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Case Report

# Gestational Gigantomastia: Case Report and Review of Treatment Options

**Versha Pleasant[1*], Ellen Chapel[2], Adeyiza Momoh[3], Amanda Manorot[1], Alissa Carver[4]**

[1]Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Michigan, USA

[2]Department of Pathology, University of Michigan, Ann Arbor, Michigan, USA

[3]Department of Plastic Surgery, University of Michigan, Ann Arbor, Michigan, USA

[4]Wilmington Maternal-Fetal Medicine, Wilmington, North Carolina, USA

***Corresponding author**: Versha Pleasant, Department of Obstetrics & Gynecology, University of Michigan, Ann Arbor, Michigan, USA

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## Abstract

Gestational gigantomastia is a rare and devastating condition involving rapid and excessive enlargement of the breast tissue during pregnancy or postpartum. We review the workup, assessment, and care of a patient with gestational gigantomastia with superimposed mastitis. Conservative treatment, medical management, and surgical options should be explored with patients. It is also important for providers to be cognizant of the psychological impact of this condition.

**Keywords:** Gigantomastia; Gestational; Pregnancy; Breast; Macromastia

## Introduction

Gigantomastia (also called macromastia or mammary gigantism) is a rare and devastating condition which involves rapid and excessive enlargement of the mammary tissue. While there have been cases of gigantomastia that occur spontaneously, there are reports of pregnancy-associated gigantomastia (called gestational gigantomastia, gestational macromastia, pregnancy-induced gigantomastia, or gravid macromastia). With gestational gigantomastia, the underlying cause is unclear [1]. While there are some options for conservative management as well as medical therapy, the literature suggests that surgery is the most effective and definitive treatment for many patients [1]. This article discusses a case of gestational gigantomastia with superimposed mastitis and explores various options for clinical management as outlined in Figure 1.

### Case Presentation

A 21-year-old African American gravida 1 para 1 was admitted for severely painful, enlarged breasts on postpartum day 5 after an uncomplicated spontaneous vaginal delivery at 39 weeks and 3 days. The patient stated that breast enlargement began approximately 5 months into her pregnancy, with increasing breast size from her baseline D cup and progressive pain. These symptoms significantly worsened one day after vaginal delivery, with areas of the breasts becoming hard and nodular. There was delayed milk let down and minimal output in attempts to breastfeed. She also noted fever and chills at home. Her medical history was significant for major depressive disorder diagnosed several years prior in which she was started on escitalopram. Family history was significant for a maternal great-aunt with breast cancer at an unknown age and a remote maternal relative with lymphoma at an unknown age. At time of admission, the patient was taking ibuprofen and acetaminophen as needed, topical dapsone and clindamycin for acne, and a daily prenatal vitamin. She had no known drug

allergies. On exam, the patient was tachycardic to 112 beats per minute, blood pressure was 135/81, and temperature was to 101.1 Fahrenheit. BMI was 29 kg/m2. Breasts were notably enlarged with mild bilateral erythema. There was edema and skin dimpling in the dependent inferior areas of both breasts, with the left breast slightly larger than the right. The skin was intact with no ulceration, skin breakdown, or necrosis noted. There was minimal lactation from the right nipple. Physical exam was otherwise unremarkable. Regarding lab work and imaging, the patient had a leukocytosis of 14.0 x $10^9$/L and a lactate of 0.6 mmol/L. Sepsis workup was performed which included negative blood cultures and negative urine culture. Chest X-ray was performed, which was challenging to interpret due to "large body habitus and soft tissues of the chest wall" that obscured view and created increased opacity. The patient was diagnosed with gestational gigantomastia with superimposed mastitis. She was treated initially with cephalexin, then subsequently switched to vancomycin and piperacillin/tazobactam. The concern for malignancy was low due multiple factors including bilateral presentation of symptoms, age, lack of strong family history, and absence of other risk factors. However, bilateral breast ultrasound was performed for further assessment. Breast ultrasound was notable for probably benign findings, specifically bilateral fluid collections posteriorly in the upper central breasts for which there was consideration of therapeutic and diagnostic aspiration. There was severe bilateral skin thickening measuring up to 1.2 cm on the left and superficial hypoechoic masses in the left upper central breast. However, there was no definite drainable fluid pocket. Diffuse heterogeneous echogenicity with dense vascular breast tissue was observed bilaterally, with areas of prominent palpable nodularity. The decision was made to proceed with core needle biopsy of representative target tissue of the left breast to rule out underlying pathology. Ultrasound-guided core biopsy demonstrated benign breast tissue with lactational change (negative for atypia and malignancy).

A Gynecologic Breast Specialist was consulted who recommended skin punch biopsy, breast compression, and consideration of dopamine agonists if lactation increased. The following referrals were recommended: General Surgery for discussion of surgical options, Infectious Disease to evaluate and narrow antibiotics, and Rheumatology to rule out autoimmune disorders. A skin punch biopsy was performed to evaluate an area of skin dimpling at the edge of the left nipple-areolar complex. Pathology demonstrated subtle dermal edema, mild nonspecific perivascular chronic inflammation, and focal angioproliferative changes (Photos 1a-1b). Compression with a breast binder was performed to discourage milk production and to provide the patient with additional support. Dopamine agonist therapy was considered but ultimately not pursued because the patient was early in her postpartum course and milk production was still minimal. Finally, daily clinical breast exams were performed to evaluate the skin for any areas of necrosis. Infectious Disease recommended continuation of the antibiotic regimen. Rheumatology did not recommend further workup due to absence of any other symptoms or history suggestive of autoimmune conditions. General Surgery was consulted, with recommendations against imminent surgical intervention due to the acute infection and continued treatment of underlying mastitis. Referral to Plastic Surgery was suggested for discussion of future surgical options. The patient was discharged on hospital day 5 with normal vitals and in fair condition. She was prescribed a 2-week course of linezolid. She was afebrile by the time of discharge, with a white blood cell count of 6.9 x $10^9$/L. At her 1-week follow up with Infectious Disease, she was noted to be clinically improving on linezolid. Repeat left breast ultrasound was recommended if there were still areas of induration to ensure no mass or abscess. She had a follow up postpartum visit 1 month after hospital discharge. At that time, her score from the Edinburgh Postnatal Depression Scale was 11. She reported that mood was worse in the first 2 weeks postpartum but had since improved. She denied suicidal ideation. Despite this, referral to Social Work was placed. The patient was offered medication for mood but declined (escitalopram was not listed in the patient's active medication list at that time). Two attempts were made by social workers to contact the patient without success. Approximately 1 month later, repeat bilateral breast ultrasound was performed and demonstrated suspicious lesions with "large bilateral masses/conglomerates of masses in the medial aspects of both breasts, corresponding to palpable areas". Right and left ultrasound-guided core biopsies of representative masses demonstrated benign breast tissue with extensive nodular ischemic necrosis, suggestive of infarction (Photo 2a). An adjacent area of viable breast parenchyma in the left breast biopsy was additionally notable for prominent stromal edema (Photo 2b). The sample was also cultured and was negative for fungal elements or leukocytes. Anaerobic culture was notable for rare coagulase negative staphylococcus and rare cutibacterium (Propionibacterium) avidum. The patient was seen 2 months later by Plastic Surgery, and reduction mammoplasty was discussed and offered. The patient's surgery was originally denied insurance coverage but then subsequently approved and scheduled almost 1 year later. In the meantime, the patient underwent bilateral breast ultrasound with benign findings, noting an "overall significant decrease in the size of the biopsy proven benign bilateral breast masses, consistent with an improving inflammatory process and clinical diagnosis of pregnancy related macromastia." However, when the patient was evaluated immediately prior to the scheduled surgery, she was deemed to have lost a significant volume of breast tissue since her prior exam. There was concern that surgery would substantially decrease remaining breast volume and may

compromise the nipple-areolar blood supply. Though surgery was initially deferred, mastopexy is being explored as another option due to persistent symptoms such as significant ptosis and recurrent inframammary rashes.

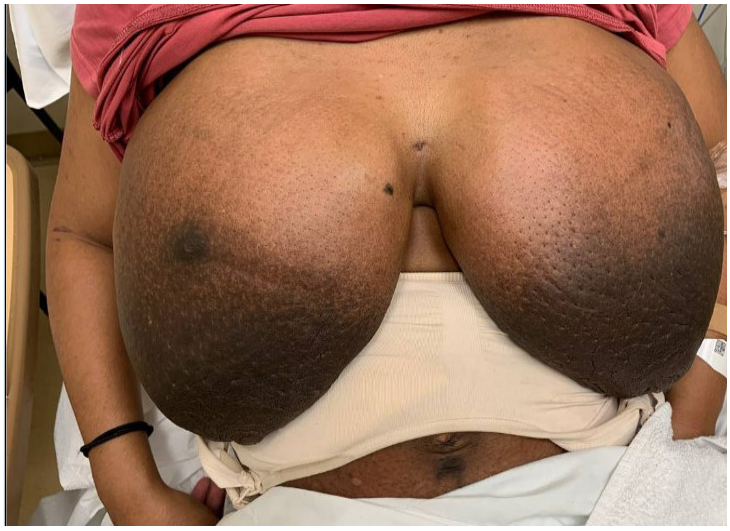
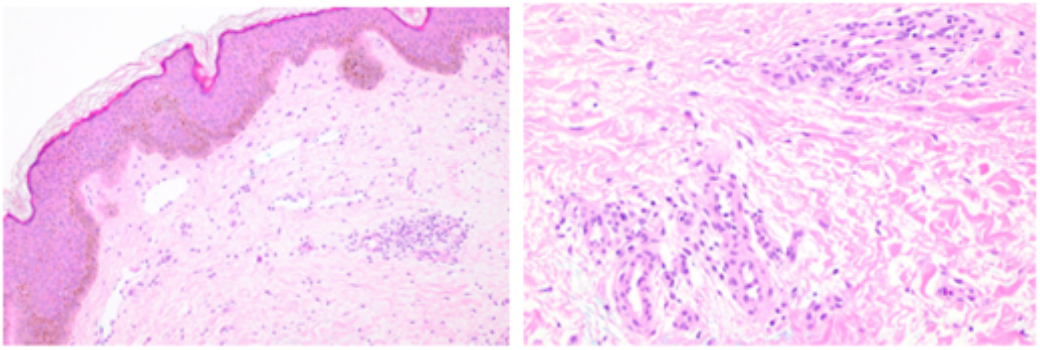
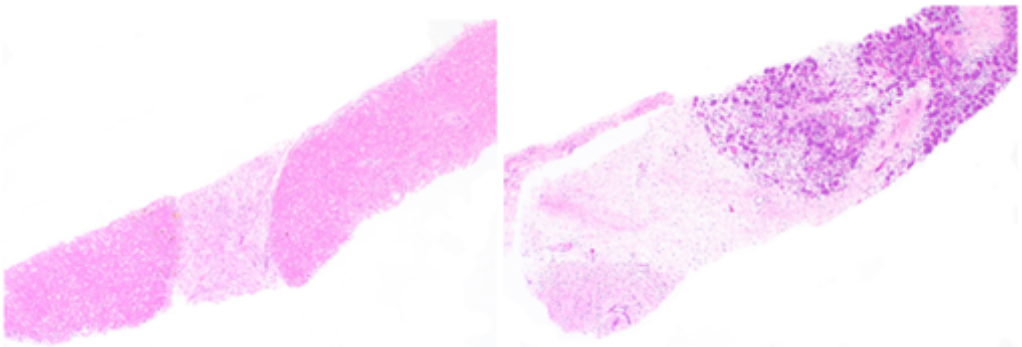


**Image 1:** Photograph of gestational gigantomastia upon admission postpartum.



**Skin punch biopsy:** Photo 1a:Mild dermal edema and nonspecific superficial perivascular chronic inflammation.

Photo 1b**:** Albeit only focally apparent, subtle angioproliferative changes surrounding small dermal vessels were noted.



**Breast core biopsy:** Photo 2a:Extensive ischemic-type necrosis, consistent with parenchymal infarction. Photo 2b:While viable lobular acini showed no significant pathologic change, the inter- and intralobular stroma demonstrated prominent tissue edema.

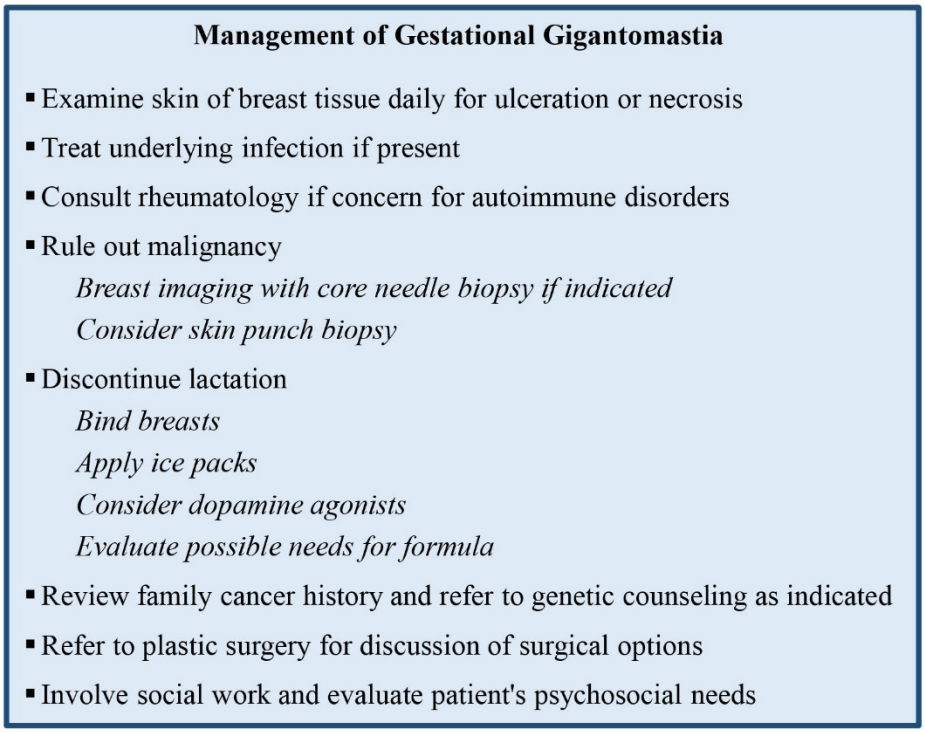



**Figure 1:** Management of Gestational Gigantomastia.

## Discussion

### Review of Gigantomastia

### Etiology and Risk Factors

Gigantomastia is a rare condition in which patients present with excessive enlargement of the breast tissue. There have been case reports suggesting an association with certain medications (such as penicillamine [2,3], bucillamine [4,5], cyclosporine [6], prednisolone [7], and cortisone [8]). Some case reports have demonstrated gigantomastia in patients with pre-existing autoimmune conditions such as myasthenia gravis [9], systemic lupus erythematosus [10], chronic arthritis, or thyroiditis [11]. However, many cases of gigantomastia are idiopathic. Typically gigantomastia involves only mammary tissue, yet there are reports of other complications such as pulmonary hypertension [12]. While this pathology can occur outside of pregnancy, gestational gigantomastia is estimated to occur in 1 in 28,000-100,000 pregnancies worldwide [13-16]. It is hypothesized that both gestational and juvenile gigantomastia are hormonally mediated. However, the role of hormones in the disease process is still unclear. Although some cases in the literature have been known to regress (as was the case for the patient in this case report), available data suggest that the majority of cases of gestational gigantomastia do not spontaneously resolve at the conclusion of the pregnancy.

**Presentation and Demographics**

There is no clear consensus regarding the definition of gestational gigantomastia. It is largely a clinical diagnosis based on rapidly and excessively enlarging breast tissue during pregnancy or postpartum. However, one adopted diagnostic criteria for gestational gigantomastia has been enlargement of the breast tissue by an excess of 1500 g per breast [17]. Another proposed criteria for gigantomastia in general is excessive breast tissue that meets or exceeds 3% of the patient's total body weight [18]. Both of these definitions can pose challenges— the former, in that the breast tissue cannot be fully weighed until after removal and, the latter, in that body weight distribution is different during pregnancy. Patients with gestational gigantomastia often present with rapid, excessive enlargement of the breast tissue, frequently during the first- and second-trimester of pregnancy [19], but also with possible development in the postpartum period. This enlargement is commonly bilateral but can also be unilateral [20]. Patients with gestational gigantomastia are usually within the 2nd or 3rd decades of life (corresponding to the window of fertility and reproduction). Associated complaints include hyperesthesia, neck/back pain, skin changes, mobility limitations, social anxiety, and difficulty finding comfortable or supportive garments. Numerous countries have produced case reports citing gestational gigantomastia, suggesting that this condition can occur across racial and ethnic demographics. One systematic review of all case reports and short case series on gestational gigantomastia published in English between 1976 to 2016 demonstrated 50 case reports that were distributed largely in North America, Europe, and Asia, but also occurring in Africa, Australia, South America and the Far East [19].

**Fetal implications**

There is no strong data to suggest that uncomplicated gestational gigantomastia alone has direct fetal implications. Additional fetal surveillance for this condition is generally not universally implemented. However, a worsening maternal clinical status in the setting of gestational gigantomastia could have sequelae on fetal status as well and should be treated appropriately and promptly. Necrosis, bleeding, or infection may lead to sepsis, multi-organ failure, and maternal and/or fetal death [21-23]. Discretion should be utilized by obstetric providers in discussion with a multidisciplinary team and the patient regarding delivery timing in the setting of worsening maternal status or refractory infection.

**Pathology**

Gestational gigantomastia is a clinically apparent condition without well-defined histologic changes. Skin punch biopsy is often performed to rule out inflammatory breast cancer. Histological changes in these samples often include dilated dermal lymphatics, chronic inflammation, and lymphangiectasia, compatible with sequelae of massive parenchymal enlargement. Pathologic characterization of parenchymal sampling is limited, though pseudoangiomatous stromal hyperplasia (PASH) and lymphangiectasia have been reported [24]. Lactational change is an expected finding in the given physiologic setting. Interestingly, breast biopsies in this patient did not show epithelial or other proliferative changes to account for massive parenchymal enlargement. However, prominent stromal edema was apparent in this case. Although the etiology of gestational gigantomastia has yet to be elucidated, this observation would seem to suggest that primary parenchymal hyperplasia may not fully account for the clinical manifestations. Given the extent of marked breast enlargement, cutaneous and parenchymal complications such as infection, ulceration, and necrosis are not uncommon, all of which may be exacerbated by lymphatic and venous stasis [19].

**Treatment**

Treatment for gestational gigantomastia is multifaceted and multi-disciplinary. It is critical to involve multiple teams early in the disease process to ensure that the patient receives prompt and comprehensive care. These teams may involve obstetricians (both General and Maternal-Fetal Medicine specialists), Gynecologic breast specialists, Breast Surgical Oncology, Plastic Surgery, and Breast Radiology. As needed, Dermatology and Rheumatology involvement can be considered if there is concern for underlying dermatologic or autoimmune etiology.

**Conservative management**

Conservative management of gestational gigantomastia should be performed continuously throughout (and not in place of) the workup process. The skin should be routinely evaluated for any breakdown, ulceration, or necrosis. If tissue breakdown is noted, Dermatology and/or wound healing specialists should be consulted for further input as needed. The patient should be assessed for concurrent infection, as ulceration and breaks in the skin due to stretching could increase the risk of infection. Furthermore, patients in pregnancy and postpartum are independently at risk for mastitis. They should be assessed and treated appropriately with antibiotics, with a low threshold to reimage with ultrasound if there is concern for breast abscess. Due to the large breast size associated with this condition, patients may experience breast, neck, and back pain. One case report noted the development of muscle hypertrophy in the shoulder, neck, and back to accommodate the increased breast weight [20]. Patients are unlikely to find bras that provide appropriate support. While some patients may elect to have custom bras made, breast binders (designed for use after breast surgeries for support and compression) can be used either individually or combined to accommodate the size of the enlarged breasts.

Compression is recommended to discourage milk production and can provide the patient added support. The concurrent use of ice packs to the tissue for limited periods of time may also be beneficial for analgesia and to discourage milk production.

**Ruling out malignancy**

There is no literature to date suggesting that patients with gestational gigantomastia in isolation carry an increased risk of breast cancer. However, there have been case reports of underlying lymphoma discovered during the evaluation of gestational gigantomastia [25-27]. Given the extreme manifestation of this condition along with the increasing prevalence of early onset breast cancer in the U.S., it is always recommended that malignancy be ruled out. Breast imaging and subsequent biopsy should be performed if indicated. Close communication with Radiology is recommended due to the rare nature of these cases. While core needle biopsy should be pursued for any suspicious lesions observed on imaging, the risk of subsequent milk fistula should be considered and core biopsy should be approached with caution. Milk fistulae can create further complications by prolonging wound healing and increasing infection risk. While inflammatory breast cancer is uncommon in reproductive-age patients, this should still be included on the differential diagnosis. Due to skin thickening, hypertrophy, and edema, there may be pronunciation of follicular orifices that mimic pea d'orange. Skin punch biopsy should be considered for any suspicious area of the skin. While patients should have early and ongoing reviews of family cancer history throughout their life regardless of breast pathology, this condition represents a relevant juncture to explore and document family cancer history. Practitioners should inquire about and document any cancer diagnoses from family members of both maternal and paternal lineages. If indicated, the person should be referred to genetic counselling and testing if they meet National Comprehensive Cancer Network criteria [28] in order to identify any germline mutations for hereditary breast cancer. Patients also have the option to undergo genetic testing in the absence of clinical indications.

**Discontinuing milk production**

Lactation should be avoided due to subsequent increasing hypertrophy of the breast tissue. Bromocriptine (an ergot derivative and dopamine D2 agonist) inhibits milk production by reducing prolactin release from the pituitary gland. It has been used in the setting of treatment of hyperprolactinemia (for certain prolactinomas) and in Parkinson's disease. In pregnancy, the data do not suggest an increased risk of birth defects or low birth weight, but with some suggestion of increased pregnancy loss (aPOR 3.7; 95% CI: 1.8-7.4) or preterm birth (aPOR 3.6; 95% CI: 1.5-8.3) [29]. While it was previously utilized to suppress postpartum lactation, bromocriptine is no longer used for this indication due increased risk of vasospasm and adverse events such as seizures, stroke, psychosis, and death [30]. Bromocriptine should not be used for patients with a history of preeclampsia and cardiovascular diseases, especially in the postpartum period. For these reasons, cabergoline is preferred over bromocriptine [31]. Cabergoline is another dopamine agonist used for hyperprolactinemia, Cushing disease, and Parkinson's disease. It has been used to inhibit postpartum lactation or engorgement in the setting of pregnancy loss or termination. Regarding safety in pregnancy, it is considered Category B (no risk in animal studies and no adequate studies in human models) [32]. A 12-year prospective observational study did not demonstrate any increased risk of miscarriage or fetal malformation with cabergoline use during pregnancy [33]. Research suggests that cabergoline is more effective than bromocriptine in inhibiting lactation, with a more acceptable side effect profile. Common side effects include headache, dizziness, nausea, and vomiting. Rare but severe side effects could include cardiac valvulopathy and extra cardiac fibrotic reactions [32]. There is a lower risk of psychosis (although still a risk) in those with prior history of mental illness [34]. Furthermore, cabergoline as with other dopamine agonists should also be avoided in patients with hypertensive disorders of pregnancy (such as preeclampsia) unless in situations where benefits grossly outweigh risk [32]. However, data from systematic reviews demonstrate that cabergoline is generally safe and effective when used postpartum for lactation suppression [35,36]. Other medications have also been explored in patients with various degrees of breast hypertrophy. A case report of juvenile breast hypertrophy revealed some benefit from treatment with tamoxifen [37]. However, tamoxifen should be avoided in pregnancy due to case reports of teratogenicity [38-42] and cumulative increased venous thromboembolism risk. It should be noted that while cessation of lactation was recommended and able to be achieved for the patient in this case report, this may be challenging or not universally plausible for patients in low-resource settings in which formula may not be available.

**Psychological impact**

There is a paucity of data exploring the subsequent emotional impact of those who experience gestational gigantomastia, likely due to the rarity of this condition. However, the psychological and social disability should be considered. Gestational gigantomastia is a painful, disfiguring condition. It occurs at a time when patients may already be undergoing other dramatic physical and physiologic changes that occur either during pregnancy or in the postpartum period. It is also at a time when patients are at high risk of depression or worsening mental health disease. The inability to breastfeed/chestfeed may be devastating for patients who desire to both nourish and emotionally bond to their infant.

While the research is conflicting, some data suggest that patients having lactational challenges may be more likely to experience postpartum depression [43,44], although the direction of this correlation is not yet fully established. As needed, social workers can be consulted to explore the various physical and emotional needs of the patient. Engagement with the patient's partner and support network should be employed. Therapy and involvement of psychiatric professionals may be indicated.

### Surgery

There is no universal and standard treatment for gestational gigantomastia. While the patient in our case report did demonstrate some clinical improvement, these patients may still experience persistent symptoms that impact quality of life. As complete spontaneous resolution of the condition is unlikely, surgery is largely considered the mainstay of treatment of gestational gigantomastia [19]. While reduction mammoplasty is commonly employed, there is still the possibility of recurrence of the condition (either spontaneously or in the setting of a future pregnancy [45]). Mastectomy could reduce (but not necessarily eliminate) the risk of recurrence but carries additional considerations, such as inability to breastfeed/chestfeed in the future and possible need for breast reconstruction procedures [19,45]. Regarding optional timing of surgery, there are significant physiologic fluid shifts that occur during pregnancy that should be considered. Increases in overall plasma volume and cardiac output incur a greater risk of major hemorrhage during surgery that have both maternal and fetal implications. Lobular proliferation and increased blood flow to the breast parenchyma occur [46]. Therefore, while optimal timing of surgery has not been clearly defined, awaiting for discontinuation of milk production could potentially decrease risk of galactoceles and infection (though existing data do not definitively support this). Patients should be routinely referred to Plastic Surgery for a discussion of surgical options and risks.

### Conclusion

Gestational gigantomastia is a rare condition that can impact patients during pregnancy and in the postpartum period. This rapid and excessive enlargement of breast tissue can be painful, disfiguring, and emotionally devastating to the patient. Breastfeeding/chestfeeding is generally not recommended to avoid worsening hypertrophy and edema. Breast binding is encouraged for adequate support and to discourage milk production. The tissue should be continuously evaluated for areas of skin ulceration and necrosis, and infection should be appropriately treated. Breast imaging should be performed to rule out malignancy, with skin punch and core needle biopsies as indicated (but taking into consideration the high risk of milk fistula formation with core needle biopsy). While dopamine agonists can be considered to definitively halt milk production and decrease prolactin, these medications have potentially serious side effects that should be considered. Although there have been cases of reversal of the condition after pregnancy, many cases will persist postpartum, necessitating surgery for definitive treatment. Patients should be continuously assessed for any social and mental health needs during treatment of this condition.

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