Granular Cell Tumor of the Breast Imitating a Malignant Tumor: A Case Report and Review of Literature

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Abstract
A 22-year-old woman with no family history of breast cancer developed a painful breast tumor in the inner lower quadrant of the left breast. After surgical consultation, ultrasound examination was advised. On ultrasound, the mass demonstrated malignant features such as non-parallel orientation, hypoechogenicity, spiculated margins, posterior shadowing, peripheral vessels on color Doppler and increased stiffness in the tissue surrounding the tumor. Before biopsy, mammography was performed. The mass had higher density than fibroglandular tissue, margins were ill-defined (spiculated) and had no microcalcification. BIRADS 5 category was pre-assigned. Core biopsy revealed granular cell tumor (GCT). The patient is undergoing regular follow-up. Granular cell tumor is rare and generally benign, however, it typically demonstrates malignant features clinically and on obtained diagnostic images. This article highlights the variety of imaging features accompanying benign breast tumors.

Keywords: Breast Cancer; Breast Ultrasound; Granular Cell Tumor; Schwann Cells

Introduction
Granular cell tumor is a neuroectodermal tumor derived from Schwann cells [1]. The skin and the subcutaneous tissue are the most common sites, however, it could also arise in the head and neck region, especially in the tongue where it was first described in the 19th century and also in the gastrointestinal and respiratory tracts and extremities. Breast origin is as many as 8% of all cases of granular cell tumors [2] and they represent only 0.1% of all breast tumors (1). Malignant transformation is observed in up to 2% of breast granular cell tumor cases [2]. The patient age with GCT ranges from 19 to 77 years [2,3].

Case Report
A 22-year-old woman presented with a 6-months history of a palpable mass in the lower inner quadrant of her left breast and left breast pain without nipple discharge. Physical examination revealed a 2 cm firm mass located at 8 o’clock with normal overlying skin. There was no associated axillary, supraclavicular or infraclavicular adenopathy. About six years prior to the current examination, the patient underwent excision of a benign lesion (fibroadenoma) from the same breast – a postoperative scar at 3 o’clock was noted. Apart from that and a history of anxiety disorders, her past medical history was unremarkable. She had also no family history of breast cancer. Ultrasonography (US) and mammography (full-field digital mammography,
FFDM) were performed. Upon ultrasound examination, a deeply hypoechoic lesion with spiculated margins, echogenic halo, irregular shape and very intensive acoustic shadowing (Figure 1), causing difficulties in making exact measurements was demonstrated. Approximate size was 19 x 21mm. Peripheral vascularity was noted (Figure 2), as well as highly increased stiffness in shear wave elastography (E max 300 kPa) on the periphery of the lesion (Figure 3). No axillary, supraclavicular or infraclavicular lymphadenopathy was found, similarly no other lesions in both breasts were identified. The morphology of the postoperative scar in the outer quadrants of the left breast was normal.

Mammography in mediolateral oblique and craniocaudal projections showed an irregular, spiculated mass in the lower inner quadrant of the left breast, with no associated calcifications (Figure 4).

The imaging features were considered as highly suspicious for malignancy in both US and FFDM and BIRADS 5 category was assessed. An ultrasound-guided core needle biopsy was

![Figure 1: B-mode presentation of the tumor - deeply hypoechoic lesion with spiculated margins, echogenic halo, irregular shape and very intensive acoustic shadowing.](image1)

![Figure 2: Peripheral vascularity of the lesion is seen.](image2)

![Figure 3: Shear wave elastography – periphery of the lesion is hard (E max 300kPa).](image3)

![Figure 4: FFDM finding of the lesion in the lower inner quadrant of the left breast. A. Mediolateral oblique projection. B. Craniocaudal projection.](image4)

![Figure 5: GCT composed of sheets of cells with infiltrative architecture and abundant eosinophilic granular cytoplasm (arrow). Hematoxylin and eosin staining, × 200.](image5)
Figure 6: GCT. S-100 positive staining (arrow), × 100.

Figure 7: GCT. CKAE1/AE3 negative staining (arrow), x 100.

Discussion

According to the literature, breast cancer among women under 40 years of age is rarely observed. In women younger than 30, the incidence rate is 1 out of 220 patients (0.45%), which makes it slightly higher than the incidence rate of GCT [4]. Clinically GCT is a breast cancer mimicker, usually presenting as a painless mass, able to cause nipple and skin retraction or infiltrate pectoralis fascia or muscles. Histologically, GCT is composed of sheets of spindle cells, containing abundant eosinophilic cytoplasmic granules (PAS+), with the fibrous tissue interspersed among those cells. The tumor causes the infiltration of the adjacent tissue, which often presents as spicules on diagnostic images (Figure 2, 3, 4). Therefore, on US examination and FFDM it can be mistaken for breast carcinoma. Moreover in biopsy specimens, it could be difficult to distinguish GCT from invasive apocrine cell carcinoma, because both of them contain eosinophilic granules [2]. Franburg-Smith et al. [6] demonstrated six histological features indicating malignancy: necrosis, spindle cell presence, cells with large nuclear bodies, increased mitotic activity, high nuclear to cytoplasmic ratio and pleomorphism. Meeting 2 or more criteria allow to classify the tumor as histologically malignant, 1 or 2 criteria denote the lesion atypical, whereas if only pleomorphism is observed, but none of the other criteria are present, the tumor is described as histologically benign [6].

The US and FFDM findings are not specific for GCT, as we presented in this case. On FFDM most of them display malignant features, having high density, irregular shape and spiculated margins. Same goes with the ultrasound appearance which leads the radiologist to suspect a malignant breast tumor. On US the shape of the tumor is usually elliptical, the margins are not circumscribed, there is lack of capsule and a shadowing behind the tumor is visible. The echogenicity could be various (dominate hypoechoic or anechoic), because of the anisotropic effect. Typically it is avascular on Doppler US. A less common manifestation is a circumscribed mass and an oval shape on US and FFDM. [6] Abreu et al. published a series of five GCT. The FFDM findings were nonspecific, all five lesions presented as masses, 3/5 exhibiting spiculated margins, one showing circumscribed and one indistinct margins. In all the cases evaluated, ultrasound showed nonparallel orientation, irregular shape, heterogeneous echogenicity, 3/5 lesions had spiculated margins similarly like on FFDM. On MRI (magnetic resonance imaging) the signal intensity on T1 and T2-weighted images is generally lower than that seen in breast cancer, whereas, the enhancement is heterogeneous [7,8]. Our case is clinically and radiologically similar to few reports published in the literature [1,6]. In differential diagnosis, invasive carcinoma, fat necrosis and fibromatosis should be taken into account. While the histology is benign, excision is always advised. Our patient was directed for surgery, with a recommendation from our pathologist to perform wide excision.

Conclusion

It is essential to exclude breast cancer before a decision of surgical treatment of GCT is to be made. It is crucial to obtain credible and detailed pathological verification, therefore a
core needle biopsy is necessary. To sum it up, clinical and imaging overall view of the tumor tends to mimic malignancy.

**Conflict of Interest**

All contributing authors declare no conflict of interest.

**Funding**

This work was financially supported by the National Centre for Research and Development (NCBiR) under the grant agreement LIDER/24/0088/L-11/19/NCBR/2020

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