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Idiopathic Granulomatous Mastitis - Experience in Two Australian Hospitals

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Abstract

Background: Idiopathic granulomatous mastitis is a rare inflammatory condition of the breast. Despite scientific advances, there remains uncertainty around aetiology and optimal treatment algorithms.

Methods: A retrospective observation study of 21 female patients treated at two major metropolitan health networks in Australia.

Results: The most common presenting symptoms were palpable lump (100%), pain (81%) and erythema (33%). Average time to diagnosis was 144 days, with average time to treatment 57 days. Five patients underwent operative excision, with complete remission in 80% of cases. Abscess drainage was used in 8 patients, requiring an average of 2.1 procedures for complete resolution after an average of 89 days. Antibiotic monotherapy was successful in three cases but failed in six cases. Average time to clinical improvement was 94 days, and time to complete remission was 157 days. Risk factors for prolonged treatment included larger lesions, smoking, and non-Caucasian ethnicity.

Conclusion: Idiopathic granulomatous mastitis mimics of other breast diseases, leading to delayed diagnosis and disparate initial management. Further research can help earlier identification of these patients to establish earlier treatment.

Keywords: *Granulomatous Mastitis; Mastitis; Breast Diseases; General Surgery; Observational Study*

Abbreviations

IGM: Idiopathic Granulomatous Mastitis; ANOVA: Analysis of Variance

Introduction

Idiopathic granulomatous mastitis (IGM) is a rare inflammatory condition of the breast. It is characterised by noncaseating granulomatous inflammation of the breast lobules. Whilst the aetiology of IGM is uncertain, risk factors include past pregnancy and breastfeeding, autoimmunity, *Corynebacterium kroppenstedtii* infection [1,2], tuberculosis, smoking, α1-antitrypsin deficiency, and sarcoidosis [3].

The treatment options for IGM are varied, and include antibiotics, anti-inflammatory medications, corticosteroids, and methotrexate, as well as abscess drainage and surgical excision. Close observation has achieved good outcomes in some patients with early disease and mild symptoms [3,4].

These treatment options have varying efficacy. Surgery significantly improves the rate of complete remission, compared to steroids, antibiotics and drainage, whilst steroid treatment improves the rate of complete remission, compared to antibiotics, abscess drainage, and methotrexate. The necessary duration of treatment, however, is uncertain [5,6].

This disease has a relapsing and remitting course, with certain groups more likely to recur. Risk factors for recurrence include bilateral disease, purulent nipple discharge, nipple inversion, skin lesions, abscess formation, and failure of non-operative treatment [7].

Here we describe the experience of two Australian breast surgical units (Austin Health and Northern Health), and the duration of therapy required to attain clinical improvement and complete remission.

Materials and Methods

We performed a retrospective observational study of patients treated between 2018 and 2023 at two major metropolitan health networks in Australia. All female patients treated in an inpatient or outpatient setting with a histological diagnosis of idiopathic granulomatous mastitis were included in the study. Patients with tuberculosis or fungal infection causing granulomas were excluded from the study.

Demographic details and treatment details were extracted from the patient database. This was compared with time to clinical improvement and complete remission. "Complete remission" was defined as completely healed abscess cavity, with no residual lumps. "Clinical improvement" was defined as breast abscess cavity nearly healed, or shrinking residual lumps, and absence of swelling and pain. "No effect" was defined as persistent breast cavity discharge, with unchanged residual lumps, swelling, or pain. Statistics were calculated using Minitab 20.2 (Minitab LLC). Comparative statistics were performed using the Student's T test for univariate analysis or ANOVA for multivariate analysis.

This study was ethically approved by the Austin Health Human Research Ethics Committee (HREC/91795/Austin-2022).

Results

A total of 21 patients met the inclusion criteria. Demographic details are included in table 1. All patients had records indicating followup for a minimum of 12 months after cessation of treatment. Common presenting symptoms included palpable lump (100%), pain (81%) erythema (33%), nipple discharge (29%), nipple inversion (14%), and fevers (14%). Axillary lymphadenopathy was detected clinically in 10%.

Demographics	Mean +/- Stdev
Age	39 +/- 14
Race/Ethnicity	
White	5
South Asian	5
South East Asian	3
Middle eastern	3
Greek	2
Pacific island	2
Aboriginal Australian	1
Parity	
Nulliparous	2
Parous	19

Parity	2.4 +/- 1.2
Pregnant at onset	0
Past abortion	1
Smoker	5
Laterality	
Left	9
Right	12
Bilateral	0
Presentation	
Pain	17
Lump	21
Erythema	7
Nipple discharge	7
Nipple inversion	3
Fevers	3
Lymphadenopathy	2
Size of lump (mm)	47 +/- 29
Time to diagnosis (days)	144 +/- 108
Investigations	
Mammogram (Abnormal/Total)	12/14
Ultrasound (Abnormal/Total)	20/21
Core biopsy (Abnormal/Total)	14/20
Surgical biopsy (Abnormal/Total)	7/7
Culture	
Corynebacterium kroppenstedtii	5/19
Corynebacterium minutissimum	1/19
Propionibacterium acnes	2/19
Not tested	2
Ziehl-Neelsen	0/19
Wade-Fite	0/18

Table 1: *Participant demographics, clinical presentations, and investigations performed.*

Histological assessment of the disease demonstrated granulomatous inflammation in all cases, with a specific diagnosis of cystic neutrophilic granulomatous mastitis in five cases. Histological diagnosis was delayed in all cases (144 +/- 108 days after symptom onset). Specimens were stained for *Mycobacterium tuberculosis* via Ziehl-Neelsen staining, and fungal staining via the Fite method. All stained negative for these pathogens. *Corynebacterium kroppenstedtii* was cultured in five cases. *Corynebacterium minutissimum* was cultured in one case.

Treatment modality is summarised further in table 2, and individual patient journeys are summarised in table 3.

Surgical treatment	12	
Excision	5	
Surgical drainage	2	
Percutaneous drainage	7	
No procedure	9	
Antibiotics	**Number**	**Duration (Median [Range])**
Doxycycline	5	28 [14, 60]
Flucloxacillin	3	30 [21, 56]
Clindamycin	3	18 [14, 22]
Amoxicillin/clavulanic acid	2	42 [10, 108]
Steroid	2	49 [42, 56]
Methotrexate	0	
Total symptom duration	211 +/- 126 days	187 [42, 500] days
Time from presentation to treatment start	57 +/- 60	45 [0, 203]
Time from treatment start to complete remission	158 +/- 127 days	126 [4, 475] days
Time from treatment start to clinical improvement	94 +/- 95 days	84 [4,447] days
Relapses	2	
Time to relapse		426 [28, 825] days

Table 2: *Treatment modality.*

Patient No	Age (y)	Ethnicity	Lump diameter (mm)	Initial treatment / Duration	Second-line treatment	Third-line treatment	Treatment start to clinical improvement (days)	Treatment start to complete remission (days)
1	23	White	12	Observation			84	84
2	49	White	13	Observation			120	120
3	39	Middle Eastern	53	Observation			125	125
4	37	Southeast Asian	50	Observation			204	204
5	34	South Asian	37	Doxycycline 100 mg bd 60 days			140	350
6	35	South Asian	42	Flucloxacillin 500 mg QID 30 days			30	268
7	37	White	80	Flucloxacillin 500 mg QID 21 days			29	29
8	33	South Asian	50	Prednisolone weaning dose (25mg daily - 2.5mg) 56 days			84	200

9	34	South Asian	67	Doxycycline 100 mg bd 28 days	Prednisolone weaning dose (25 mg daily - 5mg) 42 days		96	390
10	33	Pacific Island	106	Clindamycin 450 mg tds 22 days	Percutaneous drainage x2		150	192
11	35	White	100	Clindamycin 450 mg tds 18 days	Percutaneous drainage x2		159	159
12	35	Middle Eastern	45	Doxycycline 100 mg bd 14 days	Percutaneous drainage x3		49	126
13	27	South Asian	27	Doxycycline 100 mg bd 28 days	Operative drainage x1	Percutaneous drainage x1	119	207
14	36	White	13	Lesion excision			14	14
15	62	Greek	20	Lesion excision			7	7
16	82	Greek	24	Lesion excision			7	7
17	58	European	48	Lesion excision			4	4
18	40	Middle Eastern	20	Lesion excision + amoxycillin/clavulanic acid 10 days	Percutaneous drainage x1		22	246
19	25	Aboriginal Australian	30	Percutaneous drainage x3	Doxycycline 100 mg bd 140 days		447	475
20	31	Pacific Island	100	Flucloxacillin 500 mg qid 56 days	Percutaneous drainage x1		29	92
20 (relapse)	31	Pacific Island	100	Clindamycin 450 mg tds 14 days	Percutaneous drainage x2		34	34
21	30	Southeast Asian	50	Amoxycillin/clavulanic acid 42 days	Percutaneous drainage x1		98	187
21 (relapse)	33	Southeast Asian	50	Amoxycillin/clavulanic acid 108 days	Percutaneous drainage x1	Operative drainage x1	107	123

Table 3: *Patient journeys.*

Five patients underwent operative excision of the lumps. These tended to be for smaller lesions (13, 20, 20, 24, 48 mm) without fever or erythema to suggest sepsis. These generally had imaging findings concerning for cancer, or equivocal histological findings on core biopsy. Excision eradicated the disease in 80% of cases, with complete remission obtained within two weeks of the procedure. One case was complicated by wound breakdown and further abscess development, which was treated with percutaneous drainage and antibiotics. This case demonstrated clinical improvement after 22 days and reached complete remission after 123 days.

Eight patients were treated with abscess drainage. These patients had an evident drainable abscess on clinical or sonographic examination. One was drained operatively via surgical incision and drainage, six were drained via percutaneous aspiration under ultrasound guidance, and one was drained with a combination of surgical incision and percutaneous aspiration. All patients received concomitant antibiotic therapy. These patients required an average of 2.1 procedures to reach complete resolution (95% CI: 0.0-4.2, range 1 - 4). Time from final procedure to complete remission averaged 89 days (95%CI -1.6-181, range 20155).

Under the local Infectious Diseases team with microbial cultures guidance, the most commonly-used antibiotics were flucloxacillin (5 patients), doxycycline (3 patients), or amoxycillin-clavulanic acid (2 patients). Clindamycin was used in three cases after flucloxacillin failed to improve symptoms.

Three patients were successfully treated with antibiotics alone. One patient was treated with 21 days of flucloxacillin, demonstrating complete remission at 29 days. One patient was treated with 30 days of flucloxacillin, demonstrating clinical improvement at 30 days, but taking 268 days to reach complete remission. The final patient was treated with 60 days of doxycycline, demonstrating clinical improvement at 140 days and complete remission at 350 days.

Six patients failed antibiotic monotherapy. One patient failed a 28day course of doxycycline but had good success with a 42 day course of weaning prednisolone (25 mg daily weaning to 5 mg over 6 weeks), demonstrating clinical improvement at 96 days with resolution at 390 days. Five others demonstrated progression of disease with abscess formation despite doxycycline (28 day course, 2 separate patients), amoxycillin-clavulanic acid (42 day course), flucloxacillin (56 day course), or clindamycin (14 - 22 day course, 3 separate patients). These patients tended to larger mass diameter (mean 84.6 mm, 95%CI 35.2 - 134.0, range 50 - 106) and demonstrated good response to serial percutaneous abscess drainage.

Steroid monotherapy was used for one patient, who received a 56 day course of weaning prednisolone (daily 25 mg weaning down to 2.5 mg over 8 weeks) and demonstrated clinical improvement at 84 days with complete resolution at 200 days.

Four patients resolved with observation alone. These patients had smaller or indistinct lesions, (12 mm, 13 mm, 50 mm, 53 mm) and received late specialty clinic reviews, by which time they had demonstrated clinical improvement. Serial examination and serial ultrasound imaging demonstrated complete remission at a mean of 133 days (95%ci: 32 - 234, range 84204).

Two patients developed recurrences during the study period. Both were fit and healthy 3035 year old non-smokers who had last breastfed over 5 years prior. They both had large painful lesions (50 mm, 100 mm), and one had nipple discharge whilst the other had erythematous skin change. Both underwent percutaneous drainage after a failure of long course antibiotics. Both patients cultured *Corynebacterium kroppenstedtii*. One relapsed after 2 months and the other relapsed after 3 years.

Multivariate analysis demonstrated shorter treatment time and less operative treatment in Caucasian populations ($p = 0.03$). There was a trend to longer treatment in patients with larger lesions, smoking ($p = 0.42$), fevers ($p = 0.223$), discharge ($p = 0.42$), and erythema (0.40), although these were not statistically significant.

Discussion

Our case series demonstrates the wide variety of presentations and response to treatment that plagues cohesive treatment of this rare disease. Mimicry of more common breast conditions, such as breast abscess and breast cancer, led to diagnostic delay. Further research may help identify patients who should be tested for IGM early, streamlining treatment.

Whilst treatment was often started early, treatment selection was often directed towards other breast diseases. Abscesses were often treated akin to lactational or periductal breast abscesses, with percutaneous or open drainage and flucloxacillin, following the Australian

antibiotic guidelines. Non-abscess lumps were often investigated with core biopsy and then resected if biopsy indeterminate, or treated non-operatively if biopsy confirmed granulomatous mastitis. This non-operative treatment was guided by infectious diseases and rheumatology, leading to a wide variety of treatment approaches in this disparate group of patients.

A consensus statement has recently recommended a diagnostic and treatment algorithm for management of IGM [8]. Dissemination of this research may aid familiarity with this rare condition and streamline management. Further testing of this algorithm will help determine whether it is applicable to the Australian context.

Despite this piecemeal approach to patient management, we found that surgical excision and abscess drainage were the most effective treatment options, with rapid prolonged remission. Antibiotics alone were successful in only a small number of cases, with much longer duration of therapy to achieve complete remission. These findings are consistent with previous studies that have demonstrated the efficacy of surgery and abscess drainage in the management of IGM [3,5,6]. Further research may guide selection of patients for non-operative management, thereby reducing overall duration of treatment and expedite surgical treatment for those who will ultimately need it.

This study is limited by its small sample size and wide variety of treatment modalities. It highlights the variety of presentations which hinder accurate identification of these patients for the purpose of recruitment into the study.

Conclusion

This case series demonstrates that idiopathic granulomatous mastitis is a rare condition that is often detected late and managed suboptimally. Earlier identification and diagnosis amongst more common breast conditions may reduce diagnostic delay and streamline treatment decisions.

Conflict of Interest

The authors have no conflicts of interest or financial arrangements to declare.

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