

Granulomatous mastitis co-existing with breast cancer: A case report and mini-review of the literature

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Abstract. Granulomatous mastitis (GM) is a rare inflammation of the breast marked by non-caseating granulomatous lesions near the breast ducts and lobules. Reports of GM coinciding with breast cancer are rare. The present study describes the case of a patient with GM, high-grade ductal carcinoma *in situ* (DCIS), and invasive ductal carcinoma were present in the same breast. A 36-year-old woman with a 2-week history of left breast pain was found to have a large, firm lump. A core needle biopsy led to the diagnosis of DCIS and suppurative GM. The patient was initially treated with analgesics and antibiotics for 20 days. Eventually, the patient underwent a complete mastectomy with immediate reconstruction using a TRAM flap. A subsequent histopathological examination revealed invasive ductal carcinoma of no specific type, poorly differentiated, with extensive DCIS and suppurative GM. Upon the last follow-up, the patient was monitored and remained stable with no post-operative complications. Furthermore, in a literature review conducted utilizing Google Scholar and PubMed, only 13 cases of the simultaneous presence of GM and breast cancer were found. The average age of these patients was 43.07±12.10 years. Of note, 7 (53.85%) of these patients had both GM and breast cancer in the left breast, while only 2 cases (15.38%) involved the conditions in contralateral breasts. In conclusion, distinguishing between breast cancer and GM is challenging. Although the simultaneous presence of GM and breast cancer is rare, it remains essential to consider

this possibility. However, further research is required to clarify the association between GM and breast cancer.

Introduction

Granulomatous mastitis (GM) is a rare breast inflammation, affecting ~2.4 out of every 100,000 females in the USA (1). Typically, GM is defined by non-caseating granulomatous inflammation occurring near the ducts and lobules of the breast. These granulomas are often unilateral and commonly present as a solid mass in the upper outer quadrant of the breast (2).

GM can be etiologically classified into two main categories: Idiopathic GM and secondary GM. An unknown underlying cause characterizes idiopathic GM, although an autoimmune origin is widely supported due to its responsiveness to steroid therapy and its association with autoimmune disorders (3). By contrast, secondary GM results from identifiable causes, including infectious agents such as *Mycobacterium tuberculosis*, fungal or parasitic infections and bacterial pathogens, as well as systemic diseases such as sarcoidosis and granulomatosis with polyangiitis (2,3).

Based on clinical, pathological and radiological findings, GM can easily be mistaken for breast cancer and other conditions such as tuberculosis, fungal infections and syphilis (2). Moreover, the presence of GM alongside other breast pathologies, such as lobular carcinoma *in situ* and ductal carcinoma *in situ* (DCIS), underscores the complexities of diagnosing this condition (4). The present study describes a rare case of GM, high-grade DCIS and invasive ductal carcinoma (IDC) occurring simultaneously in the same breast. The report was prepared following the CaReL guidelines (5). All references cited were assessed for eligibility (6).

Case report

Patient information. A 36-year-old woman presented to Smart Health Tower, Sulaymaniyah, Iraq, with a 2-week history of pain in her left breast. She was a mother of 3 children, having

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breastfed her children for 4 years, and was currently nursing her youngest. She had a history of passive smoking, no notable previous medical or surgical history, and no family history of breast cancer.

Clinical findings. Upon an examination, a large, firm and immovable lump was detected in the upper outer quadrant of the left breast. Additionally, palpable lymph nodes (LNs) were noted in the left axilla.

Diagnostic assessment. A breast ultrasonography (US) revealed a heterogeneous area with fluid echogenicity and moderate surrounding edema in the left breast. This resulted in localized skin thickening and contour distortion at the 2 o'clock position, measuring 64x27 mm. Several reactive LNs were noted in the left axilla. The right breast and axilla appeared normal. A follow-up US revealed similar size and morphological characteristics. A core needle biopsy (CNB) of the lesion confirmed a diagnosis of high-grade DCIS with both solid and comedo patterns, along with suppurative GM. Subsequent breast magnetic resonance imaging (MRI) revealed heterogeneous non-mass-like enhancement, a small central mass measuring 18 mm, and bilateral enlarged axillary LNs (Fig. 1). Fine-needle aspiration of the bilateral axillary LNs revealed no evidence of malignancy.

Therapeutic intervention. At the initial visit, the patient was prescribed ibuprofen tablets (200 mg, one tablet twice daily) for 7 days and amoxicillin/clavulanic acid tablets (875/125 mg, one tablet twice daily) for 20 days. Following the presentation of the case of the patient at the multidisciplinary team meeting and additional investigations, the initial treatment plan included breast-conserving therapy and sentinel LN biopsy. A comprehensive pre-operative assessment was conducted, and the patient subsequently underwent surgery involving a wide local excision of the breast mass and excision of sentinel-sampled axillary LNs. Both tissue samples were submitted for histopathological examination (HPE). The 5- μ m-thick sections were fixed in 10% neutral-buffered formalin at room temperature for 24 h and embedded in paraffin. They were subsequently stained with hematoxylin and eosin (Bio Optica Co.) for 1-2 min at room temperature, and then examined using a light microscope (Leica Microsystems GmbH).

Following discharge, the patient was closely monitored with no post-operative complications. The HPE from the first surgery revealed IDC of no specific type, poorly differentiated, with extensive DCIS and suppurative GM (Fig. 2). The tumor was multifocal, and DCIS involved the inferior margin. Additionally, one of the nine LNs sampled exhibited macro-metastasis with extra-nodal extension, resulting in a pathological staging of pT1cN1a (7). A chest, abdomen and pelvis computed tomography scan confirmed the absence of distant metastasis.

The oncology team recommended a revision of breast surgery with axillary LN dissection since the patient declined a mastectomy. Consent was obtained for another surgery in the case that margin involvement was identified in the HPE. The HPE from the second operation again indicated the involvement of the inferior margin by DCIS, leading to

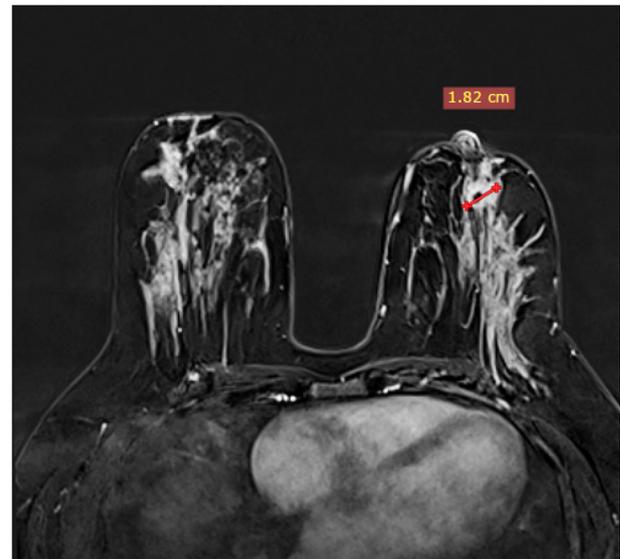


Figure 1. The breast magnetic resonance imaging demonstrates heterogeneous non-mass-like enhancement with a small central mass, measuring 1.82 cm, highlighted in the left breast.

the decision for a left completion mastectomy with immediate reconstruction using a transverse rectus abdominis myocutaneous (TRAM) flap.

The final HPE revealed high-grade DCIS without invasive components and clear resection margins. Subsequently, the patient was referred to an oncologist. The treatment regimen consisted of six cycles of chemotherapy with Docetaxel (Taxotere) 150 mg IV and carboplatin (Paraplatin) 886.9 mg IV, followed by a one-year course of trastuzumab (Herceptin) 546 mg IV. Additionally, endocrine therapy was initiated with oral exemestane (Aromasin) and subcutaneous Goserelin (Zoladex) injections. Following chemotherapy, the patient will be referred to a radiation oncologist to evaluate the need for radiotherapy.

Follow-up. Upon the last follow-up, the patient was monitored and remained stable with no post-operative complications.

Discussion

In 1972, Kessler and Wolloch (8) reported the first case of GM and noted that it may be mistaken for breast cancer due to similarities in clinical signs and presentations. These include lumps, pain, swelling, skin changes, abscesses, ulcerations, sinus tracts, fistulas in severe or chronic cases, and occasional association with axillary lymphadenopathy (8,9).

Typically, GM occurs in women of childbearing age within 5 years following their last childbirth and is extremely rare in nulliparous women. The condition often involves abscess formation, predominantly affecting the lobules, and is characterized by the absence of caseating granulomas, acid-fast bacteria, or fungi (10). The patient in the present case report was a mother of 3 children who had breastfed for 4 years and was currently nursing her youngest child.

The development of GM is considered to begin with damage to the breast ductal epithelium. This damage allows

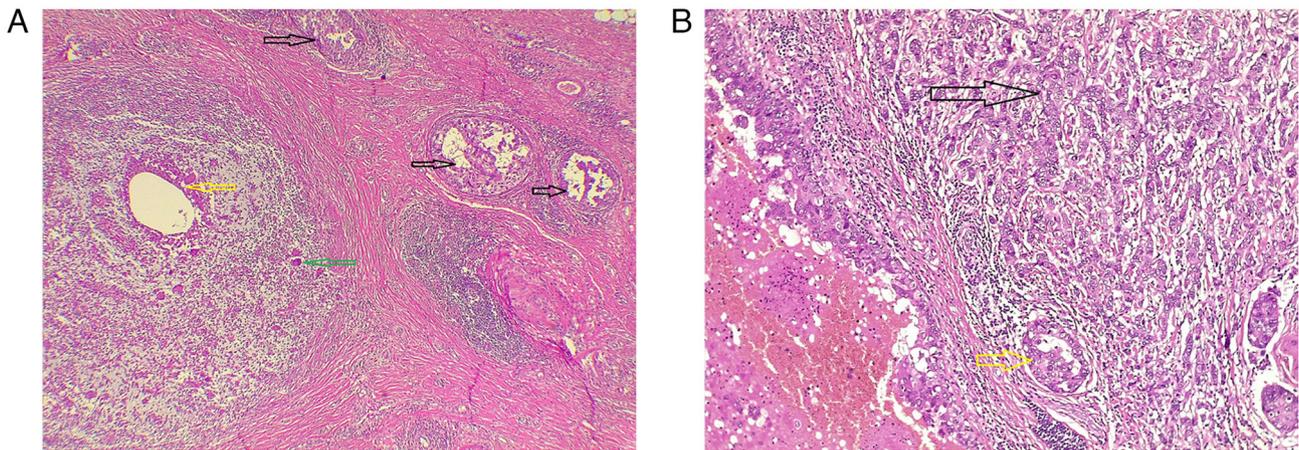


Figure 2. (A) The section shows multiple ducts, showing ductal carcinoma *in situ* (black arrows) and adjacent cystic neutrophilic granulomatous mastitis (yellow arrow), which contains multinucleated giant cells (green arrow). (B) The section shows (wide local excision) an area of invasive ductal carcinoma (black arrow) with ductal carcinoma *in situ* (yellow arrow).

luminal secretions to spread into the lobular connective tissue, triggering local inflammation. Subsequently, lymphocytes and macrophages migrate to the affected area, resulting in a granulomatous inflammatory response (2).

The diagnosis of GM can often be challenging, as ultrasound, mammography and MRI findings are typically non-specific and mainly confirm the presence of a mass, parenchymal irregularities, or multifocal lesions. Since histology remains the gold standard for diagnosis, all suspicious areas should be biopsied. For GM, chronic granulomatous inflammation is identified by giant cells, leukocytes, epithelioid cells and macrophages (11).

In some cases, patients initially diagnosed with breast cancer and treated with mastectomy and LN removal later find, through pathological analysis, that they had GM (8). Additionally, there are rare instances where individuals diagnosed with GM and managed non-invasively were later found to have breast cancer after surgery due to no significant improvement in their condition (12). The first documented association between chronic mastitis and malignancy involved five sisters with chronic mastitis, three of whom subsequently developed breast cancer (13). Whether the coexistence of GM and breast cancer is incidental or indicative of an underlying biological relationship remains uncertain. Some hypotheses suggest that chronic inflammation, as observed in GM, may contribute to carcinogenesis through sustained immune activation, cytokine release, and oxidative stress. However, current evidence does not support a direct causal link. The majority of experts consider the two conditions to be coexisting rather than causally related, with inflammation potentially unmasking or mimicking an adjacent neoplastic process (9).

The simultaneous presence of GM and breast cancer has rarely been reported in the literature (4). In a review of the literature utilizing the PubMed and Google Scholar databases, only 13 cases of simultaneous GM and breast cancer were identified (9-11,14-21). The average age of these patients was 43.07 ± 12.10 years, with ages ranging from 34 to 77 years. Among the patients, 7 (53.85%) patients had both GM and breast cancer in the left breast, while only 2 cases

(15.38%) involved the conditions in contralateral breasts. A total of 8 cases (61.54%) had a concurrent diagnosis of GM and DCIS (Table I). The case described in the present study was a 36-year-old breastfeeding woman with suppurative GM, high-grade DCIS and IDC, all localized in the left breast. This combination of findings is rare and clinically significant, as it represents only the second reported case, in which GM, DCIS and IDC were simultaneously identified in the same breast. The first such case was described by Çalış and Kilitçi (19), involving a 77-year-old woman who presented with right breast pain, edema and skin thickening near the areola. A biopsy revealed IDC and DCIS, and the final mastectomy specimen confirmed the presence of GM as well. Similar to that report, the case described herein also presented with breast pain and was ultimately diagnosed with all three pathologies following wide local excision. However, the case in the present study is further distinguished by the multifocal nature of the lesion and persistent positive margins after two surgeries, which necessitated a completion mastectomy. The breastfeeding status of the patient, commonly associated with idiopathic GM, may have contributed to initial diagnostic uncertainty, as the condition was first managed conservatively. Taken together, these features underscore the diagnostic and therapeutic complexity of managing such rare presentations.

Typically, DCIS is characterized by an abnormal growth of epithelial cells within the mammary ducts without invasion into other areas of the breast tissue. It is rarely symptomatic or clinically palpable. The lesion is enclosed by an intact basement membrane and bordered by a layer of partially continuous myoepithelial cells (9). Oddó *et al* (17) reported the case of a 44-year-old woman who presented with painful swelling in her left breast. The patient was diagnosed with GM but did not respond to any antibiotic treatments. A subsequent biopsy confirmed the presence of GM along with DCIS. Özşen *et al* (18) described a similar case of a 35-year-old woman with swelling in her right breast. Initially diagnosed with GM through a core needle biopsy, the patient underwent excisional surgery due to a poor response to treatment. The final diagnosis revealed granulomatous lobular mastitis and DCIS.

Table I. Overview of literature on the concurrent presence of granulomatous mastitis and breast carcinoma.

First author, year of publication	No. of cases	Age, years/ (sex)	Presentation	US findings	MRI findings	MMG	Treatment	Diagnosis	Location	IHC		Follow-up (Refs.)
										Positive	Negative	
Salih, 2023	1	34/F	Left breast pain for 7 days.	A full-length ectatic duct from the nipple root to the 5-7 o'clock position, with heterogeneous internal echoes, mild edema, and reactive axillary lymph nodes, suggesting GM recurrence.	A clumped non-mass-like enhancement of 20x6 mm was found in a focally ectatic duct in the left breast, with smaller foci of 4-5 mm. The total area measured 60x50 mm, with a BI-RADS score of MR-4. Additionally, a focal, heterogeneous, non-mass-like enhancement of 19x13 mm was noted in the surgical bed, 12 mm from the pectoralis major. (after a WLE).	In the central part of the left breast, below the scar line and at mid-depth, there were two rounded, scattered, faint micro-calcifications. The BI-RADS score was M2 bilaterally. (after a WLE).	A total mastectomy of the left breast and WLE of the right breast.	GM and DCIS	Left breast	ER	N/A	Disease-free after 6 months (9)
Yoshida, 2023	1	34/F	A mass and redness in the left breast.	An irregular hypoechoic area measuring over 4 cm was found in the left mammary gland.	Persistent small nodular and irregular enhancement effects were observed.	N/A	A total mastectomy of the left breast.	GLM and DCIS	Left breast	ER, PR, E-cadherin	N/A	Recurrence-free status for 18 months. (10)
Evans, 2021	1	35/F	A left breast mass.	A 60-mm irregularity with no underlying collection at the 10 o'clock position, 2 cm from the nipple.	A resectable 60-mm area in the right outer quadrant	Asymmetric density with hyperemia was found in the medial left breast. The right breast had two clusters of irregular pleomorphic microcalcifications, measuring 16x11x11 mm and 9x10x7 mm.	Oncoplastic right WLE with SLNB, subsequently requiring an axillary dissection due to Macro metastatic axillary disease.	GM and high-grade DCIS	Right breast IDC and Left breast GM	PR	HER2	N/A (11)
Zhu, 2023	3	51/F	A hard mass in the left breast for one day.	Left breast edema with dilated ducts led to the consideration of an inflammatory lesion.	Edema in the glandular layer of the left breast with dilation of the ducts.	N/A	Surgical dissection of the lesion.	GLM with solid-type high-grade DCIS.	Left breast	p63, ER, PR, HER2	N/A	N/A (14)

Table I. Continued.

First author, year of publication	Age, years/ (sex)	No. of cases	Presentation	US findings	MRI findings	MMG	Treatment	Diagnosis	Location	IHC		
										Positive	Negative	Follow-up (Refs.)
	50/F		A mass in the left breast for over six months.	Localized glandular hypertrophy in the lateral portion of the left breast, with multiple internal hypoechoic nodules, which were classified as BI-RADS grade 4a.	A suspicious mass with shadowing and enlarged ducts was observed in the left breast, suggesting the potential presence of breast cancer.	Enlarged ducts with dense calcifications that resemble gravel within the ducts.	Surgical resection of the lesion.	GLM with solid-type high-grade DCIS.	Left breast	p63, CK5/6	ER, PR, HER2	N/A (14)
	45/F		A left breast lump for two months.	Several dark, fluid-filled areas were identified, leading to a suspicion of an inflammatory lesion.	N/A	N/A	Mass resection	GLM with solid-type high-grade DCIS.	Left breast	p63, CK5/6	ER, PR, HER2	N/A (14)
Tavakol, 2022	35/F	1	Pain and a small mass in the right breast for one month; a small mass in the left breast for 6 years.	A diffuse, irregular area with microcalcifications and skin thickening (BIRADS 4b) was noted in the right UOQ. A well-defined hypoechoic mass (BIRADS 3) was seen in the left breast at 12 o'clock.	Fibroglandular, dense breast (type C). In the right UOQ, there was asymmetrical parenchymal thickening with multiple rim-enhanced masses (14-35 mm) and extensive asymmetrical non-mass enhancement (140x80x60 mm) extending to the retroareolar region, with a type 3 dynamic curve.	A large hypoechoic to heterochoic mass (150 mm) in the lateral right breast, without microcalcifications or distortion.	Conservative treatment	IGM and LCIS	Right breast	P63, CK5/6, catenin, e-cadherin	N/A	N/A (15)
Zangouri, 2022	38/F	1	A left breast mass	An irregular hypoechoic mass with tubular extensions.	N/A	A well-defined high-density mass	N/A	GM and grade III IDC	Left breast	N/A	N/A	N/A (16)
Oddó, 2019	44/F	1	Swelling and pain in the left breast.	Inflammatory changes with skin thickening, increased echogenicity, superficial fluid collections, and loss of fatty planes.	N/A	Suggestive of DCIS involvement.	A total mastectomy of the left breast	GLM and DCIS	Left breast	ER, PR	N/A	N/A (17)

Table I. Continued.

First author, year of publication	Age, years/ (sex)	Presentation	US findings	MRI findings	MMG	Treatment	Diagnosis	Location	IHC			Follow-up (Refs.)
									Positive	Negative		
Özgen, 2018	35/F	Swelling in right breast.	A heterogeneous, irregular hypoechoic area extending 3 cm from the subareolar zone in the right breast, with a 34x9 mm fluid collection near the nipple at 12 o'clock.	N/A	N/A	N/A	GLM and DCIS	Right breast	CD10, CK 5/6, p63	N/A	N/A	(18)
Çalış, 2018	77/F	Right breast pain.	Increased fibro glandular tissue with indistinct borders and an inflammatory appearance, along with a 2x2 cm non-reactive lymphadenopathy in the right axilla.	N/A	An amorphous mass with axillary lymphadenopathy and focal asymmetric opacity with calcifications in the retroareolar and outer quadrant of the right breast.	Modified radical mastectomy	IDC, DCIS, and GM	Right breast	ER, PR	E-cadherin, C-erb	N/A	(19)
Kaviani, 2017	48/F	Large palpable masses in both breasts and nipple retraction in her right breast.	Large irregular hypoechoic mass with echogenic foci and inflammation, indicating mastitis.	A single mass in the left breast measured 20x12 mm with no satellite lesions at the end of chemotherapy.	Mass-like lesions and distortion in both breasts due to highly dense breast tissue.	BCS with oncoplastic repair (round block technique) and sentinel lymph node biopsy were performed.	IDC and IGM	Left breast IDC and right breast GM	N/A	N/A	N/A	(20)
Mazlan, 2011	34/F	A right breast abscess for 8 years, and progressive loss of vision of the left eye.	N/A	Extensive scarring in the right breast appeared suspicious for malignancy.	N/A	The patient declined treatment	CGM and IDC	Right breast	ER, PR	C-erb	Passed away after 6 months	(21)

F, female; US, ultrasound; MRI, magnetic resonance imaging; GLM, granulomatous lobular mastitis; CGM, chronic granulomatous mastitis; DCIS, ductal carcinoma *in situ*; IHC, immunohistochemistry; N/A, not available; MMG, mammography; ER, estrogen receptor; PR, progesterone receptor; IDC, invasive ductal carcinoma; SLNB, sentinel lymph node biopsy; WLE, wide local excision; BCS, breast-conserving surgery; BIRADS, Breast Imaging Reporting and Data System; UOQ, upper outer quadrant.

Differentiating between breast cancer and GM can be challenging; however, it is crucial due to the significant differences in treatment strategies. Currently, histopathological diagnosis remains the most reliable method (10). Although there are no established treatment guidelines for GM, steroid therapy is commonly used as the initial approach. For patients who resist corticosteroid treatment or suffer from side effects like impaired glucose tolerance and Cushing's syndrome, adding methotrexate (10-15 mg/week) has been found effective. Incorporating methotrexate helps reduce the corticosteroid dosage and lowers the likelihood of side effects (22). However, for patients diagnosed with DCIS, treatment typically involves a combination of surgery, radiation, and endocrine therapy (9). The patient in the present study was initially treated with analgesics and antibiotics for 20 days. An HPE following a CNB of the lesion confirmed the coexistence of GM and breast cancer in the same breast. After undergoing two breast surgeries, the patient had a left complete mastectomy with immediate reconstruction using a TRAM flap.

For clinicians, this case underscores the necessity of histopathologic confirmation in all patients with suspected GM, particularly in cases when the clinical course deviates from the expected response to therapy. Breast imaging alone is often insufficient, as both GM and malignancy can present as heterogeneous, ill-defined, or mass-like lesions on ultrasound and MRI.

In conclusion, distinguishing between breast cancer and GM is challenging. Although the simultaneous presence of GM and breast cancer is rare, it remains essential to consider this possibility. However, further research is required to clarify the relationship between GM and breast cancer.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

FHK and AMS were major contributors to the conception of the study, as well as to the literature search for related studies. HAN, BOH and SHH contributed to the clinical management of the patient, assisted in data acquisition and interpretation, and participated in the literature review and manuscript preparation. SL, HOA and KMS contributed to the conception and design of the study, the literature review, the critical revision of the manuscript, and the processing of the table. LRAP was the radiologist who performed the assessment of the case. AMS and SL assisted in diagnosing the patient, contributed to the management of the patient, and participated in manuscript review. AMA was the pathologist who performed the diagnosis of the case. RMA was the oncologist involved in

the management of the patient. FHK and HAN confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for her participation in the present study.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of the present case and any accompanying images

Competing interests

The authors declare that they have no competing interests.

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