Idiopathic Granulomatous Mastitis and Breast Cancer: Three Cases and Review of 16 Previous Cases

Marzieh Mohammadi-Zavieh[1], Ramesh Omranipour[1,2], Sadaf Alipour[1,3], Maryam Sarkardeh[1,3,4]

[1] *Breast Disease Research Center (BDRC), Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*

[2] *Department of Surgical Oncology, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*

[3] *Department of Surgery, Arash Women's Hospital, Tehran University of Medical Sciences, Tehran, Iran*

[4] *Department of Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*

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Abstract- Idiopathic Granulomatous Mastitis (IGM) is an inflammatory and benign breast disease that can mimic a wide range of breast diseases (from infection to breast cancer (BC)). IGM affects women in the childbearing age and is more prevalent in Asia. According to similarity of IGM and BC presentation and different treatment pathways, it is important to distinguish between these two diseases. We present three cases; the first one is a 42-year-old woman with IGM 2 years after treatment of a stage two breast carcinoma; and the second and third one is a 46-year-old and 41 years old ladies with breast cancer 4 and 13 years after being diagnosed with IGM. Although the occurrence of IGM and cancer in an individual patient is rare, physicians should be aware of this possibility.

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Introduction

Idiopathic Granulomatous Mastitis (IGM) is an inflammatory breast disease that mostly involves women in the reproductive age (1). The clinical presentation of IGM can mimic a wide range of breast diseases from breast cancer (BC) to infectious conditions. It can present as masses, skin thickening, peau d'orange, skin or nipple retraction, nipple discharge, pain, abscess, erythema, ulcer and fistula formation (2-4). In our experience, the prevalence of IGM has increased in recent years.

The present literature contains reports of patients harboring both IGM and BC (5-9). Recently, one of our BC patients who was under surveillance was diagnosed with IGM (case 1). Thereafter, we searched our BC database for another similar record. We found 2 patients (cases 2 and 3) who had a history of IGM before their BC. Although the occurrence of BC and IGM in a patient may be accidental, we believe that breast surgeons should be aware of this possibility. In this paper, we present our three cases and then review all the cases that have been reported in the literature up to now.

Case Report

Case 1

A 42-year-old woman with the history of a hormone receptor positive, HER2 positive invasive ductal carcinoma (IDC) of her right breast came to our follow-up clinic with the chief complain of pain and lump sensation in the lateral part of her left breast. She had undergone neoadjuvant chemotherapy, mastectomy and two-stage reconstruction, post-mastectomy radiation and anti-HER2 therapy for her cancer two years ago. She has been taking Tamoxifen since the previous year .

In her recent breast examination, new-onset periareolar erythema, nipple inversion and an underlying palpable tender thickening were detected in the left breast (Figure 1). Breast ultrasound (US) revealed a 50*29*22 mm mass-like lesion with undefined borders and dilated

Corresponding Author: M. Sarkardeh
Breast Disease Research Center (BDRC), Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 9151736991, E-mail address: maryam.sarkardeh@yahoo.com

ducts containing debris and extending toward the nipple. The US findings were interpreted as BIRADS4 by the radiologist, although considered in favor of focal mastitis. The mammogram showed a focal density in the central outer part of the breast (Figure 1). Core needle biopsy under US guidance was performed, and the histological assessment revealed severe infiltration of mixed inflammatory cells, predominantly small lymphocytes, micro-abscess formation around lobules, and dilated destructed ducts; compatible with IGM. There was no finding in favor of malignancy; the specimens were reviewed by a second pathologist who confirmed the diagnosis while tuberculosis and fungal infection were excluded.

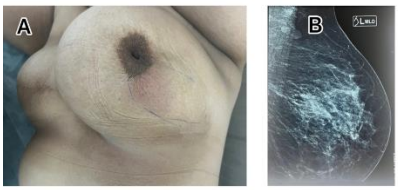

Figure 1. Clinical presentation (A) and mammography (B)

Considering the mild presentation of mastitis, treatment started with Naproxen 500 mg bid and after two weeks, the area of inflammation had enlarged, and a small draining fistula had appeared over an abscess. Due to rarity of this situation and lack of proper response, open drainage and biopsy from the abscess wall was done, and the IGM diagnosis was confirmed. The medical treatment continued, the lesion became smaller, and the inflammation subsided in the next months.

Case 2

A 46-year-old lady with a history of corticosteroid therapy for IGM 4 years ago was referred to our clinic for a suspicious palpable mass in the same quadrant of the same breast. The IGM presentation was silent from 2 years ago. On imaging a hypoechoic irregular speculated mass with indistinct margins were seen. Core needle biopsy of the lesion confirmed triple negative breast cancer. This was treated by neoadjuvant chemotherapy, mastectomy and Sentinel Lymph Node Biopsy (SLNB) and post mastectomy radiotherapy.

Case 3

A 41-year-old female with a history of left breast IGM treated by low dose corticosteroid 13 years ago, came to our clinic with a new mass in her contralateral breast; and no sign of IGM in the previous breast. Breast ultrasound showed a 22×20-millimeter irregular and hypoechoic BIRADs 5 mass, and ultrasound-guided core needle biopsy confirmed BC. She was treated by neoadjuvant chemotherapy, breast conserving, SLNB and adjuvant radiotherapy.

Discussion

IGM was presented for the first time in 1972 by Kessler as a lesion that clinically simulates a wide range of malignant or inflammatory breast diseases (10). Although the etiology of IGM is not fully known yet, several possible etiologies such as trauma, oral contraceptive pills (OCP), pregnancy and breastfeeding, hyperprolactinemia, autoimmune diseases, smoking, diabetes mellitus and hypothyroidism have been proposed (2,11). Our three presented patients had none of the risk factors, except for hormone-dependent factors as short-term OCP consumption, two pregnancies and breastfeeding for 48 months around 20 years ago in case 1. Case 2 had a history of three pregnancies, 2 term childbirths and one abortion, and her last breastfeeding was 9 years before the IGM presentation.

IGM mostly happens in women at reproductive age about 50% of patients are between 30-40 years old, and is defined as a benign lesion (1,2,10). Recently, cases of synchronous and rarely metachronous occurrence of breast cancer and IGM have been reported.

A thorough search of the present literature yielded 16 reported cases of IGM associated with breast cancer; Table 1 presents the patients and disease characteristics of these 16 cases. The first case was reported in 2011 (9).

IGM prevalence is higher in Asia and the Middle East (18). Among the 16 reported cases, 14 patients (86.6%) were from Asia. The average age of all the patients was 45.6 years, and 81.2% of them (13 patients) were in the premenopausal period. Considering the higher incidence of BC in younger age (40-50 years) in Asia compared with western countries (60-70 years) (19,20), and the higher prevalence of IGM in this area, BC should be considered as a differential diagnosis by physicians who manage breast diseases.

In 10 out of the 16 reported cases (about 62.5%), IGM and BC coexisted at the same time and in eight of them both diseases involved the same breast, this finding implies the need of a precise breast physical exam and imaging in patients with IGM-like presentations.

Nine patients (56.2%) had IDC, and ductal carcinoma in situ (DCIS) was seen in 7 patients (43.8%). In terms of the molecular tumor subtype, 10 tumors (62.5%) were estrogen receptor positive, 5 cases were HER2 positive, and 2 patients were triple negative BC. Most of these reported cases belong to the recent 5 years, this could be

explained by better recognition of IGM by clinicians and pathologists; alternatively, this can be due to an increased incidence of IGM.

In this study we present 3 patients with metachronous IGM and BC. In the first case, in a rare condition, IGM occurred contralaterally 2 years after BC; this is the first case of metachronous contralateral IGM presenting in a BC survivor in the existing literature. In the second and third cases BC occurred 4 and 13 years after IGM respectively.

Whether the occurrence of IGM and BC is a coincidence, or the result of a causal association cannot be concluded for now. The rarity of this mutual occurrence is not completely against a causal theory, because this could be due to the rarity of IGM. However, the differences in the time of presentation of BC and IGM relative to each other and the variability of the same vs. other side presentation among the 16 cases weakens the probability of a causal effect. An interesting point is the dependency of both IGM and breast cancer on female sex steroids. This might be a cause for the occurrence of both diseases in an individual.

For now, the only point that can be said for sure is that whatever the reason, considering the possibility of this co-occurrence, as well as the similarity of some of the signs of the two diseases, physicians should pay attention not to miss any of these diagnoses. A new finding in the breast of a patient with previous IGM is not always a recurrence of the disease and might be BC; and vice versa.

Table 1. Features of 16 cases of IGM associated with breast cancer

Cases*	Country	Year of publication	Age	Side	Histology	Molecular Subtype	Chronology of IGM and BC	Laterality of IGM and BC
Case 1	Iran	2024	42 years old pre-menopausal state	left	IDC	ER (+), PR (+), HER2 (3+)	After BC	contralateral
Case 2	Iran	2024	46 years old pre-menopausal state	right	IDC	Triple negative	Before BC	same side
Case 3	Iran	2024	41 years old pre-menopausal state	right	IDC	ER (+), PR (+), HER3 (3+)	Before BC	contralateral
Case 4 (8)	China	2024	51years old postmenopausal state	left	DCIS	ER (-), PR (-), HER2(1+)	Concurrent	same side
Case 5 (8)	China	2024	50 years old pre-menopausal state	left	DCIS	ER (-), PR (-), HER2(3+)	Concurrent	same side
Case 6 (8)	China	2024	45-year-old pre-menopausal state	left	DCIS	ER (+), PR (+), HER2(3+)	Concurrent	same side
Case 7 (6)	Iraq	2023	30 years old pre-menopausal state	Left	DCIS	ER (+)	Before BC	same side
Case 8 (7)	Japan	2023	34 years old pre-menopausal state	Left	DCIS	ER (+), PR (+)	Concurrent	same side
Case 9 (16)	Iran	2022	38 years old pre-menopausal state	Left	IDC	Unknown	Before BC	same side
Case 10 (17)	south Asia	2021	39 years old pre-menopausal state	right	IDC	ER (+), HER2(-)	Concurrent	contralateral
Case 11 (12)	Chile	2019	44 years old pre-menopausal state	left	DCIS	ER (+), PR (+)	Concurrent	same side
Case 12 (13)	Turkey	2018	35 years old pre-menopausal state	right	DCIS	p63 and CK5/6 around ductal myoepithelium (+)	Concurrent	same side
Case 13 (14)	Turkey	2018	77 years old postmenopausal state	right	IDC	ER (-), PR (-), HER2(3+)	Concurrent	same side
Case 14 (5)	Iran	2016	48 years old pre-menopausal state	left	IDC	ER (+), PR (+)	Concurrent	contralateral
Case 15 (15)	Tunis	2013	77 years old postmenopausal state	right	IDC	ER (+), PR (+), HER2(0)	Concurrent	same side
Case 16 (9)	Malaysia	2011	34-year-old pre-menopausal state	right	IDC	ER (+), PR (+), HER2(0)	Before BC	same side

*All the cases were female patients

Although less frequent than BC recurrence, a new finding in favor of malignancy in the breast of a BC survivor might be IGM. Also, despite the high rate of recurrence of IGM, a new mass or other sign in a previous IGM patient may be caused by BC. The presentation of both diseases in an individual, ipsilaterally or contralaterally, is a rare occurrence. However, more than a few cases have been reported, and this important point must always be considered when approaching these cases.

References

1. Wolfrum A, Kümmel S, Theuerkauf I, Pelz E, Reinisch M. Granulomatous Mastitis: A Therapeutic and Diagnostic Challenge. Breast Care (Basel) 2018;13:413-8.
2. Anoush K, Azizi M, Soleimani V, Rezvani A, Azmoudeh Ardalan F, Jahanbin B. Idiopathic Granulomatous Mastitis: Diagnosis and Histopathologic Features. Arch Breast Cancer 2022;9:272-8.
3. Yaprak Bayrak B, Cam I, Eruyar AT, Utkan NZ. Clinicopathological evaluation of idiopathic granulomatous mastitis patients: A retrospective analysis from a tertiary care hospital in Turkey. Ann Diagn Pathol 2021;55:151812.
4. Ozel L, Unal A, Unal E, Kara M, Erdoğdu E, Krand O, et al. Granulomatous mastitis: is it an autoimmune disease? Diagnostic and therapeutic dilemmas. Surg Today 2012;42:729-33.
5. Kaviani A, Zand S, Karbakhsh M, Azmoudeh Ardalan F. Synchronous Idiopathic Granulomatosis Mastitis and Breast Cancer: A Case Report and Review of Literature. Arch Breast Cancer 2016;4:32-6.
6. Salih AM, Pshtiwan LRA, Abdullah AM, Dhahir HM, Ali HO, Muhialdeen AS, et al. Granulomatous mastitis masking ductal carcinoma in situ: A case report with literature review. Biomed Rep 2023;20:17.
7. Yoshida N, Nakatsubo M, Yoshino R, Ito A, Ujiie N, Yuzawa S, et al. Concurrent Granulomatous Mastitis and Ductal Carcinoma in Situ. Cureus 2023;15:e38377.
8. Zhu J, Miao X, Li X, Zhang Y, Lou Y, Chen H, et al. Granulomatous lobular mastitis co-existing with ductal carcinoma in situ: Report of three cases and review of the literature. Ann Diagn Pathol 2024:68:152241.
9. Mazlan L, SuhaiMi SN, JaSMin SJ, Nani Harlina Md latar, Sellymiah adzMan, Rohaizak MuhaMMad. Breast Carcinoma Occurring from Chronic Granulomatous Mastitis. Malays J Med Sci 2012;19:82-5.
10. Kessler E, WollochY. Granulomatous mastitis: a lesion clinically simulating carcinoma. Am J Clin Pathol 1972;58:642-6.
11. Alipour S, Tabatabaeian M, Nafissi N, Fattahiand AS, Astaraki S, Zahernia-Shahrbabaki Z, et al. Idiopathic Granulomatous Mastitis and History of Hypothyroidism: Intervening Data of a Prospective Multicenter Trial and Meta-Analysis of the Existing Literature. Arch Breast Cancer 2023;10:38-47.
12. Odd´o D, Domínguez F, G´omez N, Méndez GP, Navarro ME. Granulomatous lobular mastitis associated with ductal carcinoma in situ of the breast. SAGE Open Med Case Rep 2019;7:2050313x19836583.
13. Ozsen M, Tolunay S, Gokgoz M. Case report: ductal carcinoma in situ within a granulomatous mastitis. Eur J Breast Health 2018;14:186-8.
14. Çalıs H, Kilitçi A. Granulomatous mastitis concurrence with breast cancer. Eur J Breast Health 2018;14:58-60.
15. Limaiem F, Khadhar A, Hassan F, Bouraoui S, Lahmar A, Mzabi S. Coexistence of lobular granulomatous mastitis and ductal carcinoma: a fortuitous association? Pathologica 2013;105:357-60.
16. Zangouri V, Niazkar HR, Nasrollahi H, Homapour F, Ranjbar A, Seyyedi MS. Benign or premalignant? Idiopathic granulomatous mastitis later diagnosed as ductal carcinoma breast cancer: Case report and review of literature. Clin Case Rep 2022;10:e06323.
17. Evans J, Sisk L, Chi K, Brown S, To H. Concurrent granulomatous mastitis and invasive ductal cancer in contralateral breasts—a case report and review. J Surg Case Rep 2021;2021:rjab519.
18. Gautier N, Lalonde L, Tran-Thanh D, El Khoury M, David J, Labelle M, et al. Chronic granulomatous mastitis: Imaging, pathology and management. Eur J Radiol 2013;82:e165-75.
19. Wong FY, Tham WY, Nei WL, Lim C, Miao H. Age exerts a continuous effect in the outcomes of Asian breast cancer patients treated with breast- conserving therapy. Cancer Commun (Lond) 2018;38:39.
20. Pourriahi R, Omranipour R, Alipour S, Hajimaghsoudi L, Mashoori N, Yazadnkhah Kenary A, et al. Clinical characteristics of breast cancer patients admitted to academic surgical wards in Tehran, Iran: an analytical cross-sectional study. BMC Women's Health 2023;23:511.