

World Journal of *Clinical Cases*

World J Clin Cases 2023 November 26; 11(33): 7940-8093



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Thrice Monthly Volume 11 Number 33 November 26, 2023

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The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJCC as 1.1; IF without journal self cites: 1.1; 5-year IF: 1.3; Journal Citation Indicator: 0.26; Ranking: 133 among 167 journals in medicine, general and internal; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Zi-Hang Xu, Production Department Director: Xiang Li, Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Salim Surani, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

November 26, 2023

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

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<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Granular cell tumor of the breast: A case report and review of literature

Jun Yan

Specialty type: Medicine, research and experimental

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Mahmoud MZ, Saudi Arabia; Xu JD, China

Received: August 21, 2023

Peer-review started: August 21, 2023

First decision: August 30, 2023

Revised: September 26, 2023

Accepted: November 13, 2023

Article in press: November 13, 2023

Published online: November 26, 2023



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Abstract

BACKGROUND

Granular cell tumor (GCT) of the breast (GCTB) is a rare neoplasm that can exhibit malignant characteristics both clinically and radiologically. This tumor can also coexist and colocalize with breast carcinoma.

CASE SUMMARY

We present a patient with this uncommon tumor and discuss the diagnostic and therapeutic approaches in order to further the knowledge of GCTB and prevent misdiagnosis and overtreatment. The characteristics of the tumor, methods of diagnosis, therapy and postoperative pathological outcomes were analyzed, and relevant literatures of GCTs were reviewed. The patient underwent surgery after core needle biopsy, and the excised neoplasm was sent for pathological examination. Histological analysis revealed nests of cells with abundant pink granular cytoplasm, confirming the diagnosis of GCTB.

CONCLUSION

As manifestations of GCT and malignancy can mimic each other, a careful histological examination is essential before major surgery. Treatment consisting of complete excision with close clinical follow-up is recommended.

Key Words: Granular cell tumor; Breast; Neoplasm; Tumor; Literature review; Case report

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Core Tip: Granular cell tumor of the breast is a rare neoplasm that can exhibit malignant characteristics both clinically and radiologically. This tumor can also coexist and colocalize with breast carcinoma. This could result in the potential misdiagnosis of breast carcinoma and overtreatment of patients. We report a patient with this tumor and discuss the methods of diagnosis and treatment. As manifestations of the disease and malignancy can mimic each other, a careful histological examination is essential before major surgery. Complete excision with close clinical follow-up is recommended.

Citation: Yan J. Granular cell tumor of the breast: A case report and review of literature. *World J Clin Cases* 2023; 11(33): 8044-8049

URL: <https://www.wjgnet.com/2307-8960/full/v11/i33/8044.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v11.i33.8044>

INTRODUCTION

Granular cell tumors (GCTs) were first described by Abrikossoff in 1926[1]. These tumors can occur in any part of the body, but are commonly observed in the skin, oral cavity, digestive tract, and subcutaneous tissue. The overall incidence of GCTs in surgical specimens is 0.03%[2]. Breast involvement has been reported in 15% of cases[3]. One to two percent of these lesions can be malignant, with a poor prognosis and few curative options besides surgery[4]. GCT of the breast (GCTB) can mimic breast carcinoma both clinically and radiologically, making it difficult to distinguish from breast malignancies. In order to improve the understanding of GCTB and prevent misdiagnosis and overtreatment, we report a patient with GCTB, who was admitted to our hospital. A brief review of the literature was conducted to further our understanding of this unique disease.

CASE PRESENTATION

Chief complaints

A 57-year-old woman presented in December 2021 with a lump in her left breast, which had been palpable for approximately 4 mo.

History of present illness

The tumor had not significantly increased in size since its discovery.

History of past illness

The patient had previously undergone bilateral breast augmentation surgery.

Personal and family history

The patient had no family history of breast cancer.

Physical examination

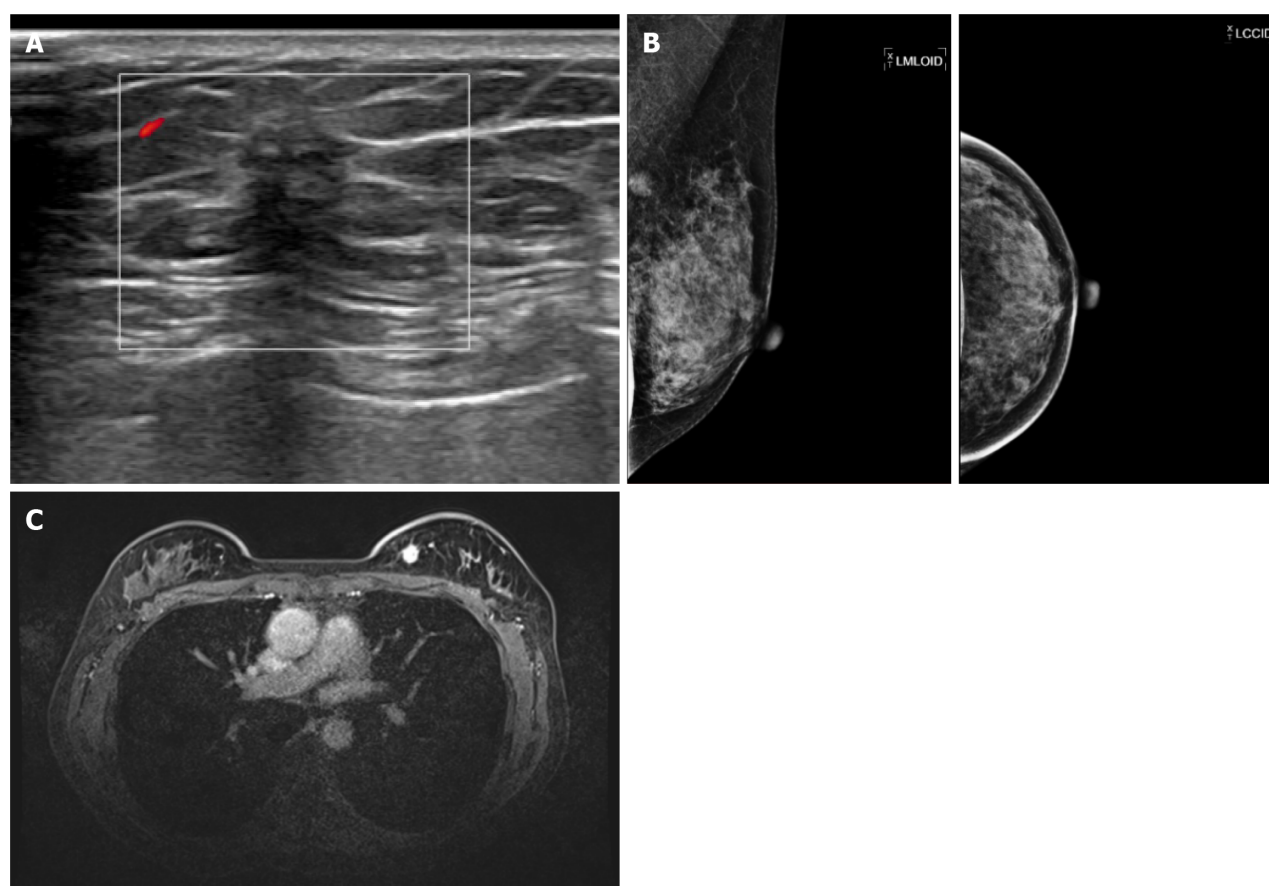
Physical examination revealed a spherical, firm, mobile, painless lump measuring approximately 1 cm in diameter and was 5 cm from the nipple in the upper outer quadrant of the left breast. No lymphadenopathy, skin retraction, discharge, thickness or dimpling was observed.

Laboratory examinations

No evident abnormalities were detected.

Imaging examinations

A standard mammogram showed a 13 mm × 12 mm dense poorly circumscribed tumor in the inner upper quadrant of the left breast. No suspicious calcification or enlarged lymph nodes were found. There were no previous mammograms available for comparison. Ultrasonography demonstrated a hypoechoic nodule, measuring approximately 9.8 mm × 10.6 mm × 9.1 mm at the 10-11 o'clock position close to the margin of left breast gland. The nodule was irregular, with a high depth to width ratio, indistinct, no envelope, the internal echo was non-uniform, a mild posterior shadow was seen without significant peripheral vascularization. No evidence of distant metastasis was found. Magnetic resonance imaging (MRI) revealed a heterogeneous enhanced round mass with a spiculated microlobulated indistinct margin, measuring 9 mm × 8 mm × 9 mm in the left breast at the 10 o'clock position, with a slightly higher signal intensity than adjacent glandular tissue in T1 and T2-weighted sequences. Following contrast administration, heterogeneous enhancement was observed with a slow initial increase in signal intensity followed by a plateau. There were no indications of implant rupture (Figure 1).



DOI: 10.12998/wjcc.v11.i33.8044 Copyright ©The Author(s) 2023.

Figure 1 Imaging photos. A: Sonography demonstrated a hypoechoic nodule, measuring about 9.8 mm × 10.6 mm × 9.1 mm at the 10-11 o'clock position close to the margin of left breast gland; B: Mammogram showed a 13 mm × 12 mm dense poor-circumscribed mass in inner upper quadrant of the left breast; C: Magnetic resonance imaging revealed a heterogeneous enhancing round-shaped mass with an spiculated microlobulated indistinct margin, measured 9 mm × 8 mm × 9 mm, located at 10 o'clock position of left breast.

FINAL DIAGNOSIS

Given the suspicion of breast malignancy, core needle biopsy was performed. Histologic assessment indicated a GCTB.

TREATMENT

The patient underwent wide local excision of the tumor.

OUTCOME AND FOLLOW-UP

The tumor was identified as a GCT on the basis of its histological characteristics. Six months after surgery, the patient is still doing well.

DISCUSSION

GCTs were first described by Abrikossoff in 1926[1]. These tumors can occur in any part of the body. The overall incidence of GCTs in surgical specimens is 0.03% [2]. Breast involvement is observed in 15% of cases [3]. GCTs can occur in all age groups and genders; however, in general, GCTs are almost twice as common in women as in men, predominantly affecting patients in their fourth to sixth decades [2-4]. With a poor prognosis and few curative options besides surgery, one to two percent of these lesions may be cancerous [5]. GCTB mainly occurs in females similar to breast malignancies, but has also been reported in the male population, accounting for 6.6% of all GCTB cases [6]. GCTB frequently resembles malignant neoplasms both clinically and radiologically, making it challenging to distinguish from breast cancers.

Previously, most cases of GCTB were symptomatic; however, with improved breast screening, more asymptomatic cases are being detected. Though some patients have experienced discomfort, pruritis, skin retraction, thickness or dimpling, and reactive lymphadenopathy at presentation, the majority of these tumors are painless, smooth, slow-growing solitary nodules. They can also be multicentric, and even coexist and colocalize with breast carcinoma[1,7]. Therefore, GCTB is difficult to distinguish from carcinoma clinically.

Radiological findings of GCT can be nonspecific in the breast, and are often indistinguishable from those of breast malignancies. They can be small, round, well-circumscribed masses, but also present as indistinct, stellate, sometimes combined with hypodense rims, spiculated with or without calcifications, and skin thickening, associated with the pectoralis on mammography[8].

These tumors on ultrasound are frequently heterogeneous, solid, and poorly defined masses with a posterior shadow and a high depth to width ratio, which often denotes malignancy. Similar to mammography, GCTB on ultrasound has a wide range of properties[9]. The appearance of GCTB on MRI is variable. Benign characteristics such as gradual augmentation, high end intensity, and equal or low signal on T1 and T2 weighted sequences may be present. In addition, malignant features such as fast enhancement, rim enhancement, washout phenomenon, irregular and indistinct lesions may also be observed[10,11]. MRI may be useful in delineating the extent of disease, the presence of aggressive features and contralateral screening; however, no specific features of GCTB have been outlined and GCTB can closely resemble primary breast malignancies[12,13].

To date, only one study has investigated the positron emission tomography/computed tomography features of GCTB. In this case, no evidence of focally enhanced tracer accumulation was revealed. The lesion displayed an average standardized uptake value of 1.8 indicating a benign lesion. Pathological investigation identified this tumor as GCT which infiltrated the subcutaneous and muscular tissue with no mitotic activity. Given the high sensitivity and specificity of positron emission tomography/computed tomography for malignant masses, further study and health economics evaluation are required[12]. Although GCTB are mostly benign, a conclusive pathological diagnosis is essential before surgery to avoid unnecessary radical treatment. Ultrasound guided percutaneous core biopsy of the tumor is well established as the diagnostic procedure for suspicious lesions. While fine needle aspiration cytology smear interpretation has diagnostic challenges including delicate cell membrane and cytoplasm, and insufficient material for immunohistochemical procedures, core biopsy is able to provide specimens that retain their native intracellular architecture to facilitate specific histological diagnosis[14,15]. Pre-operative histological confirmation with core biopsy may contribute to avoiding mastectomy and axillary dissection[16].

Despite the fact that GCTs are often benign, 1%-2% of these lesions can be malignant[5]. Fanburg-Smith *et al*[17] outlined six features including necrosis, increased mitotic count (greater than 2 per 10 high power fields), spindle tumor cells, nuclear pleomorphism, prominent nucleoli, vesicular nuclei, and a high nuclear to cytoplasmic ratio in 1998. If three of these six features are present this is indicative of malignancy, and is atypical if only two features are seen.

It was previously widely accepted that GCTs were derived from Schwann cells of the peripheral nervous system due to the presence S-100 protein[18]. Additionally, GCTs also stained positive for CD68, neuron-specific enolase, vimentin, CD57, CD56, SOX-10 and inhibin[1,19,20]. However, a subset of S100-negative “non-neural” GCTs has been identified[21-25]. The histogenesis of GCT is still debatable at this time.

Complete excision with negative margins and close clinical follow-up is the gold standard treatment strategy for GCTB. Axillary lymph node evaluation, including sentinel lymph node biopsy and lymph node dissection, is only indicated for malignant GCTB[6]. Since the approval of pazopanib for advanced soft tissue sarcomas and metastatic soft tissue sarcomas in the phase III trial, several patients with malignant GCTs have demonstrated a response following treatment with this drug. Establishing the mechanism of action responsible for the disease response *via* limited instances is challenging due to the overexpression of multiple genes by the tumor and various targets of medicines. Clinical trials and appropriate cell lines or mouse models are essential to ascertain the exact mode of action responsible for the tumor response[26-30]. Given the absence of randomized clinical trials on this particular lesion, it is currently believed that there is a limited role for adjuvant therapy, and there is no current standard chemotherapy regimen and radiation therapy for this specific tumor[1].

The prognosis of benign GCT is excellent. However, patients with malignant GCT have a poor prognosis. Malignant GCT has an overall cause-specific survival rate of 74.3% after 5 years and 65.2% after 10 years, respectively. Patients with tumors larger than 5 cm had a worse chance of survival (90.0% *vs* 51.3%, respectively; $P = 0.02$) than patients with tumors smaller than 5 cm. The prognosis was much worse for those who had regional or distant metastases at the time of diagnosis[31].

In this report, we describe a rare breast neoplasm that was radiologically indicative of a malignant tumor but was later determined to be a benign GCTB following extensive local excision. Complete imaging analysis and biopsies could be of significant assistance in making the diagnosis and avoiding invasive procedures. Following a review of the literature, clinical trials and gene research are still required for a deeper knowledge of this rare condition.

CONCLUSION

GCTB is a rare disease and can often resemble breast cancer. In the present case, the patient had imaging characteristics of a malignant tumor; however, histologic analysis revealed that the lesion was benign. A thorough imaging evaluation and core needle biopsy are necessary prior to major surgery. Complete excision with negative margins and close clinical follow-up is currently the gold standard treatment strategy for GCTB. Clinical trials and objective molecular data before treatment initiation are needed for deeper knowledge of malignant GCT and the development of effective treatment.

FOOTNOTES

Author contributions: Yan J performed this research, reviewed the articles and wrote the manuscript.

Informed consent statement: The patient provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The author reported no relevant conflicts of interest for this article.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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Country/Territory of origin: China

ORCID number: Jun Yan 0009-0009-4392-5832.

S-Editor: Wang JJ

L-Editor: A

P-Editor: Zhao S

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