Idiopathic Granulomatous Mastitis (IGM): A "Thumbs Down" Benign Breast Condition

Julia Curry, PA-C, MPAS

Allina Health Cancer Institute at Abbott Northwestern Hospital

Surgical Oncology Department

02/24/24

Allina Health

1

Objectives

- Case Presentation
- Define Idiopathic Granulomatous Mastitis (IGM) and describe epidemiology
- Discuss proposed pathogenesis and etiologies of IGM
- Share features of IGM clinical presentation and differential diagnosis
- Outline appropriate work up / evaluation and discuss diagnostic challenges
- Discuss treatment options and patient outcomes
- Present ongoing efforts to increase understanding of IGM
- Emphasize importance of patient support and multidisciplinary approach
- Discuss if there is an association between IGM and malignancy

2

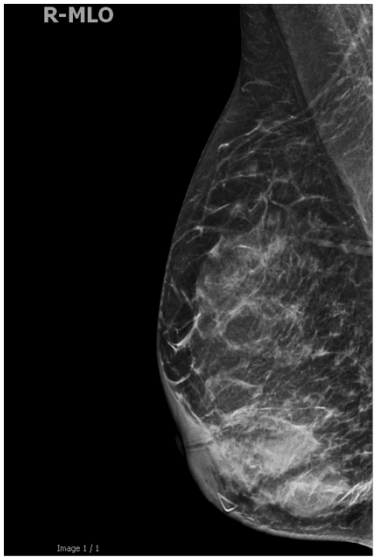
Case Presentation

- 44 y/o healthy female presented with tender RIGHT breast lump for 1-week
- History of mastitis with breastfeeding (4 years ago)
- No personal or family history of malignancy, no nipple piercing, nonsmoker
- Exam notable for 5 cm palpable mass with overlying erythema, no axillary lymphadenopathy

3

Case Presentation

- Diagnostic BILATERAL mammogram and RIGHT breast US, with aspiration yielding 4 cc purulent fluid
- Empiric antibiotic treatment with Doxycycline started
- Aerobic cultures with 2+ Gram positive bacilli resembling *Corynebacterium* – further identified as *C. kroppenstedtii*
- Discussion with infectious disease (ID) and transitioned to Linezolid with symptomatic relief

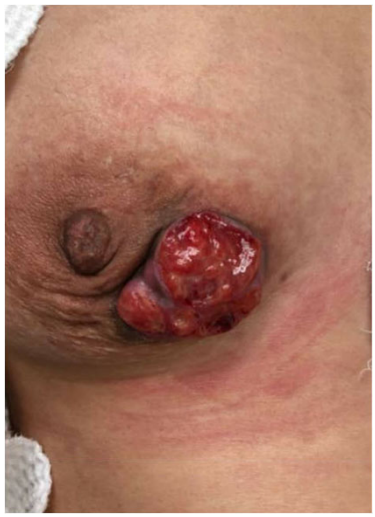


There is skin thickening around the RIGHT areola. Ill-defined mass medial RIGHT breast at the site of the palpable finding.

4

Case Presentation

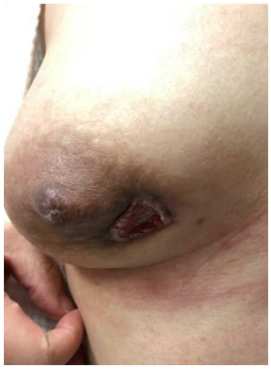
- Presented 2-months later with exophytic granulation tissue at original site of aspiration
- Diagnostic imaging with US-guided biopsy confirmed diagnosis of cystic neutrophilic granulomatous mastitis
- Prolactin measured 8.31 (WNL)
- She was offered oral steroid therapy, but declined
- Patient preferred to start a longer course of Doxycycline

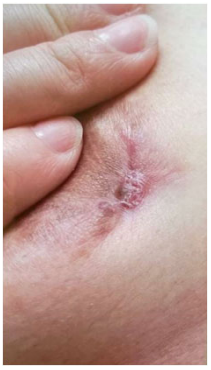


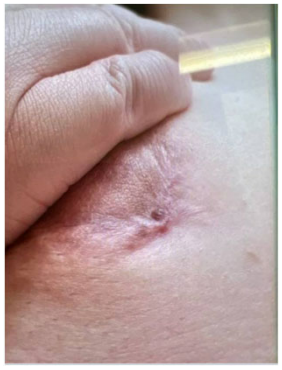
5

Case Presentation

- Ultimately referred to ID for consideration of Rifampin after lit review
- Complete symptom resolution after 8-months of Rifampin treatment







6

What is Idiopathic Granulomatous Mastitis?

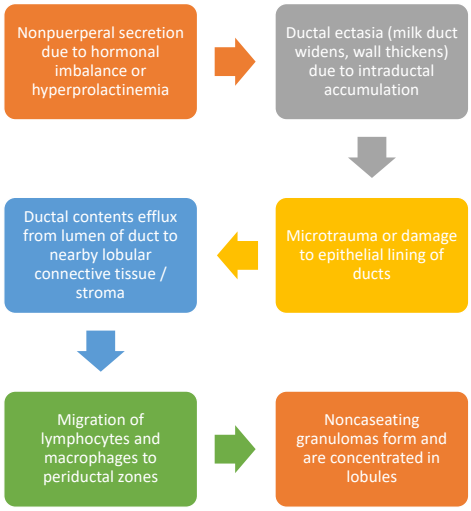
- First described in 1972 by Kessler and Wolloch, again in 1977 by Cohen (1,2)
- IGM is a rare, chronic, benign inflammatory condition of the breast (12)
- Considered the "non-specific" subgroup of granulomatous mastitis (4)

Demographics

- Prevalence 2.4 / 100,000 with rate 0.37% in USA – likely underestimated (2)
- Most commonly affects women of childbearing age with history of pregnancy and lactation within 5-years; rarely occurs in nulliparous women and men (7, 12)
- Any ethnicity could be affected, but studies report higher incidence in women of Asian, Middle Eastern, Hispanic ethnicity (2)

7

Pathophysiology and Etiology of IGM



Exact etiology of IGM remains unknown (2), but there have been proposed precipitating factors.

- Infection with *Corynebacterium*
- Alpha-1 antitrypsin deficiency
- Oral contraceptive (OCP) use
- History of lactation, pregnancy
- Hyperprolactinemia
- Smoking
- Trauma
- Autoimmune disease

8

Clinical Presentation

- Heterogeneous disease, variable presentation (5)
- Unilateral, painful breast mass in any quadrant; rarely bilateral (12)
- Erythema and swelling in 50% of patients (4)
- Abscess in approximately 37% of patients (4)
- Sinus or fistula formation secondary to disease progression or prior biopsy / aspiration (2)
- Axillary lymphadenopathy in 13-40% of patients (12)
- Onset over weeks to months (2)
- Symptoms may persist from 2-24 months (2)

9

Differential Diagnosis: What else could it be?

(2, 12)

- Breast cancer, inflammatory breast cancer
- Infectious mastitis – periductal mastitis, bacterial mastitis, Actinomyces abscess
- Idiopathic granulomatous mastitis, cystic neutrophilic granulomatous mastitis
- Tuberculosis, cat-scratch disease, leprosy (bacterial causes of granulomatous reactions)
- Histoplasmosis, cryptococcosis, coccidiomycosis (fungal causes of granulomatous reactions)
- Foreign body reaction / granulomas – silicone, beryllium
- Autoimmune – Crohn's disease, sarcoidosis, vasculitis (giant cell arteritis, Takayasu's arteritis, Churg-Strauss syndrome)

10

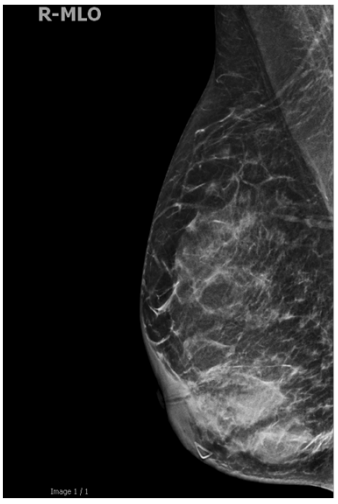
Diagnostic Evaluation of IGM

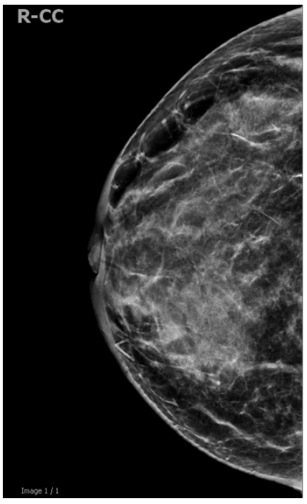
Imaging findings are non-specific and often mimics malignancy (7)

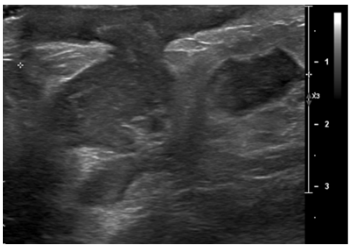
- Mammogram – Unilateral focal or regional asymmetry most common pattern (2, 6)
  - Lesions may be mammographically occult due to dense breast composition (2, 6)
  - Overlying skin thickening has been demonstrated in 63% of mammograms (7)
- Ultrasound – Hypoechoic mass (or contiguous masses), possibly fluid collections with associated skin fistulas in 7-54% of cases (2, 6, 8)
  - Hypervascularity may be detected by Doppler (6)
  - Axillary lymphadenopathy seen in 15-55% of cases (6)
- MRI – Variable findings, but can show heterogenous, ill-defined masses and non-mass enhancement (6, 8)
  - May help identify extent of disease (2)

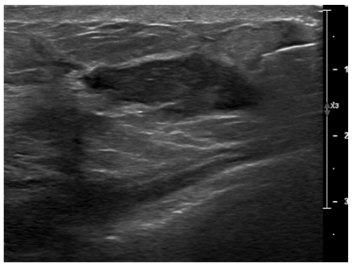
11

Mammogram and US images of case patient:









12

Diagnostic Evaluation continued…

Biopsy is gold standard for diagnosis of IGM; core needle biopsy 96% sensitive (2, 5, 6)

Histopathologic features:

- Non-necrotizing granulomas with localized infiltrate of multinucleated giant cells, epithelioid histiocytes, lymphocytes, and plasma cells (2, 6)
- May show sterile micro-abscesses with neutrophilic infiltrates (2, 6)
- Inflammation extending into adjacent lobules (2, 6)
- Additional stains for mycobacteria (AFB special stain) and fungal organisms (GMS fungal stain) to rule out infection-associated granulomas (2)
- Cystic neutrophilic granulomatous mastitis is a subtype of IGM in which *Corynebacterium* species is often isolated (6)

13

Histopathology examples from Elaine Houlihan et al. in *Idiopathic granulomatous mastitis: a 5-year retrospective review of cases in a tertiary centre in Dublin, Ireland* (16)

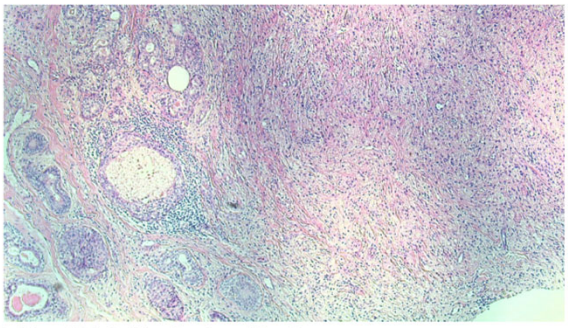


Figure 3 High power H&E showing lobulocentric granulomatous inflammation.

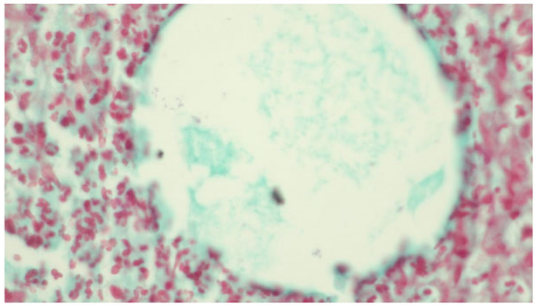


Figure 6 Gram stain showing Gram-positive bacilli within the cystic spaces.

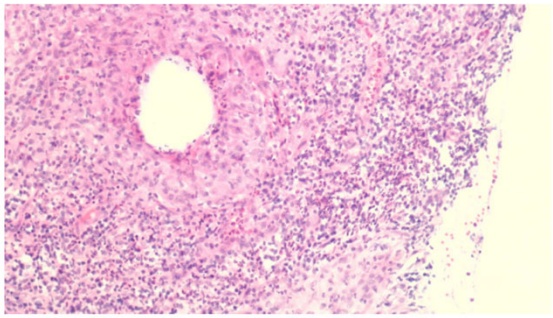


Figure 5 High power H&E of a cystic space with surrounding neutrophils and histiocytes.

14

Treatment Options for IGM

No consensus of optimal treatment for IGM, remains a self-limiting disease (2)

Multidisciplinary approach to evaluation and treatment is essential (2)

- Observation – 50% of mild cases resolve spontaneously (2)
  - Supportive care, pain management with NSAIDs (meloxicam), follow up (12)
- Antibiotics – Empiric course possibly started by time of presentation (2, 12)
  - Obtain cultures and cater antibiotic to result if growth is present, discontinue if NGTD
  - *Corynebacterium* antibiotic coverage with Augmentin or Doxycycline; 2 weeks or more

15

Treatment Options for IGM continued…

- Steroids – First-line approach for moderate to severe IGM (2)
  - Systemic:
    - Frequently been reported with up to 80% success (12)
    - Dose range of Prednisone 10-60 mg / day or Prednisolone 30-60 mg / day with gradual taper over weeks to months (12)
    - Potential adverse effects often deter clinicians and patients to pursue this modality
  - Topical:

    Cetin in 2019 (10)
    - Group T: Prednisolone 0.125% twice daily applied to affected area vs. Group S: PO Methyprednisolone 60 mg vs. Group C: Topical + PO Methyprednisolone 4 mg → **83.3% response similar in all three groups**

    Altintoprak in 2015 (11)
    - Prednisolone 0.125% twice daily every other day x 4 days with 3 days off, repeating weekly for 8.2 weeks → **complete symptom control in all patients** and 10.7% relapse over 37.2 months of follow up (no adverse effects observed)

16

Treatment Options for IGM continued…

- Steroids – First-line approach for moderate to severe IGM (2)
  - Local steroid injection (LSI) / intralesional:

    Cabioglu in 2023 (13)
    - LSI with triamcinolone acetonide every 4 weeks (median of 4 injections) plus topical triamcinolone acetonide 0.1% pomade vs. LSI with low-dose PO Methylprednisolone 4-16 mg / day (median of 8 weeks)
    - At median of 12 months (range 2-42 months of follow up), no difference was found in complete response rates between LSI group (52%) versus LSI with PO steroid (53.9%)

- Immune Modulators – Used in patients not responsive to steroids
  - Methotrexate 10-15 mg / week for 3-6 months with 83% symptom resolution rate and 17% recurrence rate (2, 12)
    - It is teratogenic! Contraindicated for women who plan to become pregnant, are pregnant, or are lactating

17

Treatment Options for IGM continued…

- Other medical therapies
  - Case series of 16 IGM patients treated with steroids + Bromocriptine 5-10 mg / day, where 31% had a favorable response (2)
  - Antituberculosis therapy

    Liu 2018 (14)
    - 22 patients with IGM in China all of whom received triple antituberculosis therapy (rifampin, isoniazid, ethambutol) for 6-12 months
    - During a median follow up of 40 months, 18 / 19 remaining patients in the study had achieved a complete clinical response with no observed recurrence; improvement at 3 months noted
- Surgery
  - Approaches include wide local excision, lumpectomy, mastectomy, percutaneous drainage of abscess / fluid collection (12)
  - Reserved for medically refractory or progressive disease (2)
  - Associated with poor cosmetic outcomes and high recurrence rates if entire affected area is not excised (2, 12)
  - Idiopathic Granulomatous Mastitis Registry by American Society of Breast Surgeons

18

Non-Pharmacologic Treatment for IGM

Wound care!

May require daily dressing changes or referral to WOC in certain cases

Patient support and counseling

Perseverance is key!

There is no "quick fix" ☹

Set realistic expectations!

Keep an open mind!

19

Is there an association between IGM and CA?

- Rarely observed to occur simultaneously, but prior cases have prompted discussion of possible correlation → **NO causative link has been demonstrated** (15)
- Clinical presentation of IGM should always prompt work up to rule out cancer
  - Perform a comprehensive history and exam
  - Pursue BILATERAL diagnostic imaging and biopsy if BILATERAL symptoms
- Persistent or prolonged symptoms beyond the "2-24 month" period → further diagnostic work up is reasonable
- Otherwise, follow-up per provider based on treatment and overall outcome with initiation of annual breast screening at 40 years old

20

Key points

- IGM is a rare, chronic, BENIGN inflammatory breast condition
- Etiology and pathophysiology are unknown, but some theories exist
- Diagnosis is frequently delayed as it is not often recognized early
- Work up should include breast imaging (bilateral), but GOLD STANDARD of diagnosis is core needle biopsy of lesion(s)
- No universally accepted treatment approach; should be catered to patient and severity of disease
  - Conservative / supportive, medical therapy, or surgical excision, wound cares
- Take a multidisciplinary approach

21

References

1. Kessler E, Wolloch Y. Granulomatous mastitis: a lesion clinically simulating carcinoma. Am J Clin Pathol. 1972 Dec;58(6):642-6. doi: 10.1093/ajcp/58.6.642. PMID: 4674439.

2. Dilaveri C, Degnim A, Lee C, DeSimone D, Moldoveanu D, Ghosh K. Idiopathic Granulomatous Mastitis. Breast J. 2024 Jan 25;2024:6693720. doi: 10.1155/2024/6693720. PMID: 38304866; PMCID: PMC10834090.

3. Williams GT, Williams WJ. Granulomatous inflammation--a review. J Clin Pathol. 1983 Jul;36(7):723-33. doi: 10.1136/jcp.36.7.723. PMID: 6345591; PMCID: PMC498378.

4. Altintoprak F, Kivilcim T, Ozkan OV. Aetiology of idiopathic granulomatous mastitis. World J Clin Cases. 2014 Dec 16;2(12):852-8. doi: 10.12998/wjcc.v2.i12.852. PMID: 25516860; PMCID: PMC4266833.

5. Chalmers R, McClellan P, Silva V, Shutt N, Restini C. Red flags for the differential diagnosis of granulomatous mastitis: a case report. J Med Case Rep. 2020 Nov 10;14(1):215. doi: 10.1186/s13256-020-02563-x. PMID: 33168069; PMCID: PMC7654600.

6. Wolfrum A, Kümmel S, Theuerkauf I, Pelz E, Reinisch M. Granulomatous Mastitis: A Therapeutic and Diagnostic Challenge. Breast Care (Basel). 2018 Dec;13(6):413-418. doi: 10.1159/000495146. Epub 2018 Nov 23. PMID: 30800035; PMCID: PMC6381909.

7. Brennan ME, Morgan M, Heilat GB, Kanesalingam K. Granulomatous lobular mastitis: Clinical update and case study. Aust J Gen Pract. 2020 Jan-Feb;49(1-2):44-47. doi: 10.31128/AJGP-08-19-5042. PMID: 32008263.

8. Sripathi S, Ayachit A, Bala A, Kadavigere R, Kumar S. Idiopathic granulomatous mastitis: a diagnostic dilemma for the breast radiologist. Insights Imaging. 2016 Aug;7(4):523-9. doi: 10.1007/s13244-016-0497-2. Epub 2016 May 10. PMID: 27164916; PMCID: PMC4956625.

9. Taylor GB, Paviour SD, Musaad S, Jones WO, Holland DJ. A clinicopathological review of 34 cases of inflammatory breast disease showing an association between corynebacteria infection and granulomatous mastitis. Pathology. 2003 Apr;35(2):109-19. PMID: 12745457.

10. Çetin K, Sıkar HE, Göret NE, Rona G, Barışık NÖ, Küçük HF, Gulluoglu BM. Comparison of Topical, Systemic, and Combined Therapy with Steroids on Idiopathic Granulomatous Mastitis: A Prospective Randomized Study. World J Surg. 2019 Nov;43(11):2865-2873. doi: 10.1007/s00268-019-05084-x. PMID: 31297582.

22

References

11. Altintoprak F, Kivilcim T, Yalkin O, Uzunoglu Y, Kahyaoglu Z, Dilek ON. Topical Steroids Are Effective in the Treatment of Idiopathic Granulomatous Mastitis. World J Surg. 2015 Nov;39(11):2718-23. doi: 10.1007/s00268-015-3147-9. PMID: 26148520.

12. Bland, K. I., Copeland, E. M., Klimberg, V. S., & Gradishar, W. J. (2017). *The Breast: Comprehensive Management of Benign and Malignant Diseases*. Elsevier Inc. https://doi.org/10.1016/C2014-0-01946-6

13. Cabioglu N, Uras C, Mutlu H, Sezgin D, Emiroglu S, Dulgeroglu O, Yilmaz R, Tukenmez M, Arikan AE, Kara H, Muslumanoglu M. Local steroid injection in severe idiopathic granulomatous mastitis as a new first-line treatment modality with promising therapeutic efficacy. Front Med (Lausanne). 2023 Oct 4;10:1251851. doi: 10.3389/fmed.2023.1251851.

14. Liu L, Zhou F, Zhang X, Liu S, Liu L, Xiang Y, Guo M, Yu L, Wang F, Ma Z, Li L, Gao D, Zhang Q, Fu Q, Yu Z. Granulomatous Lobular Mastitis: Antituberculous Treatment and Outcome in 22 Patients. Breast Care (Basel). 2018 Oct;13(5):359-363. doi: 10.1159/000487935. Epub 2018 Jul 5. PMID: 30498422; PMCID: PMC6257198.

15. 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 Dec 7;2021(12):rjab519. doi: 10.1093/jscr/rjab519. PMID: 34888031; PMCID: PMC8652020.

16. Houlihan E, Ryan K, Mannion J, Hennessy G, Dunne B, Connolly E, O'Connell B. Idiopathic granulomatous mastitis: a 5-year retrospective review of cases in a tertiary centre in Dublin, Ireland. J Clin Pathol. 2023 Sep 12:jcp-2023-209028. doi: 10.1136/jcp-2023-209028. Epub ahead of print. PMID: 37699697.

23

To Contact Me

Julia Curry, PA-C, MPAS

E: julia.curry@allina.com

Allina Health

24