Review Article

Idiopathic granulomatous mastitis

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Abstract: Idiopathic granulomatous mastitis (IGM) is a rare, benign breast condition characterized by multiple draining sterile breast abscesses. This condition of unknown etiology commonly presents in young, parous women with a recent history of lactation and of Mediterranean or Hispanic descent. IGM commonly presents unilaterally with localization in the upper outer quadrant but can present in any quadrant or both breasts concurrently. This disease can mimic breast cancer on various imaging modalities causing concern as well as presenting with erythema, breast edema, breast pain, and sinus tract formation. IGM is diagnosed through the exclusion of all other common pathogens and diseases as well as distinct histological findings of non-caseating granulomas and multinucleated giant cells upon core needle biopsy. IGM is a self-limiting disease and can self-resolve on an average of 5 months, but treatment modalities are recommended to help manage the symptoms. Treatment methods range from observation, steroids, methotrexate and surgical excision with relapse commonly occurring. Currently, no consensus within the literature exists on the best treatment strategy. Each treatment method has various advantages and disadvantages, therefore this review aims to provide focused, up-to-date guidance on of IGM. This review specifically highlights each treatment method, showcases studies on different treatment modalities in a comprehensive table, and provides a precise algorithm for clinicians on the workup and treatment of IGM.

Keywords: Idiopathic granulomatous mastitis (IGM); treatment; corticosteroids; methotrexate; steroid injections

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Introduction

Idiopathic granulomatous mastitis (IGM) is a benign inflammatory breast condition first described in the literature in 1972 (1). Also referred to as idiopathic granulomatous lobular mastitis, it is a rare and chronic condition characterized by relapsing sterile, draining breast abscesses. IGM is challenging clinically, as it mimics the presentation of a bacterial abscess or breast cancer. Often, the diagnosis of IGM is given when all other differential diagnoses are excluded. IGM usually presents in premenopausal women who were recently pregnant or lactating (2-4). It can occur in any race but does have a higher incidence in Hispanics (3,5-7) and people of Mediterranean descent (8).

Despite being present in the literature for the last fifty years, many things are still unknown about this complex, inflammatory disease. First, the etiology remains unclear despite many research studies investigating this disease. Many hypotheses exist for the exact mechanism of action, but an amplified autoimmune response is considered one of the top theories (1,9). Second, the gold-standard treatment modality for this disease remains highly debated within the

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literature with no clear consensus on the recommended treatment. The recommended treatments range from observation, steroids, methotrexate, surgical excision, and unique combinations of these treatment approaches (10). In this review, we aim to provide a clear overview of IGM as well as analyze the common treatment modalities highlighted in the literature.

Methods

A PubMed search was used to identify all articles regarding the diagnosis and treatment of IGM. A total of 616 articles from the time frame of 1972 to June 2020 were identified utilizing the search term of "granulomatous mastitis". Each article was analyzed for the main finding of the study as well as the recurrence rate. Few articles were prospective randomized trials and many were retrospective analyses or case studies identifying the success of various treatment regimens. All pertinent articles are included online: https://cdn.amegroups.cn/static/public/ABS-2020-BBD-03-supplementary.xlsx. Institutional review board approval was not obtained since only published studies were analyzed for this review article.

A summarized version of the appendix is included in this paper (*Table 1*) which highlights the type of study performed, number of subjects included, which treatment modalities were compared, recurrence rates as well as findings and recommendations. *Table 1* was created from the appendix by first identifying the different treatment modalities and then identifying how many published articles, in the conclusion of the manuscript, supported that treatment modality. Manuscripts supporting the various treatments were grouped together. Treatment groups that contained less than ten publications had every article included in the table. If a treatment group had more than ten published studies, then the articles were selectively chosen to be added to *Table 1* if they (I) had a sample size larger than 20 subjects and (II) contributed to the field through multiple citations, robust data, supported conclusions and low recurrence rates. With the presented conflicting arguments of each treatment modality highlighted, this review will give treatment guidelines for clinicians as well as a simplified management algorithm.

Review results

Diagnosis

Presentation

IGM presents clinically as a palpable breast lesion(s) (*Figure 1*) that vary in size from 1–5 cm, with an array of other symptoms such as tenderness, overlying skin induration, erythema, sinus tract formation, or breast edema which can clinically mimic a breast abscess or breast cancer on various imaging modalities (1,3,30-32,54-56). IGM commonly presents unilaterally (3) in the upper outer quadrant of the breast (3,4,31), but can be found in any quadrant as well as in both breasts concurrently (27). The palpable, erythematous breast lesion(s) are sterile abscesses often accompanied by the development of spontaneous fistulae or sinus formation.

Inflammation of Cooper's ligaments can occur, causing nipple inversion or retraction (9). In 13% to 40% of women, enlarged, palpable reactive lymph nodes are noted on exam (3,4,56). Systemic symptoms, such as a fever, are generally absent from the objective findings (8). An essential component of this challenging disease is recognizing the complex presentation to avoid unnecessary surgical interventions and excessive antibiotics. Clinicians diagnose IGM when all other differential diagnoses are excluded, and specific pathologic findings on core needle biopsy are present.

Imaging

In addition to the clinical symptoms mimicking other diseases, the imaging can also present ambiguously. Mammography findings can include an ill-defined density with speculated margins along with associated overlying skin thickening (*Figure 2*) (56,57). On ultrasound, IGM displays abscess formation with tubular extensions or hypoechoic mass (*Figure 3A*), with or without enlarged lymph nodes (*Figure 3B*) with mild concentric cortical thickening (3,56,57). Magnetic Resonance Imaging (MRI) shows IGM as one or many masses with a ring or nodular enhancement (*Figure 4*) (57). Since IGM is a chronic disease that needs monitoring for a significant amount of time, MRI's can help evaluate the extent of the disease at presentation as well as monitor progression following the reduction and resolution of lesions with time (9).

Biopsies

IGM is confirmed with specific histopathological findings obtained from a core needle biopsy of the abscess wall. The hallmark pathological finding of IGM is the presence of multinucleated giant cells, plasma cells, polymorphonuclear leukocytes, lymphocytes, and occasionally sterile microabscesses (*Figure 5*) (3,4,31,56,58). A core needle biopsy is preferred over an excisional biopsy or fine-needle

Table 1 Comprehensive summary of high-impact treatment publications

Type of treatment	Authors	Journal	Year	Total number of subjects	Type of study	Recurrence rate (n, %)	Treatment modalities compared	Findings and recommendations
Observation	Pandey *et al.* (5)	*The Breast*	2014	49	Prospective case series	0 (0.0%)	Compared patients with IGM to observation, surgery, and steroid therapy	Recommended observational approach for painless cases; for painful cases, recommended against surgical treatment, favoring steroids
	Ma *et al.* (11)	*Breast Care*	2020	970	Systemic review and meta-analysis	N/A	Reviewed 21 studies that compared surgical excision, steroids, abscess drainage, antibiotics, and observation	Concluded that observation for early IGM patients is beneficial
	Bouton *et al.* (12)	*The American J of Surg*	2015	37	Retrospective chart review	3 (11.1%)	Compared antibiotic treatment, drainage, excision, and observation	Proposed that IGM is a self-limited condition which will resolve spontaneously without treatment
	Mahlab-Guri *et al.* (13)	*IMAJ*	2015	17	Case series	1 (25.0%)	Compared oral steroids to oral steroids plus MTX and excision	The recommended treatment of choice is observation; corticosteroids recommended in severe cases
	Hur *et al.* (14)	*JKSS*	2013	50	Retrospective chart review	1 (12.5%)	Five treatment groups: observation, antibiotics, steroid, drainage, and surgical excision	Concluded that observation is recommended when lesions were small and symptoms were mild
	Davis *et al.* (15)	*Surgery*	2019	120	Retrospective chart review	19 (16.6%)	Analyzed observation only	Recommended observation; with resolution occurring at an average of 5 months
Surgery	Yabanoglu *et al.* (16)	*The Breast*	2015	77	Comparative study	0 (0.0%)	Compared steroids and surgical excision	Wide surgical excision was the preferred approach for treating patients with IGM because of the low recurrence rate
	Alrayes *et al.* (17)	*The Breast*	2019	29	Retrospective chart review	0 (0.0%)	Surgical excision only	Authors concluded that surgical excision is recommended for the treatment of IGM
	Korkut *et al.* (18)	*Eurasian J Med*	2015	73	Retrospective chart review	4 (11.1%)	Compared incision and drainage, surgical excision, and corticosteroids	Surgical excision is recommended for IGM resolution; corticosteroids recommended in select patients
	Hur *et al.* (14)	*JKSS*	2013	50	Retrospective chart review	1 (8.3%)	Compared five treatment method groups: observation, antibiotics, steroid, drainage, and surgical excision	Concluded that surgery was best treatment modality when a lesion was determined to be mass forming or a localized abscess due to fast recovery and high success rate
	Erozgen *et al.* (19)	*Breast Cancer Res Treat*	2010	25	Retrospective chart review	N/A	Compared oral steroids and surgical excision	Authors proposed that surgical treatment is the first line treatment due to corticosteroid therapy having extensive complications
	Kok *et al.* (20)	*Surgeon*	2010	43	Retrospective cohort study	10 (25%)	Compared surgical excision and corticosteroids	Recommended treatment with complete surgical excision and drainage as first-line therapy
	Yau *et al.* (21)	*Ann Plast Surg*	2010	31	Retrospective chart review	1 (3.2%)	Compared surgical excision and antibiotics	Concluded surgical intervention as an effective method for treating IGM
Oral steroids	Deng *et al.* (22)	*J of Clin Pathology*	2017	65	Retrospective case report	12 (18.5%)	Oral corticosteroids only	Authors concluded that an effective treatment option is corticosteroids after removal of the lesion using the Mammotome biopsy system
	Cetin *et al.* (23)	*World J Surg*	2019	124	RCT	20.70%	Compared the different steroid administration modalities of topical, systemic, and topical plus systemic	Concluded that oral, systemic steroids are 80% effective for complete response with 20% recurrence rate
	Mahmodlou *et al.* (24)	*Electron Physician*	2017	48	Retrospective cohort study	3 (6.25%)	Oral corticosteroids only	Authors concluded that steroid therapy is an effective treatment modality for IGM
	Aghajanzadeh *et al.* (25)	*The Breast*	2015	206	Retrospective chart review	11 (5.5%)	Compared the treatments of surgical excision, oral steroids, steroids plus methotrexate, steroids plus bromocriptine, and surgery plus steroids plus antibiotics	Recommended oral corticosteroids as the first line of treatment
	Pandey *et al.* (5)	*The Breast*	2014	49	Observational prospective cohort study	9 (20.5%)	Compared subjects with IGM to observation, surgery, and steroid therapy	Authors recommended steroid therapy as an effective non-surgical option
	Montazer *et al.* (26)	*Asian Pac J Cancer Prev,*	2020	30	RCT	N/A	Contrasted high and low dose corticosteroids	Concluded that high dose prednisolone is more beneficial than low dose prednisolone due to having a higher success rate with lower recurrence; could reduce the need for surgery
	Mizrakli *et al.* (27)	*Surg Today*	2015	49	Retrospective chart review	N/A	Compared oral corticosteroids, antibiotic therapy, and surgical excision	Authors concluded that systemic corticosteroids are an appropriate treatment option for IGM
	Shin *et al.* (28)	*BMC Women's Health*	2017	34	Retrospective chart review	5 (25.0%)	Compared wide excision, corticosteroids, and abscess drainage	Recommended first line treatment should be steroid therapy with or without abscess drainage
Oral steroids + surgical management	Wang *et al.* (29)	*J of Invest Surg*	2019	200	Retrospective chart review	8 (5.1%)	Compared steroid therapy alone to surgical excision after steroid therapy	Authors concluded that surgery after steroid therapy is a more satisfactory treatment for IGM than steroid therapy alone
	Akcan *et al.* (30)	*Breast Care*	2014	74	Retrospective chart review	0 (0.0%)	Analyzed surgical excision with or without oral corticosteroids	Recommended systemic steroid therapy with surgical resection as first-line treatment
	Oran *et al.* (31)	*The Breast*	2013	46	Retrospective chart review	0 (0.0%)	Compared surgical excision, steroid therapy, and steroid therapy plus surgical excision	Authors concluded that surgical excision plus steroid therapy is first line management for recurrence

Table 1 (*continued*)

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Type of treatment	Authors	Journal	Year	Total number of subjects	Type of study	Recurrence rate (n, %)	Treatment modalities compared	Findings and recommendations
	Gurleyik *et al.* (32)	*J Breast Cancer*	2012	19	Retrospective chart review	1 (5.2%)	Compared oral corticosteroids and consecutive surgical excision after follow-up	Recommended the first line treatment of IGM is corticosteroids followed by consecutive surgical excision of the remaining lesions
	Karanlik *et al.* (33)	*Breast Care (Basel)*	2014	60	Prospective, non-randomized observational study	0 (0.0%)	Compared low-dose oral corticosteroid therapy alone to low-dose corticosteroid therapy followed by surgery	Concluded that surgical excision after steroid therapy is more advantageous treatment option than steroid therapy alone
Oral steroids + methotrexate	Sheybani *et al.* (34)	*The American College of Obstetricians and Gynecologists*	2015	22	Prospective cohort study	N/A	Compared oral steroids to oral steroids plus methotrexate	Concluded the treatment of choice is corticosteroids and methotrexate, with or without surgery
	Aghajanzadeh *et al.* (25)	*The Breast*	2015	206	Retrospective chart review	16 (28.6%)	Compared the treatments of surgical excision, oral steroids, steroids plus methotrexate, steroids plus bromocriptine, and surgery plus steroids and antibiotics	Authors recommended oral steroids plus methotrexate when patient is prone to a recurrence
	Kim *et al.* (35)	*ANZ J. Surg*	2003	5	Case reports	0 (0.0%)	Analyzed methotrexate and corticosteroid usage in surgical-resistant cases	Recommended a low weekly oral dose of methotrexate plus corticosteroids in surgical-resistant cases
Topical steroids	Altintoprak *et al.* (36)	*World Journal of Surgery*	2015	47	Retrospective chart review	3 (10.7%)	Analyzed topical steroids only	Concluded that topical steroids are a recommended treatment modality for IGM characterized by skin changes and the benefit of no steroid side effects
	Altintoprak *et al.* (37)	*Korean J Intern Med*	2011	1	Case report	0 (0.0%)	Analyzed topical steroid usage with a low dose oral steroid	Authors recommend topical steroids for IGM management
	Cetin *et al.* (23)	*World J Surg*	2019	124	RCT	5 (14.7%)	Compared the different steroid administration modalities of topical, systemic, and topical plus systemic	Concluded that topical steroids are first line treatment due to the decrease in side effects
	Gunduz *et al.* (38)	*The Breast*	2014	11	Case report	2 (18.2%)	Analyzed topical steroids only	Authors concluded topical steroids are an effective therapeutic approach
Steroid injections	Tang *et al.* (39)	*Journal of Surgical Research*	2020	49	Retrospective cohort study	0 (0.0%)	Compared the treatment methods of observation, steroid injection, and surgical resection	Authors concluded that intralesional steroid injection is an effective treatment option
	Kim *et al.* (40)	*J of Surgical Ultrasound*	2016	15	Retrospective cohort study	0 (0.0%)	Authors compared steroid injections with or without oral steroid administration	Intralesional steroid injection of Triamcinolone is an effective treatment modality for IGM
	Alper *et al.* (41)	*The Breast*	2020	28	Prospective cohort study	0 (0.0%)	Analyzed steroid injections only	Injection of steroids for the treatment of IGM is an effective method with minimal complications
	Munot *et al.* (42)	*European Journal of Surgical Oncology*	2012	4	Case reports	0 (0.0%)	Analyzed steroid injections only	Authors recommend injection of steroids into the breast cavity; all patients had a complete clinical and radiological response with no side effects
Methotrexate and other agents	Raj *et al.* (43)	*Rheumatology*	2004	3	Case reports	N/A	Compared the treatment modalities of methotrexate plus corticosteroids and methotrexate plus azathioprine	Recommended the use of methotrexate with azathioprine without long-term steroids use to avoid steroid side effects
	Wang *et al.* (44)	*The Breast*	2019	1	Case reports	0 (0%)	Investigated the treatment method of methotrexate plus etanercept	IGM was successfully treated with etanercept combined with methotrexate
	Schmajuk *et al.* (45)	*J Rheumato*	2009	2	Case reports	0 (0%)	Analyzed the treatment of methotrexate alone	Authors recommend treatment utilizing methotrexate as a solo therapy
	Farouk *et al.* (46)	*World J Surg*	2017	30	Prospective case report	0 (0%)	Examined Rifampicin as a solo medical therapy for IGM	Concluded that Rifampicin is an effective solo medical therapy for IGM, can be used as an alternative to corticosteroids and surgery
	Akbulut *et al.* (47)	*Breast J.*	2011	108	Case reports	2 (12.5%)	Investigated methotrexate plus corticosteroids as a treatment regimen	Methotrexate can prevent complications in IGM cases without steroid side effects
	Steuer *et al.* (48)	*JAMA Dermatology*	2020	32	Case reports	N/A	Compared antibiotics and antibiotics plus methotrexate	Authors concluded first line IGM treatment is doxycycline twice daily followed by the second line treatment being methotrexate
	Haddad *et al.* (49)	*The Breast*	2020	17	Retrospective cohort study	3 (17.6%)	Analyzed methotrexate only	MTX monotherapy is beneficial for the treatment of IGM
	Postolova *et al.* (50)	*J Rheumatol*	2020	19	Case reports	3 (15.8%)	Analyzed the usage of methotrexate after failed treatment with antibiotics, prednisone, and surgical intervention	Authors recommend methotrexate for patients who failed treatment with antibiotics, prednisone, and surgical intervention
Comparative studies	Azizi *et al.* (51)	*The Breast*	2020	474	Retrospective cohort study	N/A	Compared patients in four groups: medical treatment only, surgical treatment only, a combination of medical and surgical treatment, and no treatment (self-resolving)	Concluded that the most common treatment was medical therapy

Table 1 (*continued*)

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Type of treatment	Authors	Journal	Year	Total number of subjects	Type of study	Recurrence rate (n, %)	Treatment modalities compared	Findings and recommendations
	Wang *et al.* (29)	*J of Invest Surg*	2019	200	Retrospective chart review	N/A	Compared surgery after steroid therapy and steroid therapy alone	Authors concluded that surgery after steroid therapy is a more satisfactory treatment for IGM than steroid therapy alone
	Ma *et al.* (11)	*Breast Care*	2020	970	Systemic review and meta-analysis	N/A	Reviewed 21 studies that compared surgical excision, steroids, abscess drainage, antibiotics, and observation	Recommended observation for early IGM patients
	Steuer *et al.* (48)	*JAMA Dermatology*	2020	32	Case reports	N/A	Analyzed antibiotics and methotrexate	Authors concluded first line IGM treatment is doxycycline twice daily followed by the second line treatment being methotrexate
	Cetin *et al.* (23)	*World J Surg*	2019	124	RCT	N/A	Compared different steroid administration modalities of topical, systemic, and topical plus systemic	Concluded that topical steroids are first line treatment due to the decreased side effects
	Atak *et al.* (52)	*Breast Dis.*	2015	40	Retrospective chart review	N/A	Authors compared the treatment methods of antibiotics and anti-inflammatory agents, steroids, abscess drainage, and surgical excision	Concluded that surgical excision is the best treatment modality for IGM
	Akcan *et al.* (30)	*Breast Care*	2014	74	Retrospective chart review	N/A	Compared surgical excision with or without oral corticosteroids	Authors recommend systemic steroid therapy with surgical resection as first-line treatment
	Oran *et al.* (31)	*The Breast*	2013	46	Retrospective chart review	N/A	Three different treatment modalities were examined: surgical excision, steroid therapy, and steroid therapy plus surgical excision	Authors concluded that surgical excision or steroid therapy is first line
	Hur *et al.* (14)	*JKSS*	2013	50	Retrospective chart review	N/A	Five treatment method groups: observation, antibiotics, steroid, drainage, and surgical excision	Concluded that surgery be best treatment modality when a lesion is determined to be mass forming or localized as an abscess due to fast recovery and high success rate
	Kayahan *et al.* (53)	*Breast Care*	2012	31	Retrospective cohort study	N/A	Analyzed the treatment methods of surgical excision. Abscess drainage, or steroid therapy	Authors concluded that excision was a superior treatment modality compared to steroid therapy by providing less complications and faster healing
	Sheybani *et al.* (34)	*The American College of Obstetricians and Gynecologists*	2015	22	Prospective cohort study	N/A	Compared oral steroids to oral steroids plus methotrexate	Concluded the treatment of choice is corticosteroids and methotrexate, with or without surgery
	Pandey *et al.* (5)	*The Breast*	2014	49	Prospective case series	N/A	Compared the treatment modalities of observation, surgery, and steroid therapy	Concluded that the majority of women did not need surgical treatment; recommended observation for painless cases and steroid therapy as an effective nonsurgical option
	Karanlik *et al.* (33)	*Breast Care (Basel)*	2014	60	Prospective, non-randomized observational study	N/A	Analyzed low-dose oral corticosteroid therapy alone to low-dose corticosteroid therapy followed by surgery	Concluded that surgical excision after steroid therapy is more advantageous treatment option than steroid therapy alone
	Aghajanzadeh *et al.* (25)	*The Breast*	2015	206	Retrospective chart review	N/A	Compared the treatments of surgical excision, oral steroids, steroids plus methotrexate, steroids plus bromocriptine, and surgery plus steroids plus antibiotics	Authors recommended oral corticosteroids as the first line of treatment
	Tang *et al.* (39)	*Journal of Surgical Research*	2020	49	Retrospective cohort study	N/A	Compared the treatment modalities of observation, steroid injections, and surgical excision	Authors concluded that intralesional steroid injection is an effective treatment; surgical resection is not necessary for most patients
	Yabanoglu *et al.* (16)	*The Breast*	2015	77	Comparative study	N/A	Authors compared conservative management (steroids) *vs.* surgical excision	Found that wide surgical excision is the preferred approach for treating patients with IGM because of the low recurrence rate
	Shin *et al.* (28)	*BMC Women's Health*	2017	34	Retrospective chart review	N/A	Compared the different treatment modalities of wide excision, steroids after incision and drainage, and antibiotic therapy	Steroid therapy with or without abscess drainage may be the first choice of treatment; recommended against wide excision

Figure 1 Clinical presentation of IGM in two separate patients.

Figure 2 Mammography imaging demonstrates asymmetric densities mimicking breast carcinoma and enlarged lymph node.

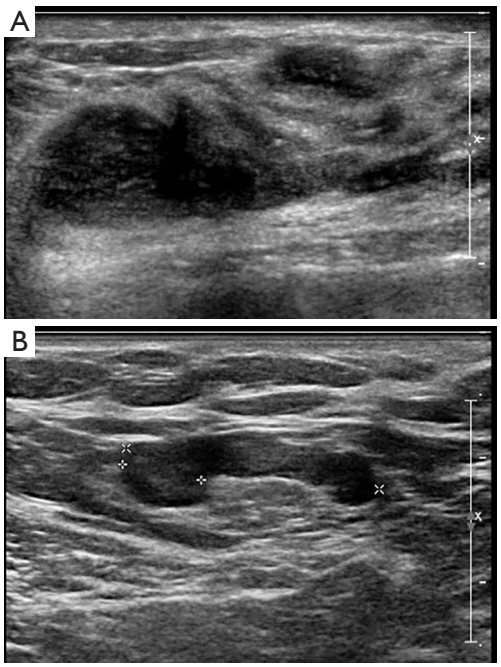

Figure 3 Ultrasound images of IGM. (A) Ultrasound findings of breast parenchyma with ill-defined abscess cavities and (B) ultrasound findings of IGM showcase enlarged axillary lymph node with eccentric cortical thickening.

aspiration (FNA) because it completely characterizes the lesion, is less disfiguring and rules out malignancy (31). If an abscess is present, drainage should occur by FNA and cultures should be obtained to rule out any infectious etiology such as aerobes, anaerobes, fungal infection (periodic acid-Schiff), as well as microorganisms such as Corynebacterium (Gram stain), or acid-fast bacilli (Zeihl-Neelsen) (3,59). Other plausible pathogens should be ruled out at this time including mycobacterial, parasitic, or mycotic origins (1,9,27). Tuberculosis mastitis should also be eliminated from the differential diagnosis through

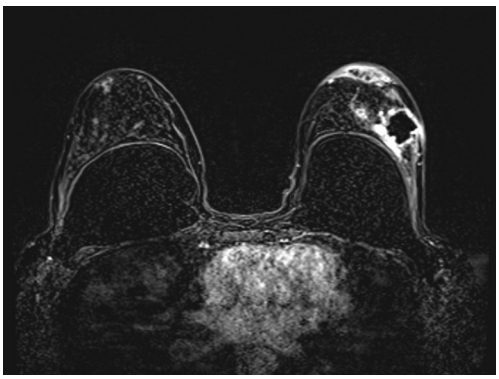

Figure 4 MRI with nodular ring enhancement of the IGM areas in the left breast.

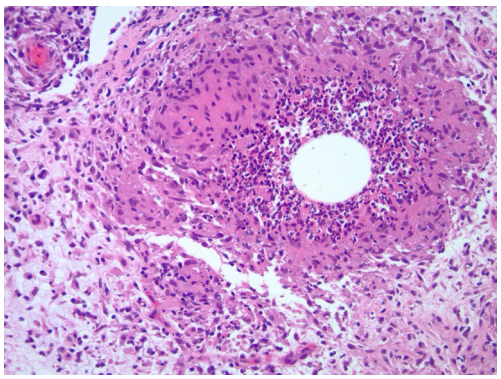

Figure 5 Photomicrograph of tissue specimen shows granulomatous inflammation with non-caseating granulomas and multinucleated giant cells (H and E, ×20).

a purified protein derivative (PPD) serum test, skin test, or chest x-ray in addition to the tissue staining for the acid-fast bacilli. Autoimmune etiologies like sarcoidosis or foreign material should be excluded through blood work examining antinuclear antibody (ANA), rheumatoid factor, C-reactive protein, and alpha-I-antitrypsin (1,9,27).

Etiology

The etiology of IGM remains unclear, although a correlation is well documented with recently pregnant or lactating women (51). Many studies support the hypothesis of an autoimmune component (1,9). Other theories suggest an association of hormonal imbalance, oral contraceptives (31), smoking (60), corynebacterium (28), unknown microbiological agents (8), and α1-antitrypsin deficiency (8) whereas other studies have refuted these associations (8,30). It is speculated that the pathology is from local trauma or changes to the ductal epithelium allowing for luminal secretions to be present in the lobular connective tissue, therefore causing lymphocyte and macrophage migration, triggering a granulomatous response within the breast (9). Further research is needed to isolate the exact mechanism of IGM, which would allow for a more personalized treatment approach.

Treatment

Currently, no standardized treatment for IGM exists. Treatments are decided through analyzing each patient's presentation, the severity of the symptoms, the size of the lesions, the overall health of the patient as well as the surgeon's preferred treatment method. Many treatment algorithms are present throughout the literature, but none have been widely accepted (3,4,27,31,54,55,61). Although a benign disease, effective treatment is necessary to manage the symptoms and prevent the recurrence of the disease. Recurrence and relapse rates for IGM have varied from 20–50% (3,57,62) causing stress for the patient and the treating physician. Importantly and reassuringly, IGM is a self-limiting disease resolving within 2 to 24 months of onset, regardless of the treatment modality used (4,57). A variety of treatment methods have been utilized to relieve the patient's chief complaints such as observation, various forms of steroids, immune modulators and surgical excision. This review will outline each treatment method and give an algorithm up-to-date with the current research. An extensive literature review of IGM treatment modalities is presented (*Table 1*).

Antibiotics and pain management

Since IGM is a disease of exclusion, it is essential upon presentation to rule out any infectious agents while beginning a workup, as bacterial abscesses are more common. Therefore, a bacterial etiology must be before diagnosing IGM. All abscesses should be aspirated or drained followed by broad-spectrum antibiotics during the period of diagnostic evaluation. Acceptable antibiotics include sulfamethoxazole and trimethoprim, amoxicillin/clavulanate (4), doxycycline (48) as well as metronidazole.

For symptomatic pain relief, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Advil) and celecoxib (Celebrex) are the drugs of choice to help with the inflammatory pain that corresponds to the IGM masses (3). Opiates are rarely required for this level of pain

management (3).

Observation

IGM is known to be self-limiting; therefore a more conservative treatment method used is observation of the abscesses with regular clinic examinations (14). Many patients present with an array of symptoms and abscess sizes, but if the symptoms are mild to painless along with small lesions, observation may be the first line of treatment, as it will self-resolve (5,11-13,15). Patients need to be reassured that IGM does resolve, but the time to resolution can average 5 months (15). Once the diagnosis of IGM is confirmed, and infections etiology including Corynebacterium is ruled out, patients do not necessarily need to maintain on long-term antibiotics. However, physicians also need to follow patients during observation to ensure no signs of other opportunistic bacterial infection occur due to the open skin areas.

Surgical treatment

Surgical treatment methods vary from abscess drainage, wide surgical excision, and mastectomy. Although the literature has demonstrated that wide surgical excision has been successful (4,14,16,17,20,30,31,53,63), recurrence rates range from 0% to 50% (16,30,64). When completing a wide excision, the goal is a complete removal of the questionable area including fistula tract, affected skin, with a lesion free margin ranging from 5 to 10 mm (3,30).

Much debate still exists about the benefits of surgical excision. Since newer treatment methods have evolved within the last ten years, the utilization of surgical intervention as a first-line therapy has reduced (5,13,28,29). If the patient has a single small lesion, surgical excision could be considered but high recurrence rates are likely. Additionally, there are side effects to surgical excision such as poor cosmetic results, extensive scarring, as well as delays in both would healing and fistula formation (28,32,33). Although mastectomy in severe cases has been described, so has recurrence after mastectomy, so this approach is not optimal.

Steroids

The utilization of steroids for IGM was first published in 1980 (65) and remains today the first-line treatment. Steroids are administered in three different ways: oral, topical, or injections.

Oral steroids are still commonly used and have documented success rates up to 80% (22), but still have the chance for relapse. The prescribed range for IGM is 10–60 mg/day of prednisone or 30–60 mg/day of prednisolone (27) with a gradual taper over the following weeks to months (30). Additional treatment options include 16 mg prednisolone twice a day for two weeks (36) or 1 mg/kg of prednisolone for three weeks (3). Unfortunately, the high rates of IGM resolution with use of oral steroids come at a price: systemic side effects. The side effects range from glucose intolerance and insomnia to cushingoid features. In addition, patients can potentially relapse when discontinuing treatment a few months later (3), however an extra course of steroids can be prescribed when that occurs.

Clinicians prescribe topical steroids as a popular alternative to oral steroids due to having less systemic side effects. Case reports all show positive results and endorse the usage of topical steroids (23,36-38). The pharmacological agent of choice is prednisolone ointment (0.125%) twice a day for 1–3 months (23,36). The recurrence rates for topical steroid use range from 10–18% (23,36-38). In a study published by Cetin *et al.*, the steroid administration routes of topical, systemic, and topical plus systemic steroids were examined and topical steroids had the best results with the lowest recurrence rate of 14.7% (23).

Steroid injections directly into the IGM lesions are the newest advancements in the treatment of IGM and given the reported effectiveness and decreased recurrence rates (39-42), should be considered as the first-line therapy for any newly presenting IGM patient. Steroid injections are based on the well-established techniques for treating arthritic diseases. Steroid injections for IGM were first described in 2012 with a small sample size, but a very low recurrence rate (42). Many newer studies have reported no recurrences with steroid injections along with a faster resolution time compared to other treatment modalities (39-42). The prescribed dose is Kenalog-40 (triamcinolone 40 mg/mL) ranging in volume from 2–4 mL (80–160 mg) mixed with lidocaine as a local anesthetic (39). The injection into the IGM lesion(s) is completed under ultrasound guidance and repeated every 1–2 weeks until resolution. A potential complication of this treatment modality is skin atrophy (39), but otherwise it holds a great deal of promise as a minimally invasive first-line treatment approach.

Immune modulators

Methotrexate (MTX), an immunosuppressive agent, has also been successful in the treatment of IGM. This method is an alternate therapeutic option for any patient who is unresponsive to steroid therapy (3,49). MTX can be given

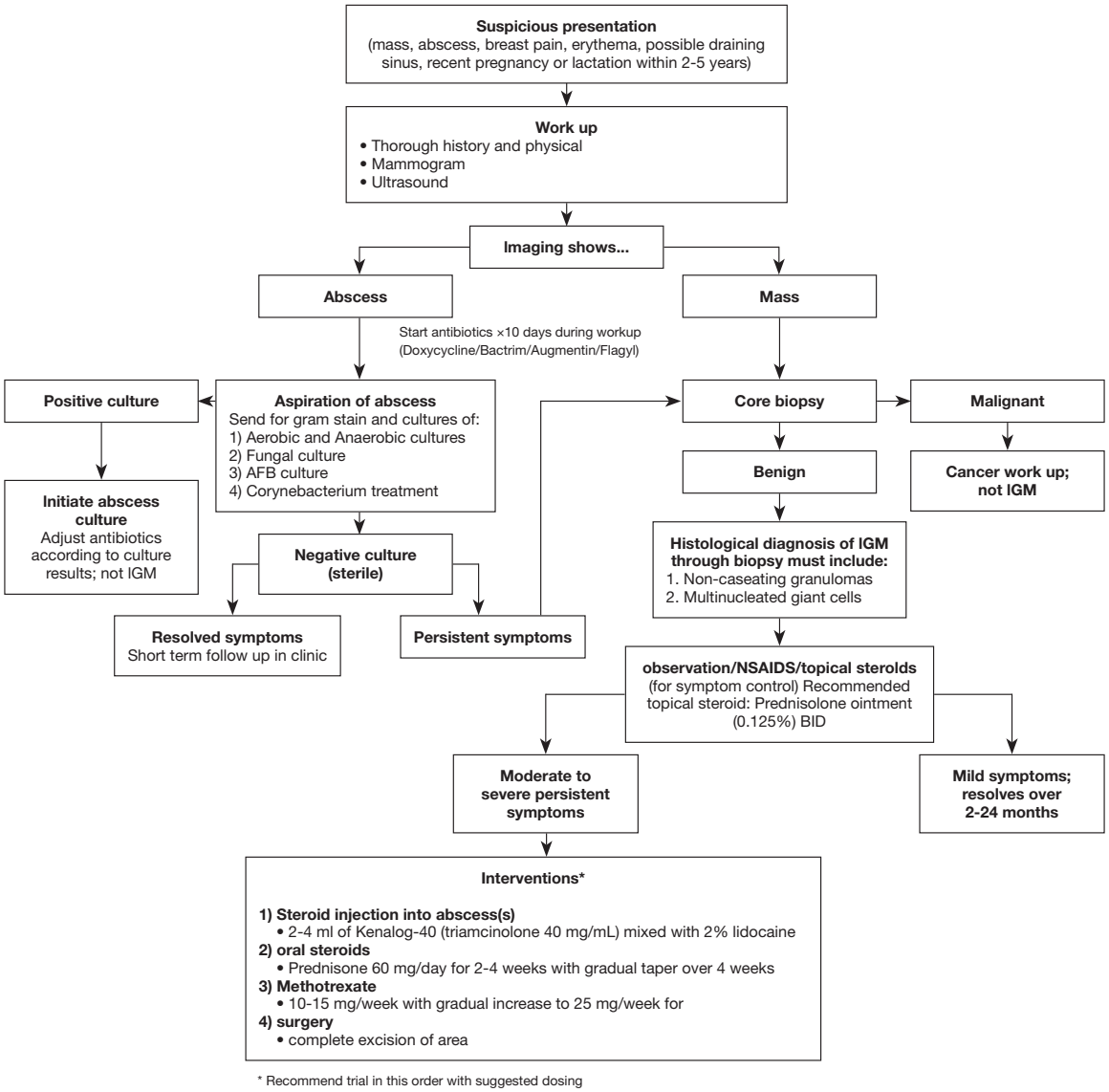

Figure 6 Diagnosis and treatment algorithm for idiopathic granulomatous mastitis.

with other treatment modalities such as steroids (25), but a recent study has shown promising effects of this treatment modality on its own demonstrating that by 15 months of treatment, 94% of patients had disease improvement along with 75% achieving remission (50). The pharmacological dosing for MTX is 10–15 mg/week and increasing to 20–25 mg/week given either orally or subcutaneously based on clinical response (50). Reported adverse effects range from elevated liver enzymes and hair loss to more mild symptoms such as nausea, decreased appetite, and mild headaches (41,50).

In the situation where the IGM lesions are not responding (or progressing) and MTX is being considered, consultation to rheumatology and infectious disease is recommended.

Studies comparing different treatment modalities

A comprehensive search was conducted over all the published literature for IGM examining the many detailed treatment studies. A comprehensive table (*Table 1*) is provided of the most significant treatment studies along with all comparative studies to date (full review: https://cdn.amegroups.cn/static/public/ABS-2020-BBD-03-supplementary.xlsx). Based on review of these comparisons,

a flow sheet reviewing work-up and management options has been complied as a reference (*Figure 6*).

Discussion

Many significant advancements in the treatment modalities for IGM have occurred within the last ten years. Still, randomized controlled trials are needed to determine which treatment modality is superior. Promising studies exist for each treatment modality, but an accurate conclusion about the best treatment modality cannot be drawn without a randomized control trial. As highlighted in the spreadsheet of treatment studies (*Table 1*), the recurrence rates for steroid injections into the abscess cavity are remarkably low in the published literature. Due to these low rates, steroid injections hold great promise and; therefore, we recommend it as the preferred treatment modality due to the high success, minimal systemic side effects and low recurrence rates.

Our comprehensive treatment algorithm (*Figure 6*) serves to provide a road map for any clinician to diagnose and treat IGM successfully. A thorough workup is critical to exclude all other differential diagnoses to detect IGM accurately. From our literature review, a comprehensive treatment plan is presented to help guide any clinician who encounters IGM in their clinic. Patients presenting with a mass suspicious for IGM should have diagnostic imaging. If an abscess is present, aspiration should be performed, sent for cultures and prophylactic antibiotics initiated. If the abscess cultures are sterile or there is a mass on imaging, a core biopsy should be performed to obtain a tissue diagnosis to confirm IGM. Based on the literature review, the authors recommend observation as the first line treatment with attention to symptom management. This includes non-steroidal anti-inflammatory medication for the pain and topic steroids to the affected area. If the symptoms worsen, use of injectable steroids into the abscess cavity can facility resolution of the breast abscesses. If no improvement or a large area of the breast is involved, oral steroids can be utilized. In refractory cases, methotrexate can be used. Surgical excision should be used sparingly, with mastectomy as a very last resort.

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Footnote

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