell Tumor/epidemiology; Pathology; Women's Health.

RESUMO

**Introdução:** O tumor de células granulares (TCG) é uma neoplasia rara e predominantemente benigna, frequentemente localizada na região da cabeça e pescoço. Comumente, afeta adultos entre 40 e 60 anos, com maior incidência em mulheres. O TCG mamário, representando de 5% a 15% de todos os TCG, demanda diagnóstico histopatológico em virtude de semelhanças clínicas e radiológicas com malignidades mamárias. Tipicamente, manifesta-se como massa solitária palpável, embora a multicentricidade ocorra em até 20% dos casos, seja em tumores mamários ou de outros sítios. **Relato do caso:** Paciente, 43 anos, com nódulo hipoecoico classificado como BI-RADS 5 na ultrassonografia, localizado no quadrante superolateral da mama esquerda, às duas horas, de formato irregular, medindo 7,0 x 6,0 mm nos maiores eixos e distando 50 mm da papila. Por ser radiologicamente suspeito, foi realizada a *core biopsy* mamária, que microscopicamente foi categorizada como lesão de potencial maligno incerto. A análise imuno-histoquímica revelou positividade para S100 e CD68, indicando origem em células de Schwann, associada à negatividade para citoqueratinas e receptores hormonais, desfavorecendo a origem epitelial dos carcinomas. A conduta terapêutica foi a exérese cirúrgica completa do nódulo, e a análise histopatológica confirmou tratar-se de TCG. **Conclusão:** Relatar essa neoplasia faz-se importante em razão da raridade da condição e sua capacidade de mimetizar cânceres mamários.

**Palavras-chave:** Neoplasias da Mama/epidemiologia; Tumor de Células Granulares/epidemiologia; Patologia; Saúde da Mulher.

RESUMEN

**Introducción**: El tumor de células granulares (TCG) es una neoplasia rara y predominantemente benigna que se puede encontrar en diversas partes del cuerpo, siendo la región de cabeza y cuello las más comúnmente afectadas. Suele ocurrir en adultos de 40 a 60 años, con mayor incidencia en las mujeres. El tumor de células granulares de mama representa del 5% al 15% de todos los TCG y, debido a características clínicas y radiológicas que pueden parecerse a las neoplasias malignas de mama, el diagnóstico histopatológico es esencial. Suele manifestarse como una masa solitaria palpable, aunque es posible la multicentricidad hasta en un 20% de los casos, ya sea en tumores de mama u otras localizaciones. **Informe del caso:** Paciente de 43 años con nódulo hipoecoico clasificado ecográficamente como BI-RADS 5, ubicado en el cuadrante superior lateral de la mama izquierda, a las 2 h, de forma irregular, de 7,0 x 6,0 mm en los ejes mayores y a 50 mm del pezón. Por sospecha radiológica se realizó biopsia central de mama, la cual microscópicamente se categorizó como lesión de potencial maligno incierto. El análisis inmunohistoquímico reveló positividad para S100 y CD68, indicando origen en células de Schwann, asociado a negatividad para citoqueratinas y receptores hormonales, desfavoreciendo el origen epitelial de los carcinomas. La actitud terapéutica fue la extirpación quirúrgica completa del nódulo, confirmándose mediante análisis histopatológico que se trataba de TCG. **Conclusión**: Informar este caso es importante debido a la rareza de la afección y su potencial para imitar el cáncer de mama.

**Palabras clave:** Neoplasias de la Mama/epidemiología; Tumor de Células Granulares/epidemiologia; Patología; Salud de la Mujer.

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## INTRODUCTION

Granular cell tumor (GCT) also known as Abrikossof tumor is a rare neoplasm, predominantly benign, with remarkable incidence in the head and neck, especially in buccal lesions located at the back and lateral edge of the tongue[1].

Accounting from 5% to 15% of all GCTs, breast GCT is gaining interest due to its clinical and radiological characteristics which often mimic breast carcinomas amidst sclerosing benign conditions as complex sclerosing adenosis. In the last years, its clinical relevance has risen with prevalence of 6.7 per one thousand cases of breast cancer in the general population, including men which respond for 6.6% of the cases. Typically, breast GCT is a palpable mass detected in nearly 70% of the cases[2].

The present case report describes a breast GCT in a 43-year old female patient, whose initial ultrasound indicated BI-RADS 5 node, highlighting the importance of the satisfactory diagnosis and treatment for this uncommon condition. The "*Hospital Erasto Gaertner*" approved the study, report number 6,144,040 (CAAE – submission for ethical review 69995423.3.0000.0098) in compliance with Directive 466/2012[3] of the National Health Council. An additional literature review at the databases PubMed, SciELO and Science Direct was performed to contextualize the case within the existing scenario.

## CASE REPORT

43-year old woman attended the first consultation with the gynecologist who identified a firm little moveable palpable node at the left breast a few months ago with no further complaints. Referred breast cancer family history, was unable to tell degree of kinship or age of the relative affected by the malignant tumor.

Digital mammogram was performed with findings within normality patterns (BI-RADS 1). However, as the breasts were dense and heterogeneous, obscuration might have impeded the detection of small nodes in the mammography. Therefore, complementary ultrasound was indicated which revealed irregular, hypoechogenic, spiculated margins imaging, with longer axis perpendicular to the skin, producing posterior acoustic shadow, findings compatible with BI-RADS 5 at superolateral quadrant of the left breast. The lesion was located at two o'clock, 5cm from the papilla, measuring 7.0 x 6.0 x 5.0 mm (Figure 1A). The areolar-papillary complexes were normal, no signs of ductal ectasia, no lymph node enlargement signs were identified at the axilla and lymph modes structures had regular echography aspect.

Ultrasound-guided core biopsy of the suspected node was performed, the microscopic analysis showed fragments of breast tissue with collagenized stroma permeated by strings of cells with ample, granular and eosinophilic cytoplasm, with round nuclei and prominent nucleoli (Figure 1B).

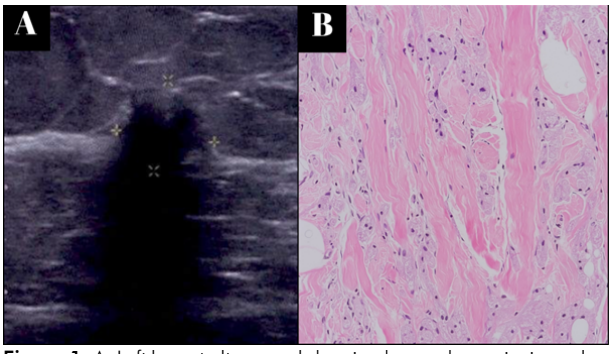


**Figure 1**. A. Left breast ultrasound showing hypoechogenic, irregular, spiculated nodule with posterior acoustic shadow. B. Optical microscopic imaging showing strings of cells with ample, granular and eosinophilic cytoplasm containing round nuclei and prominent nucleoli (optical microscopy, hematoxylin and eosin, 400x).

These findings prompted the team of pathological anatomy to classify the lesion as B3 according to the European Working Group for Breast Pathology. It corresponds to uncertain malignancy potential according to the pathologist histological evaluation; this category includes ductal and lobulated hyperplasia, lobular carcinoma *in situ*, plane epithelial atypia, papilloma, radial scars and other uncommon conditions. Samples difficult to classify histologically are described as such whether the microscopic criteria are scarce and impede more specific diagnosis[4]. For better definition, complementary immunohistochemical study was indicated for diagnostic elucidation.

The confirmation was through immunohistochemical evaluation with markers CD68 and S100, in addition to ruling out the possibility of breast carcinoma. Positivity of cells described for CD68 and S100 (Figure 2A and 2B) was found, without cytokeratin expression (CK7) or estrogen and progesterone hormone receptors. Protein CD68 represents lysosomal activity and appears positive in 90% of GCTs. Also found in neuron Schwann cells, melanocytes and myoepithelial tissue, S100 is described as a sensitive marker constantly positive in GCT[2]. Cytokeratin (CK7) are proteins expressed by epithelial lining of the cavities of internal organs and ducts of glands and their expression can indicate several types of neoplasms of this origin, therefore, the negativity disfavors the diagnosis of carcinoma[5]. From these findings, the histological context and profile of antibodies were compatible with GCT.

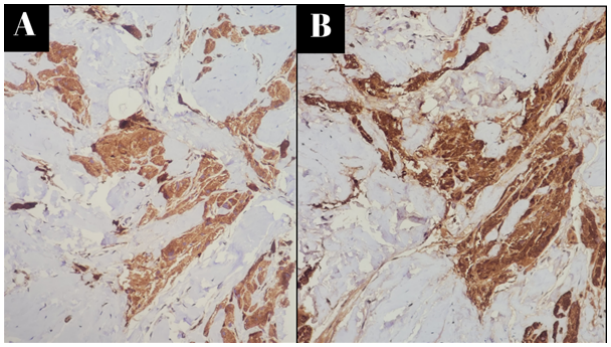


**Figure 2**. A. Immunohistochemical positivity of marker CD68. B. Immunohistochemical positivity of marker S100 (optical microscopy, immunohistochemistry, 200x)

Surgical resection was the treatment of choice with left breast segmentectomy surgery with safety margins and intraoperative evaluation. During the macroscopic analysis of the breast parenchyma of the surgical piece, a white-like, well-defined and firm mass was noticed with 0.7 cm in its longest axis. Histologically, the diagnosis of GCT was confirmed with free-resection margin.

In postoperative follow-up with the mastology team, the physical examination of the breast was normal with free axilla and supraclavicular fossa. New mammograms and ultrasound were performed after six and 12 months with benign findings. Axillary regions did not show suspicious lesions.

## DISCUSSION

Although more common at the tongue, GCT can manifest atypically on several sites, as the respiratory system, paranasal sinuses, skin and gastrointestinal system. Usually, they stand out due to their rarity accounting for 0.5% of all soft tissue tumors and more uncommon at the breast, responding for only 5% to 15% of all the cases of GCT[6-11].

These lesions can occur in patients of a wide age-range although less frequently in children. The peak of incidence occurs between the second and sixth decade of life with predilection for African born women. The prevalence of GCT compared to other human neoplasms is quite low, approximately 0.019% to 0.03%[1,12,13].

Clinically, they are firm, generally mobile and painless lumps, although variable consistency and symptomatology have already been reported. Detection by palpation occurs in 70%, mammogram screening in nearly 26% while only 4% are identified during the follow-up of patients who had already been diagnosed with some type of breast cancer. Though rare, cutaneous involvement may occur with thickening, retraction and dimpling, while lymphadenopathy is barely found[2].

Whether at the breast, predilection of GCT for the upper quadrant was noticed in the present study, possibly associated with the origin of perineural cells and distribution of the supraclavicular cutaneous sensory nerve. Epidemiological aspects emphasize the clinical relevance of breast GCT with prevalence of 6.7 cases for every thousand cases of breast neoplasms of the population[14-18]. Therefore, these peculiarities justify the inclusion of GCT in differential diagnosis of suspicious breast lumps, potentially leading to misleading diagnosis and wrong treatments, further to physical and psychological discomfort for the patients.

Usually, ultrasound reveals to what extent the neoplasm varies according to the tumor infiltration and presence of reactive fibrosis. The series of 25 cases described by Ghannam *et al.*[19] showed that in 56% of the cases, the disease presented as a solid, hypoechoic/anechoic lump frequently associated with intense posterior shadowing. For 44% of the sample, it was detected as heterogeneous echotexture and areas of hyperechogenicity or pure hyperechogenicity. Additionally, the tumor margins were usually described as spiculated, angular or indistinct but in 36% of the cases, circumscribed and well-defined lesion was reported[19].

The accurate diagnosis of GCT is reached through anatomopathological study involving macroscopic and microscopic analysis of the lesion. The assessment allows to identify the histological type of the lesion and its typical cell features: nests or polygonal string cells with abundant and eosinophilic granular cytoplasm followed by prominent collagenous stroma. The cytoplasmatic granules exhibit a strong and diffuse coloration by the Period Acid of Schiff, showing the glycoprotein nature. Regarding immunohistochemistry, strong positivity for protein S100, SOX10 was found and neuron-specific enolase. These additional approaches help the confirmation of the diagnosis and detailed understanding of the tumor[20].

Conserving surgical excision remains as the primary treatment of breast GCT, with total local excision with negative resection margins because tumor recurrence is common, mainly when the lesion is not fully resected, further to routine follow-up[2]. For benign free-margins cases, the evolution is favorable without complementary therapies. Quite rarely, for malignant GCTs, radiotherapy and chemotherapy are indicated[20]. Regarding the prognosis within the carcinogenic context, the global 5-year survival is 74.3% and 62.5% after ten years, but survival was worse for patients with tumors > 5 cm.

## CONCLUSION

It has been described the importance of GCT as well as its uncommon occurrence at the breast. Although rare

in that region, the possibility of differential diagnosis when imaging tests reveal suspicious breast lumps should never be neglected. Understanding its clinical-pathological relevance is essential, notwithstanding its predominantly benign nature, the surgical excision is imperative to differentiate from other conditions and free-margins to prevent local recurrence.

## CONTRIBUTIONS

Juliane Soldi Malgarin, Júlia Costa Linhares and Samya Hamad Mehanna contributed to the study design, analysis and interpretation of the data, wording and critical review. Sérgio Augusto Mayer contributed to the study design, analysis and interpretation of the data and wording of the manuscript. Julia Wolff Barretto contributed to the analysis and interpretation of the data and critical review. Ana Paula Martins Sebastião contributed to the collection, analysis and interpretation of the data. All the authors approved the final version to be published.

## DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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None.

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