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Spontaneous, idiopathic granulomatous mastitis in a pregnant patient: A case report and review of the literature

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ABSTRACT

Idiopathic granulomatous mastitis is a rare breast condition of unclear etiology. Its course is often rapidly progressive, slow to resolve, and can have a high rate of recurrence. Clinical presentation can mimic breast abscess, infectious mastitis, and carcinoma of the breast, generating a diagnostic challenge. Histopathological analysis is required to make the diagnosis after common conditions are excluded. There is no standard treatment, however surgical excision, steroid treatment, and observation are commonly reported approaches. Here, we describe a complex case of a multiparous patient presenting with idiopathic granulomatous mastitis at 32 weeks gestation. In this review, we highlight the importance of collaboration amongst a multidisciplinary team for effective diagnosis and treatment. We discuss the use of oral corticosteroids in the antenatal period and illustrate the patient support required to both facilitate successful breastfeeding in the postpartum period and promote recovery.

1. Introduction

Mastitis, or inflammation of the breast, may be categorized into lactational and non-lactational types [1]. Lactational or puerperal mastitis, is by far the most common form, affecting up to 30 % of breastfeeding women. It generally occurs when breaks in skin and prolonged engorgement of milk ducts support bacterial growth [1]. The resultant infection leads to symptoms of pain, swelling, erythema, and fever that can occur at any point during lactation. Cases are most common within the first 3 weeks postpartum [1]; antenatal lactational mastitis is rare. Non-lactational mastitides include periductal mastitis and idiopathic granulomatous mastitis (IGM) [1]. Periductal mastitis affects 5–9% of women internationally, is often of infectious origin, and is almost exclusively associated with tobacco use wherein the ducts are either directly or indirectly damaged by smoke exposure [1,2]. Alternatively, IGM is a rare, spontaneously arising, non-infectious, and non-neoplastic inflammatory condition of unclear etiology. When uncommon medical conditions arise during pregnancy, they are often complicated by increased apprehension on the part of both patient and care provider in terms of the potential impacts diagnosis and treatment may have on the fetus.

The primary presentation of IGM is a firm breast mass associated with intense local pain and subsequent skin ulcerations and

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fistulae [3,4]. It often progresses rapidly and is slow to resolve [3]. First documented in 1972 as a condition mimicking carcinoma [5], IGM presents a diagnostic dilemma as it imitates several other breast pathologies (lactational/infectious mastitis, abscess, and malignancy). While this condition is primarily associated with pregnancy, it has also been reported outside of the parous age range [6,7]. Here, we describe a case of IGM presenting antenatally in a multiparous patient. One goal in presenting this case is to highlight a rare condition for obstetrical care providers who do not commonly have extensive experience with breast conditions presenting in pregnancy. Additionally, we emphasize the importance of a multidisciplinary approach to the management of IGM throughout both pregnancy and the postpartum period, meeting the needs of both the parturient and the breastfeeding dyad.

2. Case presentation

A 32-year-old G3P2 reported to her midwife at 32 weeks gestation. Her obstetrical history was relevant for two prior Caesarean sections (CS). The current pregnancy had been uncomplicated apart from gestational anaemia -managed with iron supplementation - with no prior history of breast disease or infection. The patient had successfully breastfed two children in the past. At this visit she complained of left breast swelling, erythema, and pain, which was confirmed via physical exam by both the midwife and the consulting obstetrician. A breast ultrasound (US) was completed which found a single area measuring $1.2 \times 4.2 \times 3$cm suggestive of mastitis. The patient was discharged with a course of cloxacillin.

2.1. Investigations

Within five days of initiating antibiotics, the patient reported persisting symptoms. At this time, cloxacillin was discontinued and a substitution was made for cephalexin. Within 48 hours of initiating this treatment, the patient reported new symptoms including myalgias, rigors, and an aggravation of breast symptoms. A physical exam found the patient to be afebrile but with a left breast mass 10cm in diameter with significant induration and tenderness. Intravenous (IV) antibiotic treatment was initiated (2g cefazolin, every 8 hours). Due to the persistence of symptoms despite systemic treatment, a multi-disciplinary team was formed which included Midwifery, Obstetrics, Infectious Disease, Internal Medicine, Interventional Radiology, and a General Surgeon with a practice focus in IGM.

On examination, multiple palpable masses were found along the lateral aspect of the left breast; the nipple appeared within normal limits with no identifiable discharge or inflammation. The contralateral breast was examined to be normal. A repeat US, blood cultures and a core biopsy of the left breast were completed. IV antibiotic treatment did not lead to any improvement. Fetal status was monitored with daily non-stress tests and remained reassuring.

2.2. Diagnosis

Blood cultures returned negative and repeat US found multiple hypoechoic and hyperemic regions corresponding to a 15cm region of thickening within the left breast. Pathological examination of the biopsy specimen noted granulomatous inflammation with histiocytes, multinucleated giant cells, and a mixed inflammatory reaction. All microbiological stains were negative. These results supported a non-infectious and non-neoplastic cause, isolating the diagnosis of granulomatous mastitis.

2.3. Treatment

An initial treatment plan was made consisting of high dose oral steroids (prednisone, 20mg daily) with monthly reevaluation of treatment response and steroid dose. Due to concerns regarding the risk of preterm labour with steroid use (particularly with the history of two prior CS), the obstetrical team was uncomfortable initiating steroid treatment before delivery. The decision was made to treat the patient after delivery and an elective repeat CS was arranged for 39 weeks gestation.

Due to the patient's significant discomfort, and the potentially long treatment period soon to be complicated by lactation, she was anxious to begin treatment prior to delivery. Ultimately, following further consultation with our surgical expert, 40mg prednisone daily was initiated at 36 weeks 5 days gestation.

2.4. Outcome & follow-up

A healthy baby boy was delivered via an uncomplicated elective CS at 38 weeks 6 days. At this time (following 2 weeks of prednisone treatment) the patient reported reduced breast pain, however the size of the mass was unchanged. Post operatively, ibuprofen and acetaminophen were used for pain management with prednisone taken concurrently.

Due to the underlying physiology of lactation and the severity of the patient's symptoms, feeding from the left breast was discouraged. The patient opted to breastfeed from the right breast only, and to supplement the infant's nutritional needs with formula.

At 6 weeks postpartum the prednisone dose was reduced to 30mg/day with the patient reporting an improvement in her condition. With continued response, the dose was tapered to 20mg approximately 6 weeks later. Further dose reductions by 5mg occurred until symptoms resolved, and treatment was no longer required. The total steroid treatment time was 21 months.

At the conclusion of steroid treatment, a follow-up mammogram showed scattered areas of fibroglandular density and a galactocele measuring approximately 2cm. This is a normal radiologic finding consistent with prior breastfeeding. The patient was discharged from surgical follow-up. At the time of this writing, the patient has had another child and reports no recurrence of IGM.

3. Discussion

The goals of this case report were to illustrate a very rare breast condition and address a gap in the obstetric literature. Obstetrical care providers are not often called upon to manage breast conditions, as antenatal *infectious* mastitis is uncommon and *non-infectious* breast conditions such as IGM are rare. Thus, it can be difficult to know where to seek guidance when such conditions affect our patient population.

While not within the sphere of obstetrics *per se*, peri-gravidic mammary pathologies are relatively common. Midwives, family doctors, and obstetricians should be familiar with these conditions such that they feel comfortable offering advice to pregnant patients and hold an appropriate degree of suspicion concerning lesions. For example, while uncommon, infectious mastitis does occur antenatally. Recognition of the signs and symptoms of mastitis, and knowledge of the predominant causative microbes will guide treatment [1]. In addition, while only 1:1000 pregnancies are complicated by cancer, breast cancer is the form most frequently diagnosed in these patients [8]. Given that the pregnant population is usually a younger demographic than those often diagnosed with breast cancer [9], and that the physiological alterations of the breast associated with pregnancy can mimic the signs of breast malignancy (e.g., nipple discharge, hypertrophy, increased density of the tissue) [8], a diagnosis can be delayed. It is strongly advised that masses persisting for more than two weeks during pregnancy be investigated [8]. 80 % of those lesions will be benign [8], and such investigations allow for the diagnosis and appropriate treatment of rarer conditions, such as IGM.

Currently, the pathological etiology of IGM is unclear. Associations have been made with endocrine conditions such as hyperprolactinemia [10] or the hormonal variations of pregnancy [11], smoking, oral contraceptive pill use, α-1 antitrypsin deficiency [12,13], and ethnicity [14]. An etiopathogenesis of autoimmunity has received recent focus due to an association of an autoimmune cytokine profile with IGM [15], the concentrated presence of T cells in lobules destroyed by granulomas [16,17], and the clinical response of IGM to steroid treatment [17].

The lack of clarity around the etiology of IGM affects its diagnosis and treatment. As the clinical presentation of IGM mimics several more common conditions, a finding of IGM represents a diagnosis of exclusion after breast infections, other granulomatous conditions, and rarely, invasive carcinoma are eliminated [4]. While imaging findings for IGM have been described, the results are variable and of limited utility [18]. Tissue sampling and empirical response to therapy is the most effective treatment approach, with analysis of a tissue biopsy obtained through interventional radiology often most helpful in making the diagnosis. Use of a larger core biopsy needle permits the collection of increased sample-material with a single needle insertion, allowing for a more accurate histological diagnosis [19]. Histological findings are characterized by multiple non-caseating granulomas and inflammatory infiltration of neutrophils, eosinophils, giant cells, plasma cells, and lymphocytes [5,20].

There is currently no consensus on a standard treatment for IGM. In addition, due to lack of familiarity, management plans may be suboptimal [21]. Treatments including expectant management, antibiotics, corticosteroids (or other anti-inflammatories), and surgical excision have all been cited [3,4,7,21,22]. As infectious agents must be excluded as a component of IGM diagnosis, it follows that antibiotic treatment is ineffective beyond prophylaxis during invasive diagnostic procedures. While expectant management has been used and spontaneous resolution hypothesized as the natural conclusion of IGM [7], this approach tends only to be appropriate for mild manifestations of the disease, wherein patients do not experience pain.

Steroid treatment and surgical excision are the most frequently cited treatments. Surgery by wide local excision or partial/complete mastectomy was considered the first-line therapy for many years. However, such treatment is associated with a high recurrence rate of lesions, the need for repeated operations [5,16,23,24], delayed wound healing, and disfigurement [7]. It has been estimated that 50 % of reported IGM cases are initially mistaken for carcinoma. Such diagnostic confusion has led to underreporting of IGM and heightened patient anxiety. This legacy has also generated a predisposition toward surgical intervention including unnecessary mastectomies [6]. Surgical options should be considered a route of last resort.

With respect to steroid treatment, glucocorticoids, particularly prednisone, are used most often. Documented doses of oral corticosteroids range from 10 to 60mg/day [3,25–28]. While the treatment period can be lengthy [a median of 159 days has been reported [29]], oral steroid therapy is demonstrated to be effective. In addition to oral therapies, intralesional injections have been reported with promising results [30,31].

Prolonged steroid use is not universally effective and can result in side effects such as Cushing's syndrome, opportunistic infections, hypertension and glucose intolerance [26]. The use of pharmacologic agents such as methotrexate have been reported to resolve inflammation whilst avoiding the side effects of steroid use [32,33]. However, as these drugs are contraindicated in pregnancy and lactation, they are not available to the obstetric population as treatment options.

3.1. *Pregnancy & lactation – advice for obstetrical care providers*

IGM is a complex condition that demands collaboration across specialties. Our case demonstrates the added layer of complexity that presents in the gravid patient, wherein there is heightened apprehension on the part of the healthcare team. For those providing obstetrical care, it is advantageous to have an interested team member who can build familiarity and comfort with managing breast conditions. Relationships with radiologists and either general or breast surgeons who may be more acquainted with such diagnoses are also advantageous. Indeed, multidisciplinary teams have been shown to result in improved decision-making [34], and better care and outcomes for patients [35]. In our case, the advocacy of a community-based provider – who was well-integrated into the hospital-based specialist team – was essential to the patient getting care that met her needs. Given the progressively specialized nature of medicine, communication between disciplines is increasingly essential [36].

Overall, IGM requires clinical - not surgical - management and responds well to corticosteroids. Both obstetrical providers and

general surgeons benefit from developing comfort with corticosteroid use in pregnancy. While antenatal steroid use is not innocuous, and careful consideration is warranted, steroids are used during pregnancy to treat a variety of maternal and fetal conditions [37]. Prolonged courses of steroids are often indicated in pregnancy for conditions such as: autoimmune diseases (e.g., rheumatoid arthritis, inflammatory bowel disease, immune thrombocytopenic purpura) and less commonly are used in the management of refractory hyperemesis gravidarum. These drugs need not be avoided or delayed in gravid patients suffering from severe IGM symptoms. Providers can be confident that corticosteroid management of IGM is effective when any fistulae begin to close and edema resolves; doses can then be tapered. For our patient, her 40mg/day dose was gradually reduced with symptom resolution and, after 21 months of treatment, her condition had resolved. Treatment will depend on symptoms, disease extent, and patient factors [38]. Supportive care is a key management consideration as the patient is required to cope with the long-term nature of the illness [3].

With respect to lactation, breastfeeding is compatible with prednisone. With high doses of oral prednisone (>40mg/day) the most conservative management is to wait 4 hours post medication to feed due to theoretical impacts on infant growth and development [39]. This is neither strictly necessary nor supportive of the nutritional needs of the infant and is counter to the initiation of successful lactation. Frequent stimulation (every 2–3 hours) of the hypothalamic-pituitary-axis is required to stimulate and maintain Lactogenesis II and III [40]. Patient education and care supportive of their feeding goals is critical.

Opinions are inconsistent regarding whether the infant should be fed from the IGM affected breast. Physiologically, feeding on the affected side will further stimulate lactation, and potentially engorgement – increasing inflammation – in the already painful breast. It is reasonable for the patient who wishes to breastfeed to feed from one or both breasts, depending on their symptoms. Our patient opted to feed from the unaffected breast only and supplement the infant's nutritional needs with formula.

4. Conclusion

IGM is a rare breast condition that represents a diagnostic and therapeutic dilemma, particularly in the gravid patient. We share the experience reported by others that a diagnosis of exclusion including histopathological analysis was required to identify IGM in our patient. While many obstetrical care providers may be most comfortable with expectant management in the context of pregnancy, it tends not to be feasible due to the severity of the condition. While surgical approaches to IGM have historically been most common, these methods are highly invasive, associated with complications, do not prevent recurrence, and should no longer be considered first-line. We share the expertise of managing IGM with high dose prednisone, a safe and effective option during pregnancy. Our case illustrates how a multidisciplinary approach can facilitate diagnosis, treatment, and a successful breastfeeding experience.

Ethics statements

This case review was approved by the Research Ethics Board of North York General Hospital, with the approval number: #21–0027. The patient provided informed consent for the publication of their anonymised case details.

Data availability statement

The data used are confidential, and not eligible for deposit into a publicly available repository.

CRediT authorship contribution statement

Grace Liu: Investigation, Writing – original draft, Writing – review & editing. **Donna McRitchie:** Investigation, Writing – review & editing. **Elizabeth Russell:** Investigation, Writing – review & editing. **Elizabeth C. Cates:** Conceptualization, Data curation, Investigation, Resources, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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