DOI: 10.7860/IJARS/2024/68200.2973

Case Series

Surgery Section

A Case Series of Idiopathic Granulomatous Mastitis: Surgical Intervention is not the Only Option

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ABSTRACT

Idiopathic Granulomatous Mastitis (IGM) is a benign inflammatory disease of the breast that is difficult to treat, as there is no definitive protocol for management and it has a higher recurrence rate. The present case series presents five patients who exhibited clinical symptoms such as breast swelling, pain and nipple discharge, and were diagnosed with IGM. They were treated with a multimodality approach (surgical and/or conservative management) based on their symptoms. All patients were successfully treated for IGM using the multimodality approach. While a recurrence was observed in one out of five patients, it was further successfully treated with additional conservative management. The proposed multimodality treatment is effective in treating IGM. It eliminates the risk associated with surgical intervention among patients clinically diagnosed with IGM. It also eliminates the risk of corticosteroid side-effects among patients whose initial clinical diagnosis and postoperative histopathological examination is negative for IGM.

Keywords: Benign inflammatory disease, Corticosteroid treatment, Mammography, Methotrexate, Prednisolone

INTRODUCTION

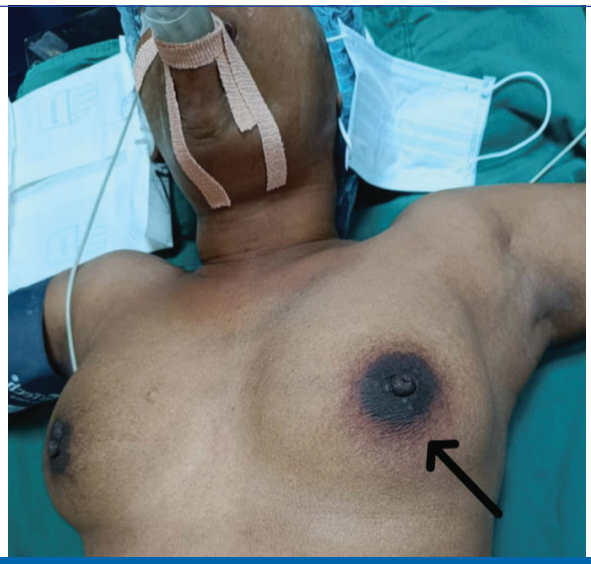
Idiopathic Granulomatous Mastitis (IGM) is a benign chronic inflammatory disease of unknown aetiology [1]. It has been reported among females from as early as 11 years to 80 years of age, particularly in those with a recent history of breastfeeding (or up to 2 years after breastfeeding) and pregnancy [2]. To date, the diagnosis and treatment of IGM remain a challenge. IGM can closely resemble breast carcinoma or benign inflammatory disorders and is often diagnosed through a process of exclusion. In the present case series, the authors have adopted and validate a diagnosis based multimodality (conventional and/or conservative management) treatment approach for treating IGM patients.

CASE SERIES

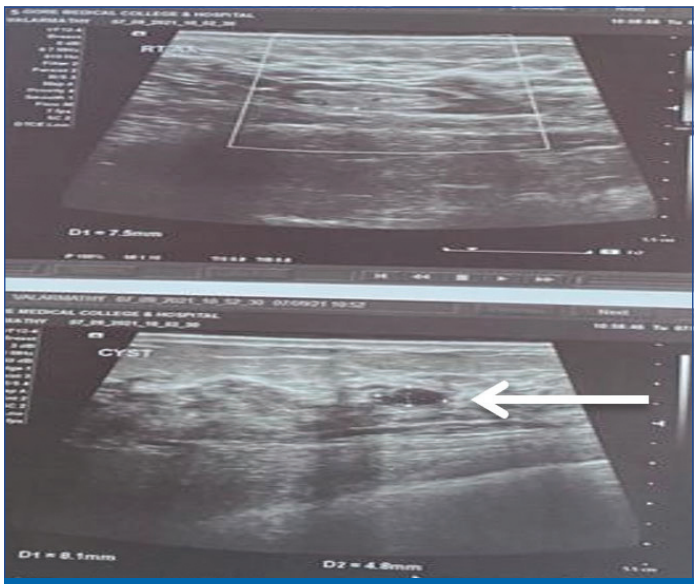
Case 1

A 38-year-old female presented with complaints of swelling in the left breast with milky discharge associated with pain for one week. She had no history of recent breastfeeding, pregnancy, trauma, fever, or swelling in the opposite breast or elsewhere in the body. She is not a smoker or alcoholic and has no history of using Oral Contraceptive Pills (OCPs). On examination, a 3x2 cm swelling was found in the upper outer quadrant of her left breast associated with milky discharge from the nipple. The swelling was hard in consistency, not freely mobile, and the skin over the swelling appeared normal [Table/Fig-1].

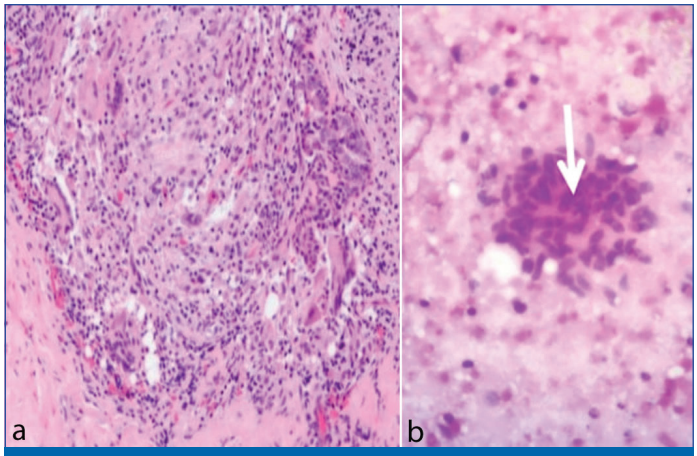
Clinically, a palpable axillary lymph node of size 1.5×1 cm was found in the left axilla. Further investigations including bilateral Ultrasonograph (USG) of the breast and axilla, and Fine Needle Aspiration Cytology (FNAC) revealed the following: a complex or complicated cyst in the left breast and a simple cyst in the right breast (with features of early mastitis) with bilateral prominent ducts [Table/Fig-2]. FNAC of the left breast indicated granulomatous mastitis. The patient was planned for excision and biopsy of the cyst, and the histopathological examination by Haemotoxylin and Eosin (H&E) stain suggested chronic granulomatous mastitis [Table/Fig-3a,b]. Special stains were negative for Acid-fast Bacilli (AFB) and Periodic Acid Schiff (PAS). The specimen was further sent for Tuberculosis (TB) culture, which turned out to be negative, as did the GeneXpert test. The patient's symptoms improved after the excision of the lump.



[Table/Fig-1]: Inflammatory changes around nipple-areolar complex (black arrow).



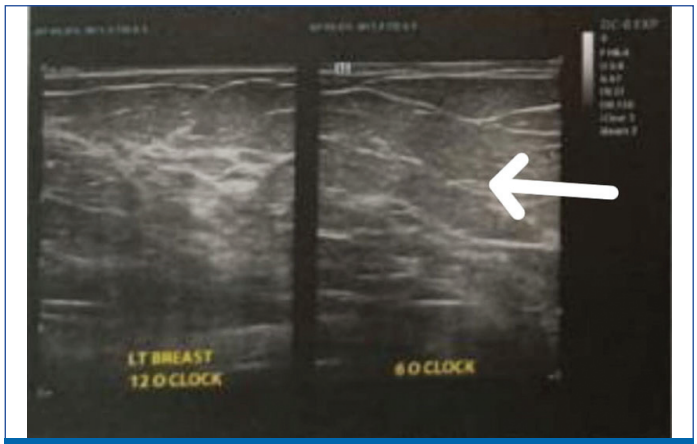
[Table/Fig-2]: USG showing complex breast cyst (white arrow).



[Table/Fig-3]: a) HPE shows cohesive cluster of epitheloid cell (H&E, 45x); b) White arrow shows granuloma formation (H&E, 100x).

The patient was followed-up after 15 days. She had the same complaints of a breast lump on the left side. On examination, a 2×1 cm swelling was present in the upper inner quadrant of the left breast, with no warmth, tenderness, firm to hard consistency, and no palpable lymph nodes. The patient was started on methotrexate and steroids after recording the baseline liver function test values. The prescribed regimen included Tablet (Tab.) methotrexate 5 mg once a week for four weeks, Tab. prednisolone 20 mg once a day in the morning, followed by Tab. prednisolone 10 mg once a day at night, for one month.

After one month of high-dose steroid therapy, the patient was followed-up, and there was a significant reduction in the size of the swelling to 1×1 cm with no associated warmth and tenderness. The same regimen was followed for the next month, and on follow-up after two cycles of high-dose therapy, there was a swelling of 0.5×0.5 cm in the left breast. At the end of three cycles of therapy, there was complete regression of the breast lump [Table/Fig-4].

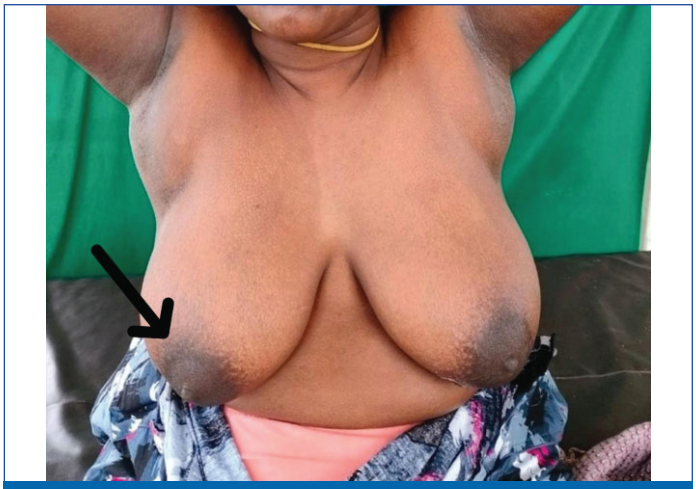


[Table/Fig-4]: Follow-up study revealing no mass on left breast (white arrow).

Case 2

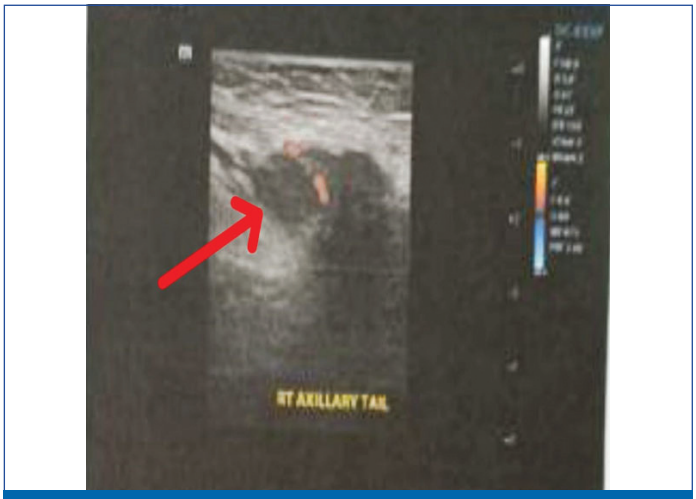
A 65-year-old perimenopausal woman presented with complaints of swelling over her right breast [Table/Fig-5], associated with pain for the past two months. She had no significant past medical history, including no previous history of tuberculosis. She was not on any chronic medication and had not used the oral contraceptive pill. She had no history of breast trauma, and there was no family history of breast cancer. She had breastfed her two children for three months each. Her first child was born when she was 24 years old and her second child when she was 36 years. She was currently in her perimenopausal period.

Clinically, there was a lump in the right outer upper quadrant, firm in consistency. The overlying skin was thickened and slightly warm. There was no associated nipple discharge or skin sinus. A single palpable axillary lymph node firm in consistency was noted in the right axilla. The opposite breast was normal.

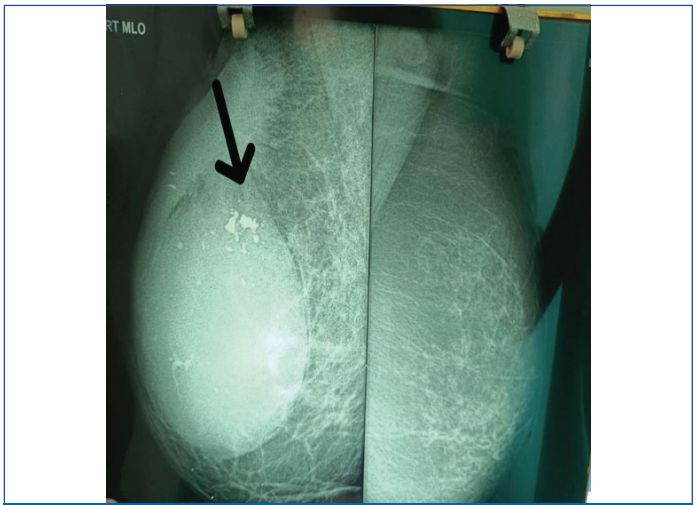


[Table/Fig-5]: Swelling in right breast (black arrow).

Ultrasound revealed an irregularly outlined, hypoechoic mass with hypoechoic tubular extensions into the breast parenchyma [Table/Fig-6]. There were no posterior acoustic features. Colour doppler demonstrated increased vascularity in the surrounding tissue, with the right axillary lymph node measuring 14×10 mm. It was round, with a thickened cortex and minimal visible fatty hilum. Mammography revealed bilateral moderately dense fibroglandular breast parenchyma in the right upper outer region, and it revealed a poorly defined area with increased density and calcification, suggesting an enlarged right axillary node with loss of fatty hilum [Table/Fig-7]. The imaging features raised suspicion for carcinoma, and ultrasound-guided core biopsy of the right breast mass and fine-needle aspiration of the right axillary lymph node were performed.



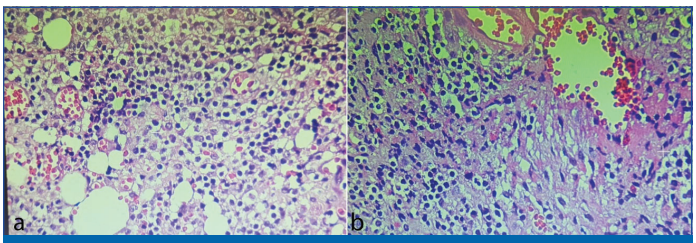
[Table/Fig-6]: USG right axillary node enlargement (red arrow).



[Table/Fig-7]: Mammography enlarged right axillary node with loss of fatty hilum (black arrow).

The core biopsy demonstrated features of granulomatous mastitis. Stains for demonstrating acid-fast bacilli (Ziehl-Neelsen) and fungal elements PAS were negative. The fine-needle aspirate of the right axillary lymph node was consistent with a reactive lymph node.

The patient was planned for excision and biopsy. All other routine preoperative investigations were done, and the anaesthetist's fitness was obtained for the excision and biopsy of the right breast lump, which was done under general anaesthesia. The entire breast lump was excised and sent for histopathological examination. The intra and postoperative periods were uneventful. The patient improved symptomatically and was discharged on postoperative day 5. The patient was reviewed with a histopathological report indicative of chronic granulomatous mastitis [Table/Fig-8a,b].



[Table/Fig-8]: a) HPE arrow shows collection of macrophages and foam cells (H&E, 45x); b) Chronic inflammatory infiltrate predominantly lymphocytes and congested vessels (H&E, 45x).

One month postoperatively, the patient started treatment with methotrexate and steroids after recording the baseline liver function test values. Tab. methotrexate 5 mg once a week for four weeks, Tab. prednisolone 20 mg once a day in the morning for one month, followed by Tab. Prednisolone 10 mg once a day at night for one month. After one month of high-dose steroid therapy, the patient was followed-up for any recurrence. The same regimen was followed for the next two months, and at the end of three cycles of therapy, there was complete regression of the breast lump.

Case 3

A 35-year-old female presented with complaints of right breast swelling associated with pain for the past two months. There was no discharge or overlying breast skin changes. She delivered her last child 18 months prior to admission and had breastfed for nine months. The patient had no significant past medical history and denied previous use of oral contraceptives, oestrogens, or recent breast trauma. Initial cultures of ultrasound-guided fluid aspiration showed no growth. She had previously received multiple courses of oral antibiotics without improvement in symptoms.

On physical examination, the patient was afebrile and there was a 3x3 cm palpable lump in the upper inner quadrant of the right breast. The skin overlying the mass was normal, and the mass was freely mobile within breast tissue. Axillary lymph nodes were not palpable. An ultrasound revealed scattered fluid collection suggestive of small abscesses. A core needle biopsy revealed chronic mastitis with focal abscess formation. The patient failed to improve with antibiotics and subsequently underwent surgical management. Cultures and special stains for bacteria, mycobacteria and fungi were negative. Histopathological examination showed IGM with multinucleated giant cells and chronic lobulitis.

The patient was started on prednisolone 20 mg and methotrexate 5 mg therapy, and follow-up was done after one month. A decrease in the size of her breast mass was noted at the end of one month. The dosage of prednisolone 10 mg was tapered over the next two months. Since the patient had a good clinical response with complete resolution of the breast mass at the 12-week follow-up visit, prednisolone was tapered off completely, and methotrexate was discontinued. Five months from treatment, the patient had no signs or symptoms of relapse.

Case 4

A 40-year-old female presented with complaints of a lump in the left breast associated with nipple discharge for the past three months. She also reported occasional pain over the lump, non radiating, and associated with low grade temperature. She had a positive history of using oral contraceptives six months back. There was no history of trauma to the breast, and no family history of breast carcinoma. Her first child was born when she was 22 years old, and she breastfed for one year.

On examination, there was fullness in the left upper outer quadrant, firm to hard in consistency. The overlying skin was normal, and serous nipple discharge was noted. No other swelling was palpable in the left upper breast. A single lymph node was palpable at level 1 of the left axilla, mobile with minimal tenderness and not associated with skin changes. The right breast and right axilla were normal. Radiological (ultrasound) investigation revealed a breast abscess. The patient was planned for operative management and drainage of pus. Pus and tissue culture sensitivity were sent and found to be IGM. After explaining the treatment course for IGM, the patient was started on steroid therapy for three months. The patient was followed-up for two years with no recurrence.

Case 5

A 45-year-old female presented to the Surgical clinic with a complaint of a lump in her right breast for the past two months, not associated with pain or nipple discharge. There is no other clinical history related to swelling. The patient has a regular menstrual history, no history of oral contraceptive use, or previous similar complaints. She had her first child at the age of 25 years, with a history of breastfeeding for eight months, and her second child at the age of 26 years with a history of breastfeeding for one year. On clinical examination, a 5×3 cm firm mass was palpable at the left outer quadrant, with normal skin over the swelling and a normal nipple-areolar complex. No other swelling is palpable elsewhere, and both axillae and the left breast were normal. Ultrasound revealed a Breast Imaging Reporting and Data System (BIRADS-3) result. The patient underwent a tru-cut biopsy which revealed an IGM. She was started on steroid therapy, and complete regression of the swelling was noted after three cycles of therapy with no recurrence.

The five cases included in the present case series study were 35-65 years. [Table/Fig-9] reports the age and patient history related to IGM. All have a history of breastfeeding for more than nine months, with no recent history of breastfeeding. Two patients had a significant history of taking oral contraceptive pills, which is an important risk factor for IGM. None of the patients had a similar illness in the past. No other significant history (such as trauma to the breast, family history of breast cancer, or breast tuberculosis) was reported among them.

Case	Age (years)	History of oral contraceptive pills consumption	History of breast feeding	History of similar illness in past	Significant history
1	38	No	Yes	No	No
2	65	No	Yes	No	No
3	35	Yes	Yes	No	No
4	40	Yes	Yes	No	No
5	45	No	Yes	No	No

[Table/Fig-9]: Age and history of female patients with IGM diagnosis.

In the clinical findings [Table/Fig-10], all cases presented with a palpable lump, mostly involving the right breast. Three patients presented with nipple discharge. Three patients presented with skin changes mimicking breast malignancy. Four patients presented with ipsilateral axillary lymph node involvement (most are reactive lymph nodes due to inflammatory swelling).

Case	Lump side and size (cm)	Quadrant	Swelling consistency	Skin changes	Nipple discharge	Axillary lymph node	The other breast	DDX
1	Left (3×2)	UOQ	Hard	No	Milky	I/L single	Normal	Inflammation abscess/galactocele
2	Right (6×7)	UOQ	Hard	Redness and dilated veins	serous	I/L single, mobile, firm	Normal	Carcinoma
3	Right (3×3)	UIQ	Firm	Inflammatory changes present	No	I/L single	Normal	Inflammatory abscess
4	Left (2×2)	LIQ	Firm to hard	Inflammation changes present	Serous	I/L single	Normal	Inflammation abscess
5	Right (5×3)	LOQ	firm	No	No	No	Normal	IGM

[Table/Fig-10]: Clinical findings of the cases.
UOQ: Upper outer quadrant; UIQ: Upper inner quadrant; LIQ: Lower inner quadrant; LOQ: Lower outer quadrant; I/L: Ipsilateral; DDX: Differential diagnosis

Three out of the five cases that were presented with differential diagnoses of an inflammatory abscess [Table/Fig-11] underwent radiological (USG) investigation [Table/Fig-11]. Following an inconclusive radiological report, they underwent surgical management for abscess drainage, and their specimens were sent for Histopathological Examination (HPE), GeneXpert test and AFB analysis. Another patient (in the postmenopausal age group) with a 6×7 cm breast lump and an inconclusive report from the invasive investigation (tru-cut biopsy) was treated with surgical excision and sent for postoperative HPE evaluation. As the invasive investigation suggested IGM for the final case, she was not subjected to surgical intervention.

Case	Differential diagnosis	Radiological investigation	Invasive investigation (FNAC/Tru-cut/Excision biopsy)	AFB	GeneXpert
1	Inflammatory abscess/ galactocele	USG: Complex cyst in the left breast and simple cyst in the right breast (has early mastitis features)	Preoperative FNAC: Aggregates of epithelioid histiocytes noted against the proteinaceous background- S/o granulomatous mastitis	Negative	Negative
2	Carcinoma	Mammogram: Irregular outlined hypoechoic mass	Tru-cut: Granulomatous mastitis	Negative	Negative
3	Inflammatory abscess	USG: Chronic mastitis and focal abscess	Postoperative HPE: IGM	Negative	Negative
4	Inflammatory abscess	USG: Breast abscess	Postoperative HPE: IGM	Negative	Negative
5	IGM	USG: BIRADS-3	Pre-op HPE: IGM	Negative	Negative

[Table/Fig-11]: Summary of radiological, invasive and special investigation.

All five cases (after surgical intervention for four cases) were treated with conservative management (corticosteroid and immunosuppressant therapy). Before treatment, all were briefed on the pros and cons of the treatment, and their consent for treatment was obtained.

Protocol

- Tab. methotrexate (5 mg), once a week×4 weeks
- Tab. prednisolone (20 mg) 1-0-0×1 month
- Tab. prednisolone (10 mg) 0-0-1×1 month

The regimen was repeated for three months. Conservative management was administered for three months, with regular monthly check-ups to assess the regression of swelling and detect any early recurrence. The summary of the treatment and follow-up (recurrence and side-effects) is detailed in [Table/Fig-12].

One patient, who had a differential diagnosis of an inflammatory abscess with a complex cyst in USG and underwent an excision biopsy, experienced a recurrence of swelling in the same spot after conservative management. Upon extending the conservative management for an additional two months, the swelling regressed completely. Furthermore, one patient (case 1) experienced the side-effects of corticosteroid therapy (skin reactions on the face), which were managed by reducing the dosage.

Case	Suspected diagnosis	Treatment done	Tab. methotrexate (5 mg) once a week×4 weeks Tab. prednisolone (20 Mg) 1-0-0×1 month Tab. prednisolone (10 mg) 0-0-1×1 month	Recurrence (Within 2 years)	Side-effects of steroid
1	A complex cyst (inflammatory abscess/ galactocele)	Excision biopsy	3 cycles	Yes	No
2	Carcinoma	Excision and biopsy	3 cycles	No	No
3	Inflammatory abscess	Incision and drainage	3 cycles	No	No
4	Inflammatory abscess	Incision and drainage	3 cycles	No	No
5	IGM	No surgical intervention	3 cycles	No	No

[Table/Fig-12]: Treatment and follow-up (recurrence and side-effects).

DISCUSSION

Idiopathic granulomatous mastitis remains a diagnosis of exclusion, and the clinical findings are often inconclusive due to granulomatous inflammation. First reported in 1972, granulomatous mastitis is clinically divided into specific granulomatous and IGM. While specific granulomatous mastitis occurs due to chronic granulomatous inflammation, the etiology of IGM mimics inflammatory breast carcinoma [3]. Studies show that autoimmunity and bacterial infection (*Corynebacterium kroppenstedtii*) are two main factors that contribute to IGM, as reported in 1996 by Binelli [4]. Physical examination resembles malignancy, and histopathological confirmation is mandatory to ensure malignancy is not missed [5]. IGM can cause nipple retraction or peau d'orange, which can mimic a malignant tumour. It also mimics breast abscesses, and chronic IGM can lead to the development of fistulae, sterile abscesses, and nipple inversion [6,7]. IGM is also observed to occur in inflammatory reactions following trauma, hormonal imbalance, and OCP use [8].

In a study conducted by Baslaim MM et al., histopathologically confirmed cases of IGM represented 1.8% of cases out of 1,106 women with benign breast disease, and up to 15% of the patients are characterised by axillary lymphadenopathy [9]. Radiological diagnoses (USG and mammogram) are non specific and indicate the presence of a tumour. The most frequent findings on mammograms and USG are an asymmetric diffuse increased density of fibroglandular tissue and hypoechoic mass lesions or nodular structures, respectively. Further histopathological diagnosis through invasive investigations (fine needle aspiration cytology, tru-cut biopsy, or excision biopsy) helps to diagnose whether the tumour is benign or malignant. Additionally, immunological indicators such

Authors	Year of publication	Total no. of cases	Age of patients	Presenting features	Aetiology	Histopathology	Treatment	Follow-up
Nguyen MH et al., [12]	2021	1	Young, parous, lactating women	Tender, erythematous breast lesions	Immune-mediated, lipophilic corynebacterium species	Non caseating granulomata and an inflammatory cell infiltrate	Multidisciplinary approach	-
Ringsted S and Friedman M [13]	2021	28	Young-middle aged, with recent pregnancy or breastfeeding	Painful, erythematous lump, with discharge in few cases, inflammatory arthritis and erythema nodosum in few	Corynebacterium and tubercle bacilli positive in few cases	Biopsy showing non caseating granulomas	Treatment for active tuberculosis, steroids, methotrexate	Few cases showed relapse
Mathew Thomas V et al., [14]	2020	2	Young-middle aged	Painful breast lump, erythema with axillary lymphadenopathy	*Corynebacterium kroppenstedtii* growth in one case	Lymphocytic infiltration and non caseating granulomas in cytology smears	Steroids in one case, doxycycline in another	Recurrence seen
Deng JQ et al., [15]	2017	65	Average age 31.2 years (19-48 years)	Inflammatory mass, firm-to hard lump in few cases	Local autoimmune disease, involving humoral and cell-mediated immunity, hyperprolactinaemia	Non caseating granulomas in biopsy, IHC-CD3, CD4, CD8, CD79a lymphocytes diffusely distributed in the lesion. Stains for IgG, IgM-negative	Corticosteroids with/without surgical removal of breast lesion	Recurrences in few cases
Wang J et al., [16]	2021	200	20-50 years	Breast lump with skin rupture	Autoimmune	Non caseating granuloma, inflammatory cell infiltrate	Corticosteroids with/without surgical therapy	Recurrence, postsurgical wound complications
Farrokh D et al., [17]	2019	32	Young-middle aged, with recent history of pregnancy or lactation	Solitary/multiple breast mass, skin ulcer, sinus tracts, and nipple discharge	Tuberculous (positive smears, tuberculosis culture, TB PCR)	Granulomas with caseation necrosis	Anti-tubercular therapy	-
Ichinose Y et al., [18]	2021	3	Older women	Lump at the site of previous surgical scar, often with erythema	Previous surgical incision	Xanthogranulomatous lesion with cystic changes and dense sclerosis, calcification, necrosis	Follow-up, tumourectomy	Resolution
Li J [19]	2019	75	Young to middle-aged parous women	Breast lump (with/without pain), nipple retraction, sinus formation, axillary lymphadenopathy	Idiopathic	Non caseating granulomas	Lumpectomy, abscess drainage or mastectomy. Follow-up with postoperative antibiotics	Resolution
Shin YD et al., [20]	2017	34	Reproductive age, with history of lactation, OCP, smoking, etc	Painful mass, erythema, fistula formation, discharge	AFB, TB-PCR negative. Methicillin-resistant *Staphylococcus aureus*-cultured in one case	Non caseating scattered granulomas composed of epithelioid histiocytes, giant cell, lymphocytes, neutrophils, plasma cells, eosinophils	Antibiotic therapy incision and drainage steroids wide excision	Partial to complete response
Alrayes A et al., [21]	2019	29	Young to middle aged	Inflamed breast mass	Unknown	Demonstration of granulomas	Surgical excision with debridement and removal of retroareolar ductal system	No recurrence in the follow-up period

[Table/Fig-13]: Summary of the findings of studies in the last five years [12-21].
IHC: Immunohistochemistry; CD: Cluster differentiation; Ig: Immunoglobulin; TB: Tuberculosis; PCR: Polymerase chain reaction; AFB: Acid-fast bacilli

as Interleukin-8 (IL-8), IL-10 and IL-11 play an important role in IGM diagnosis [10].

Yigitbasi MR et al., discovered that Il-33 and soluble interleukin 33 Suppression of Tumourigenicity 2 (ST2) receptor help to differentiate IGM from breast cancer [11]. The treatment of IGM also remains questionable as surgical management affects the treatment's effectiveness and often causes clinical depression [5]. Currently, various studies are being conducted to treat IGM through conservative management (using corticosteroids) and reduce the recurrence rate [22-24]. While the use of corticosteroids has been reported to be successful in treating IGM, the risk of side-effects (from using corticosteroids) makes it less suitable to replace surgical management for cases with inconclusive diagnosis [25].

A multimodality treatment approach, either surgical management or conservative management based on clinical diagnosis, as reported in various recent studies and in this case series, has yielded better results (patients were fully treated with no recurrence). Firstly, patients with inconclusive radiological and invasive diagnoses were initially treated with surgical management [Table/Fig-13] [12-21]. Upon a positive IGM diagnosis based on a postoperative histopathological examination, they were further treated with conservative management (corticosteroid and immunosuppressant therapy) to avoid recurrence. This helps to avoid the risk of corticosteroid side-effects among patients whose initial diagnoses are inconclusive and are diagnosed as IGM negative during the postoperative histopathological examination. This eliminates the risks and side-effects (mental and physical trauma) associated with surgical management.

CONCLUSION(S)

Idiopathic granulomatous mastitis poses challenges for both diagnosis and treatment. The authors have adopted a multimodality treatment plan that emphasises non surgical management for the treatment of IGM. When radiological and invasive investigations are inconclusive, IGM is first treated as a differential diagnosis (in cases of breast

abscess/malignancy) and subjected to surgical management. Patients are further treated with conservative management, if the postoperative investigation results in a positive IGM diagnosis. This eliminates the risk of corticosteroid side-effects on patients who test negative in the postoperative investigation. Conservative management encompasses treating patients with corticosteroid and immunosuppressant therapy for three months, with monthly follow-ups and reducing the dosage each month to help reduce recurrence and avoid the patient's dependency on corticosteroids.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Oct 27, 2023
- Manual Googling: Jan 15, 2024
- iThenticate Software: Jan 20, 2024 (11%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval Obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 26, 2023**
Date of Peer Review: **Dec 16, 2023**
Date of Acceptance: **Jan 22, 2024**
Date of Publishing: **Mar 01, 2024**