The THAI Journal of SURGERY 2021;42(2):54-60.
Official Publication of The Royal College of Surgeons of Thailand

Original Article

A Case Series of Idiopathic Granulomatous Mastitis and a Proposed Treatment Protocol

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Abstract

Objective: Idiopathic granulomatous mastitis (IGM) is a benign inflammatory breast disease. It has a poorly understood etiology. It can mimic breast cancer in clinical and mammographic findings. Some patients might improperly undergo mastectomy due to high suspicion of breast cancer. The objective of the present report is to discuss possible approaches to diagnosing and treating IGM based on a series of such patients.

Methods: This study retrospectively reviewed 17 cases of IGM. We discuss etiologic factors, clinical features, imaging findings, a variety of treatment options and outcomes. In conjunction with reviewing the literature, a treatment protocol for patients with suspected IGM was proposed.

Results: All patients were female and the median age at the time of diagnosis was 36 years (range, 21 to 53 years). Most patients (16 out of 17) were of reproductive age. In 16 patients who had undergone successful pregnancy, the last breast-feeding period was mostly less than 5 years to the onset of symptoms. All patients presented with breast mass and pain. Twelve patients underwent mammography, which were categorized as either BI-RADS 4 in 7 patients, or BI-RADS 2 in 5 patients. All patients underwent remission after various multimodality treatment approaches, including the use of corticosteroids, antibiotics, and surgery.

Conclusion: IGM is a benign inflammatory breast disease, mainly affecting women of childbearing age. Corticosteroids and wide excision play important roles in management.

Keywords: Idiopathic granulomatous mastitis, Chronic granulomatous mastitis, Granulomatous lobular mastitis

Introduction

Idiopathic granulomatous mastitis (IGM), also known as granulomatous lobular mastitis, is a benign inflammatory breast disease.[1] It was first described by Kessler and Wolloch[2] in 1972. Histologically, IGM appears as non-caseating granulomas, frequently centered on the breast lobules, with epithelioid histiocytes, multinucleated giant cells, and varying numbers of plasma cells, lymphocytes, neutrophils, and eosinophils. There should be no evidence of specific infection, trauma, foreign body, or evidence of sarcoidosis.[3-5] It has a poorly understood etiology. Possible risk factors include race[6,7], cigarette, diabetes mellitus, obesity, breast trauma, infection, oral contraceptive pill (OCP) usage, lactation, autoimmune disease[8], hyperprolactinemia[9,10], and immunologic response to milk leakage from the breast lobules.[11,12] IGM usually affects women of childbearing age.[13] It can mimic breast cancer in clinical findings and mammography.[14-16] Some patients may even undergo mastectomy due to high suspicion of breast cancer.[13,15] The main objective of the present study was to review and describe possible etiologic factors, clinical characteristics, imaging study, diagnosis and treatment of IGM, and to propose a treatment protocol.

Received for publication 23 February 2021; Revised 4 April 2021; Accepted 5 April 2021
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Methods

The present study included 17patients with a histological diagnosis of IGM (granulomatous inflammation without caseous necrosis; giant cells; confined to breast lobules; no microorganism seen) treated between January 2014 and December 2020 at Songkhla Hospital, from among 1558 breast disease patients with tissue diagnosis. Potential etiologic factors (including smoking, use of oral contraceptives, parity status, lactation status, local trauma, history of autoimmune disease, familial history of breast disease and breast cancer, and body mass index), clinical presentation, imaging study, treatment, and response to treatment were descriptively analyzed. In addition, a IGM treatment protocol was proposed based on data analysis and literature review. The study was approved by the Songkhla Hospital Ethics Committee.

Results

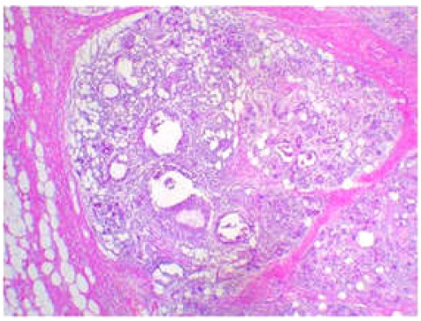
Some potential etiologic factors for IGM for patients in the present study are shown in **Table 1**. All patients were female and the median age at diagnosis was 36 years (range, 21 to 53 years). Most patients were of reproductive age and parous, only one patient was in menopause. The median BMI was 23.5 kg/m^2 (range, 17.9 to 31.1 kg/m^2). No patient had a family history of breast disease or cancer. None were smokers nor alcohol drinkers. One patient had a history of blunt trauma to her breast from falling on a table, one month before the visit due to IGM. The last breast-feeding period was mostly less than 5 years in all parous patients.

Clinical characteristics of patients with IGM and results of imaging studies are shown in **Table 2**. All patients presented with palpable mass and breast pain. Two patients (one nulliparous and one postmenopausal patient) had milky nipple discharge. No patient had axillary lymphadenopathy.

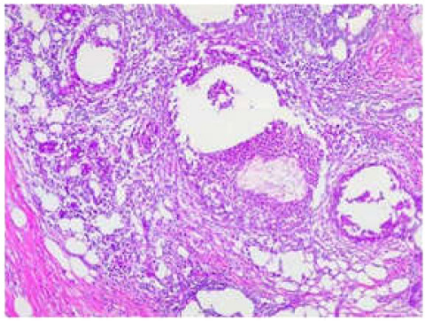
Imaging studies were performed on 12 patients. Mammography and ultrasonography were categorized as BI-RADS 4 and BI-RADS 2 in 7 and 5 patients, respectively. The diagnosis of IGM was made via excisional biopsy, core needle biopsy (CNB) or incisional biopsy. CNB failed to demonstrate IGM in 3 patients (38%). All patients were in remission after various treatments including the use of antibiotics, NSAIDs, prednisolone and surgery (**Table 3**)

Discussion

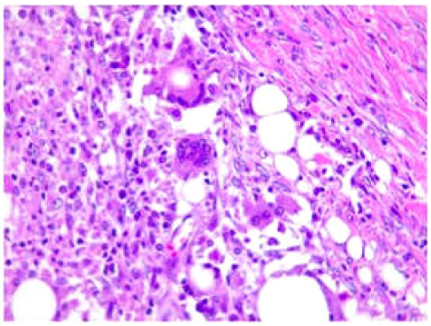
IGM is an under-recognized breast condition. There were only 17 cases among the 1558 breast tissues examined during the study period. Since multiple processes may cause granulomatous inflammation of the breast, IGM remains a diagnosis of exclusion. The pathogenetic basis of IGM may be complex or multifactorial (e.g., IgG-related disease[7,18], or with hyperprolactinemia, etc.). This may explain the wide variation in therapeutic strategies as well as the variation in success and recurrence rates.



Granulomatous inflammation centered on lobules with lymphocytes, plasma cells, epithelioid histiocytes, multinucleated giant cells and neutrophils.



There are neutrophils forming microabscesses and surrounding empty miccrocysts.



High-power view of the center of a granuloms in granylomatous mastitis shows a Langhans' giant cells surrounded by epithelioid histocytes, lymphocytes, and a few eosinophils.

Figure 1 Histopathology of idiopathic granulomatous mastitis

Table 1. Potential etiologic factors for idiopathic granulomatous mastitis for patients in the study

Patient number	AGE (years)	BMI (kg/m²)	Underlying diseases	Medication/ supplements	Parity status	Last breastfeeding period (years)
1	42	25.3	Psychiatric disease	Psychotropic drug	Nulliparous	No
2	35	20.6	No	Food supplements	Parous	1
3	43	27.7	No	DMPA	Parous	4
4	40	22.4	No	No	Parous	3
5	21	23.2	No	OCP	Parous	3
6	34	25.6	No	No	Parous	4
7	26	23.8	No	No	Parous	3
8	30	23.4	No	No	Parous	2
9	42	29.2	No	No	Parous	2
10	38	20.5	No	No	Parous	1
11	36	31.1	No	OCP	Parous	2
12	36	25.4	No	No	Parous	1
13	53	17.9	No	No	Parous	9
14	30	19.5	No	No	Parous	2
15	34	23.5	No	No	Parous	2
16	45	23.2	No	No	Parous	3
17	44	24.1	No	No	Parous	1

OCP: oral contraceptive pill; DMPA: depot-medroxyprogesterone acetate;
Patient no. 4 had silicone augmented breasts; patient no.13 was in menopause.

Table 2. Clinical and radiological characteristics of patients

Patient number	Mass size (cm)	Mass location	Nipple discharge	Presence of sinus	MMG + US category	US category	Abscess formation
1	5	R 7-11*	Milky	No	BI-RADS 4	-	No
2	6	L12	Yellow-green	No	BI-RADS 4	-	No
3	2	R6	No	No	BI-RADS 4	-	No
4	Diffuse	Diffuse	No	No	BI-RADS 2	-	No
5	2/2**	R5,10 **	No	No	-	BI-RADS 4	No
6	3	R8	No	No	-	BI-RADS 4	No
7	3	R1	No	Yes	-	-	No
8	3	R10	No	No	-	BI-RADS 4	No
9	3	R2,7***	Yellow-green	No	-	-	Yes
10	2	L1	No	No	-	-	No
11	3	L3	No	No	-	-	No
12	1,1	L3	No	No	BI-RADS 2	-	No
13	1.5,1	L3,4***	Milky/pus	No	BI-RADS 2	-	No
14	2	R3,4***	No	No	BI-RADS 2	-	No
15	2	L subareolar	No	No	BI-RADS 4	-	No
16	4,3	R2-3, R7-8	Milky	No	-	-	No
17	3	R subareolar	No	No	BI-RADS 2	-	No

* Connecting lesion; ** Lesions seen at different times; *** Different location; MMG: mammography; US: ultrasonography

Table 3. Treatment of idiopathic granulomatous mastitis in the study.

Patient number	CNB	Incision biopsy	Excision	Mastectomy	NSAIDs	Antibiotics	Steroids
1	IGM	-	-	-	Ibuprofen	Amox+clav	Prednisolone
2	Chronic mastitis	IGM	-	-	Diclofenac	Cephalexin	-
3	IGM	-	-	-	-	Dicloxacillin	Prednisolone
4	IGM	-	-	-	-	-	-
5	Inadequate	IGM	-		Diclofenac	Ofloxacin	Prednisolone
6	-	-	IGM	-	-	-	Prednisolone
7	-	-	IGM	-	-	-	Prednisolone
8	-	-	IGM	-	-	Dicloxacillin	-
9	-	IGM	-	IGM	-	Amox+clav	-
10	-	-	IGM	-	-	Dicloxacillin	-
11	-	IGM	-	-	-	Dicloxacillin Ciprofloxacin	Prednisolone
12	-	-	IGM	-	Ibuprofen	Dicloxacillin	-
13	-	-	IGM	-	-	-	-
14	-	-	IGM	-	-	Amox+clav	-
15	-	-	IGM	-	-	-	-
16	IGM	-	-	-	-	-	Prednisolone
17	IGM	-	-	-	-	-	Prednisolone

CNB: Core needle biopsy; NSAIDs: Non-steroidal anti-inflammatory drugs; IGM: Idiopathic granulomatous mastitis; Amox+clav: Amoxycillin-clavulonic acid

In the present study, a median age of 36 years at presentation is consistent with the findings in the literature, which is typically between 20 and 50 years.[15,19,20] Almost all IGM patients in the present study had previously given birth and was at reproductive age. Only one patient was nulliparous, and one patient was postmenopausal. There is probably a close relationship between IGM and hormonal status, pregnancy and lactation. This may suggest a localized immune response to extravasated secretion from the breast lobule.

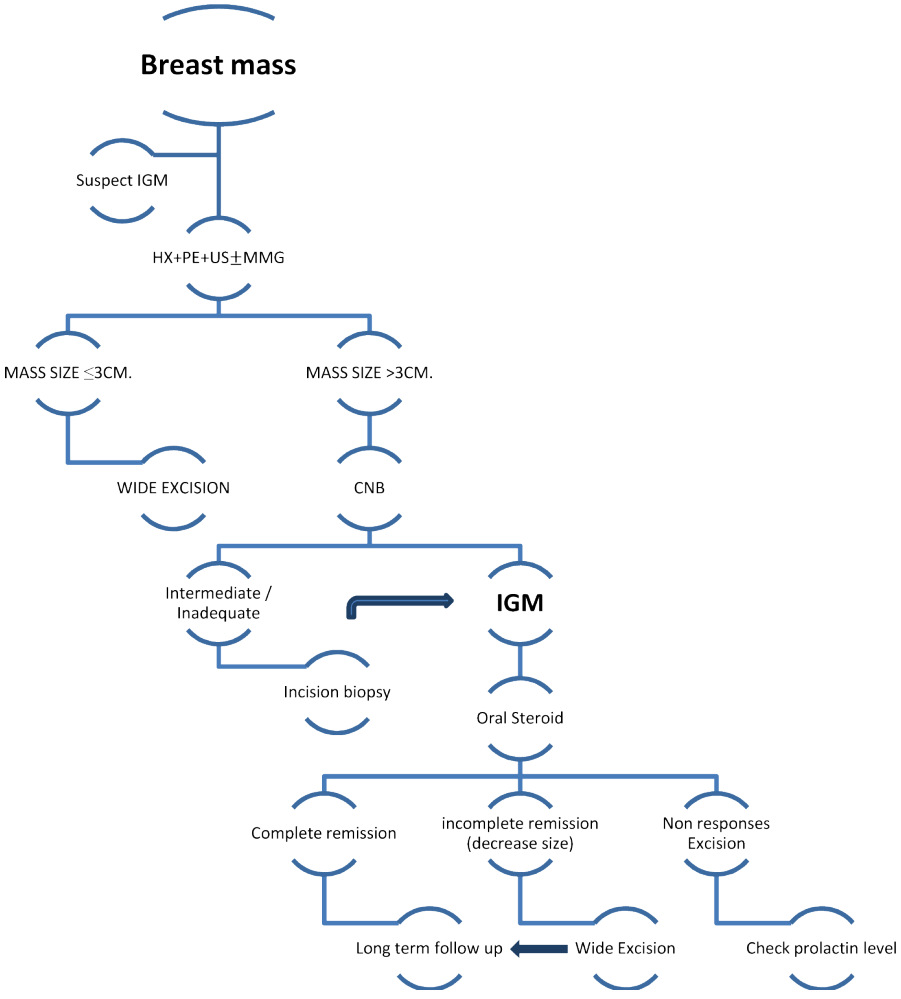
In the present study, there was no evidence that obesity, diabetes, local trauma, use of oral contraceptives, smoking and alcohol drinking have any association with IGM. Imoto et al [(15)] showed that IGM lesions were usually unilateral and can occur in every breast quadrant except the subareolar region. In the present study, subareolar lesions were present in 2 patients, therefore, IGM lesions can occur in every region of the breast.
Breast ultrasonography and mammography revealed BI-RADS 4 and BI-RADS 2 findings in IGM patients in the present study, consistent with a previous study.[16] It confirmed that there are no pathognomonic features for IGM on ultrasonography and mammography. Similar to the report of Alrayes, et al[7], CNB was able to demonstrate IGM in 62% of patients, thus confirming the utility of CNB as an initial diagnostic tool. Excision is valuable for both definite diagnosis and treatment for small lesions. In the present study, two patients with small lesions underwent excisional biopsy and subsequently are in complete remission. Alrayes, et al[7] suggested excising the inflammatory mass with negative resection margins, including the removal of retroareolar ductal system, as the preferred treatment.

For large breast lesions, complete resection may be complicated by breast volume loss and unaccepted cosmetic results. In the present study, 4 cases were in complete remission after treatment with prednisolone. This observation supported the suggestion in the literature that corticosteroids may be used as primary treatment, or to help reduce the size of lesions before surgery. Sakureica,.et al[21] and Salehi, et al[22] suggested post-operative corticosteroids to prevent IGM recurrence for resistant and complicated cases. IGM is usually sterile, therefore there is no role for antibiotics except in cases of secondary bacterial infection. One patient in the present study was treated by mastectomy. She presented with breast abscesses and inflammatory mass. After incision and drainage, the lesion recurred. She was diagnosed with

IGM after excision. She was never treated with prednisolone, but had wound complications. After 3 further operations, she ended up with a mastectomy, both to rule out breast cancer and to ease her suffering.

Currently, there is no consensus on the optimal therapeutic strategy for IGM. Zhou, et al[23] performed a meta-analysis of 10 retrospective studies involving 1,101 patients and concluded that there is no significant difference in the recurrence of IGM between surgical and conservative treatment. They strongly recommended a conservative approach to avoid wound complications, but did not compare this to side-effects and complications of corticosteroid treatment. Wolfrum, et al[24] reported only a 66% to 72% success rate of corticosteroid treatment. Hakan, et al[25] performed a comparative study of conservative versus surgical treatment in 77 patients with IGM, and reported that the average time to remission of patients who were treated conservatively was 6 months, while the average time to remission of patients who were treated surgically was 1 month. There was no recurrence in the surgically treated group after an average follow up period of 17 months, so these authors preferred wide surgical excision for treating patients with IGM.

In the present study, 8 patients were treated by excision and recovered well. According to the results of the present study and our review of the literature, we prefer wide excision for the patients with suspected IGM of size less than 3 cm, partly because we had a 38% failure rate of CNB to demonstrate IGM. Excision in this case can be both diagnotic and therapeutic without significant breast volume loss, and can also avoid the use of high dose corticosteroids. We therefore suggest an algorithm for the treatment of patients who are suspected to have IGM as in Figure 2.



Hx: History; PE: Physical examination; US: Breast ultrasound; MMG: Mammography; IGM: Idiopathic granulomatous inflammation; CNB: Core needle biopsy

Figure 2 Proposed treatment protocol for idiopathic granulomatous mastitis

Finally, as Luqman, et al[26] and Husa, et al[27] have both reported cases of breast cancer occurring in association with IGM, we also suggest long-term follow-up and thorough investigation of patients diagnosed with IGM to avoid missed cancer diagnosis.

Conclusion

IGM is an under-recognized benign inflammatory breast disease, mainly affecting women of childbearing age. Patients commonly present with palpable mass and pain at any location of the breast. IGM may present within 5 years of the last breastfeeding period. CNB is the mainstay of diagnosis. Corticosteroids and wide excision play major roles in management. Thorough investigation and long-term follow-up of patients with IGM is recommended.

Acknowledgments

Dr. Sakda Alapach, Hospital director; Dr. Piyarat Jeeravongpanich, providing pathological data; Dr. Srila Samphao and Dr. Matthew Hunsaker, providing language help and editing; Mr. Somkiet Klomkling, supporting literature

What Is Already Known On This Topic?

Idiopathic granulomatous mastitis (IGM) is a rare benign inflammatory breast disease Clinically and radiographically mimic inflammatory breast cancer. Wide excision and corticosteroids play role in treatment modality.

What The Study Adds

Coarsely Incidence rate of Idiopathic granulomatous mastitis (IGM) among the patients treated for breast pathologies. Postulated etiology, clinical and radiographical of Thai patient. Approach and management for the patients who present with IGM.

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บทคัดย่อ **Case series ของผู้ป่วย Idiopathic granulomatous mastitis และแนวทางการดูแลรักษา**

พงศธร อาสนศักดิ์

กลุ่มงานศัลยกรรม โรงพยาบาลสงขลา

ความเป็นมา: โรคเต้านมอักเสบที่ไม่ทราบสาเหตุ (Idiopathic granulomatous mastitis (IGM)) เป็นโรคเต้านมอักเสบที่ยังไม่ทราบสาเหตุแน่ชัด มีลักษณะทางคลินิกและการตรวจทางรังสีวิทยาที่อาจจะทำให้วินิจฉัยผิดพลาดเป็นมะเร็งเต้านมได้ ซึ่งจะนำไปสู่ผลการรักษาที่ไม่พึงพอใจทั้งจากผู้ป่วยและแพทย์ผู้รักษา จนถึงขณะนี้ยังไม่มีแนวทางการรักษาที่ชัดเจนสำหรับโรค IGM ดังนั้นจึงเป็นเรื่องสำคัญและมีประโยชน์ที่จะศึกษาผู้ป่วยที่มีภาวะ IGM

วิธีดำเนินการ: การศึกษาข้อมูลย้อนหลังของผู้ป่วยที่มีภาวะ IGM 17 ราย โดยศึกษาข้อมูลและปัจจัยที่อาจจะเป็นสาเหตุ ลักษณะทางคลินิก ผลการตรวจทางรังสีวิทยา แนวทางการรักษา และผลลัพธ์ของการรักษาร่วมกับการทบทวนวรรณกรรม และได้เสนอวิธีแนวทางการรักษาสำหรับผู้ป่วยที่สงสัยว่าเป็นโรค IGM

ผลการศึกษา: ผู้ป่วยทั้งหมดเป็นเพศหญิงและอายุเฉลี่ย 36 ปี (21-53 ปี) โดย 16 จาก 17 คนอยู่ในวัยเจริญพันธุ์ และ 16 คนเคยมีบุตร ส่วนใหญ่เคยให้นมบุตรครั้งสุดในระยะเวลาน้อยกว่า 5 ปี ผู้ป่วยทั้งหมดมาด้วยก้อนที่เต้านมและอาการปวดบริเวณก้อน ผู้ป่วยได้รับการตรวจ mammography 12 คน โดยผู้ป่วย 7 ราย มีผลการตรวจ เป็น BI-RADS 4 และ 5 ราย เป็น BI-RADS 2 ผู้ป่วยทุกรายมีอาการดีขึ้นหลังจากการรักษาด้วยยาปฏิชีวนะ คอร์ติโคสเตียรอยด์ การผ่าตัด หรือการรักษาหลายวิธีร่วมกัน

สรุปผลการศึกษา: IGM เป็นโรคเต้านมอักเสบของสตรีในวัยเจริญพันธุ์ ที่พบได้น้อย คอร์ติโคสเตียรอยด์และการผ่าตัด wide excision ให้ผลดีในการรักษา