CASE REPORT

UDC: 618.19-007.6-089
DOI: https://doi.org/10.2298/VSP200423031I

Juvenile gigantomastia: subcutaneous mastectomy with primary reconstruction

Juvenilna gigantomastija: supkutana mastektomija sa primarnom rekonstrukcijom

Jasmina Ivić*, Marija Dunjić*, Isidora Tamindžić†, Živorad Kocevski*, Boban Djordjević*‡, Boško Milev‡§

Military Medical Academy, *Clinic for Plastic Surgery and Burns, §Clinic for General Surgery, Belgrade, Serbia; †Specialized Hospital for Plastic, Aesthetic, and Reconstructive Surgery "MedicOne", Belgrade, Serbia; ‡University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia

Abstract

Introduction. Gigantomastia is one of the most severe anomalies of the female breasts and is caused by their pathological enlargement. Juvenile gigantomastia (JG) of the breasts is a rare disease of an unknown etiology characterized by a sudden and alarmingly rapid, continued growth of the breasts in puberty. **Case report.** We present two patients with massive bilateral JG. Both patients had normal hormonal status and denied any other health issues, including a positive family history of gigantomastia. The skin overlying the breasts was red, without ulcerations, and with visibly enlarged superficial veins. The nipples were not well defined from the surrounding skin and were positioned below the level of the umbilicus. Patients were successfully treated with a surgical technique consisting of a bilateral subcutaneous mastectomy with the primary reconstruction of the breasts using polyurethane implants and reconstruction of the nipple by the free nipple graft technique. The histopathological reports from both patients' biopsy specimens presented diffuse hyperplasia of the glandular and stromal tissue. Both patients had excellent esthetic results with minimally visible postoperative scars. **Conclusion.** Surgical management of JG is the primary means of treatment. This paper presents significant results and effects of plastic surgery, and the applied surgical method can be recommended for the successful management of JG.

Key words:
gigantomastia; plastic surgery procedures; treatment outcome.

Apstrakt

Uvod. Gigantomastija predstavlja jednu od najozbiljnijih anomalija ženskih dojki, a nastaje usled njihovog patološkog uvećanja. Juvenilna gigantomastija (JG) dojki je retka bolest, nepoznate etiologije, koju karakteriše nagli i alarmantno brzi, kontinuirani rast dojki u pubertetskom periodu. **Prikaz bolesnika.** Prikazujemo dve bolesnice sa masivnom bilateralnom JG. Obe bolesnice imale su normalan hormonski status i negirale bilo kakve druge zdravstvene probleme, uključujući porodičnu istoriju gigantomastije. Koža grudi obe bolesnice bila je crvena, bez ulceracija, sa vidno uvećanim površnim venama. Bradavice nisu bile jasno definisane u odnosu na okolnu kožu i bile su postavljene ispod nivoa pupka. Bolesnice su uspešno lečene hirurškom tehnikom koja je uključivala bilateralnu supkutanu mastektomiju sa primarnom rekonstrukcijom dojki poliuretanskim implantatima kao i rekonstrukciju bradavice tehnikom slobodnog grafa. U histopatološkim nalazima iz uzoraka biopsije obe bolesnice nađena je difuzna hiperplazija žlezdanog i stromalnog tkiva. Obe bolesnice imale su odlične estetske rezultate sa minimalno vidiljvim postoperativnim ožiljcima. **Zaključak.** Hirurško lečenje je primarno sredstvo u lečenju JG. Prikazani su značajni rezultati i efekti plastične hirurgije, a primenjeni hirurški metod može se preporučiti za uspešno lečenje JG.

Ključne reči:
hirurgija, plastična, procedure; gigantomastija; lečenje, ishod.

Correspondence to: Jasmina Ivić, Military Medical Academy, Clinic for Plastic Surgery and Burns, Crnotravska 17, 11 000 Belgrade, Serbia. E-mail: jasminaivic@live.com

Introduction

Deformities of the breasts have a cumulative psychologically negative effect on the female population that causes a feeling of decreased femininity and sexual unattractiveness. They try to hide the defects through different ways of dressing and seclusion, which in turn has an effect on their normal activities of everyday living.

The possibility of reconstruction gives hope to the patient undergoing mastectomy in terms of decreasing the possible physical and emotional effects of undergoing the procedure. The shape and symmetry of the breasts are deemed more significant than the visibility of the postoperative scars. Having a plan for the treatment of gigantomastia is crucial for the patients facing the diagnosis. It is essential for surgeons to understand the history of breast reconstruction, as it is the core of the comprehensive and all-inclusive approach to healing.

Abnormalities of female breasts have been a rising concern for many centuries. That has given a rise to what is known and performed as a reduction mammoplasty, viewed both as a science and an art form. This reduction in breast volume is performed to either alleviate clinical symptoms or improve positive body image in patients.

In the seventh century, a Greek physician, Paulus Aegina, first described breast reduction for treating gynecomastia. In 1561, a German physician Hans Schaller reported using breast amputation for treating gigantomastia. Later, in 1669, a British physician Briton William Durston reported using breast reduction for breast hypertrophy [1].

Diseases of the breasts differ extremely in their clinical presentations and mechanisms of onset and always cause a certain amount of doubt in clinicians who deal with breast pathology.

The literature describes five subtypes of gigantomastia: juvenile (also known as pubertal or virginal), gestational, idiopathic, penicillin-related, and obesity-related.

Diffuse hypertrophy of the breasts in the adolescent period, which presents either before or after the onset of menarche, is known as juvenile or virginal hypertrophy and, in extreme cases, as JG. It is defined as the extreme enlargement of the breasts, most commonly within a 6-month period, which is further followed by a continual period of gradual breast enlargement [2].

JG is a rare disorder (0.4%) characterized by excessive breast tissue enlargement and proliferation, accompanied by serious physical and psychosocial consequences. It is sporadic in nature; however, in written works, it is also described as having a positive family background [3–6].

The definition of JG is not universally accepted in literary works. It is most commonly described as an increase in breast size, which occupies over 3% of the full body mass or excess breast tissue weighing over 1.5 kg [7].

Kulkarni et al. [8] defined JG as an etiologically undefined benign progressive bilateral breast enlargement to the extent that the only means of treatment is with a surgical breast reduction, during which more than 1,800 g of breast tissue would be removed from each side, respectively.

The first case of gigantomastia described in medical literature was in 1670 in Plymouth [9]. Kupfer et al. [4] stated that the first published case of hypertrophy was in 1919 by Henry Albert.

JG can be either unilateral or bilateral in presentation, as well as either symmetric or asymmetric.

The leading characteristic of JG is that at some undetermined point during adolescence, the breasts begin to enlarge extremely and rapidly, followed by stretching of the overlying skin and a dark red discoloration; recurring mastitis and nipple deformation are also frequently present. In some cases, sudden enlargement of the breasts can also lead to ulceration of the overlying skin of the breasts.

The etiology of the onset of JG is still unclear. The main hypothesis is that the cause is a secondary hypersensitivity to certain hormones in the adolescent period, such as estrogen (ER), PR, prolactin, or growth factors. However, most of the reported cases in medical journals and other literature stated that normal hormonal levels were present [8–14]. It is also noted in the literature that some autoimmune diseases, such as systematic erythematous lupus, are linked to gigantomastia [15, 16].

In the following cases, the patients were presented to a council of specialists which consisted of a plastic surgeon, general surgeon, radiologist, endocrinologist, pathologist, pediatrician, and psychologist. Due to the nature of their clinical presentations, with large masses of fibrocystic breast tissue, as well as the excess distance between the nipples, it was decided that a subcutaneous mastectomy would be performed under general anesthesia. That would be executed with skin-sparing mastectomy, as done in the inverted-T surgical technique with reduction mammoplasty, followed by a primary reconstruction of the breasts with polyurethane breast implants and reconstruction of the areola with a free nipple transplant in the same surgical act.

It is important to state that both patients gave their full, conscious, and informed consent to be included in this case report.

Case 1

A 19-year-old Caucasian nulliparous female patient presented with slightly asymmetric bilateral JG. The patient stated that the additional growth of her already-developed breasts was noticed a year ago. In the beginning, the enlargement was both symmetric and moderate. Six months ago marked the onset of extreme breast growth, with a subtly more pronounced enlargement of the left breast.

The patient stated that the onset of menarche was at the age of 12 and that it has been since accompanied by regular menstrual cycles lasting 28 days. She denied chronic illnesses, medication use, and allergies to food and medications. The patient underwent spinal surgery for scoliosis at the age of 13.5. She negated positive family history of gigantomastia or macromastia.

The patient stated that before the onset of the described breast growth, her breasts fit a C-cup in bra size and that, in just a year, they enlarged to the presenting size. The enlarged

breasts posed as both a physical burden, causing back pain, frequent mastitis, and restriction in everyday activities, as well as a psychological burden including but not limited to social isolation and withdrawal from peer groups. Due to significant bilateral mastitis a month before the surgery, the patient was on a two-week triple antibiotic therapy.

Upon clinical examination, it was noted that there was an asymmetric hypertrophy of both breasts, with a slightly larger left breast. With the patient in the upright standing position, the breasts reached the level below the umbilicus. The skin overlying both breasts was intact, without ulcerations, distended, and dark red with a perceivably evident and dilated venous presentation. In both breasts, it was recognized that the nipples were deformed, atrophied, and inflamed (Figures 1A and 1B). On bimanual palpation, the breasts were hard and nodular. The distance between the midline and the nipple was 58 cm on the right breast and 63 cm on the left.

Hormonal levels of ER, PR, testosterone, prolactin, luteinizing hormone (LH), and follicle-stimulating hormone (FSH), as well as tumor marker analysis for CA-125, all came back within the normal physiological ranges. The patient was tested for systemic lupus, diabetes, and diseases of the thyroid gland. All test results were negative.

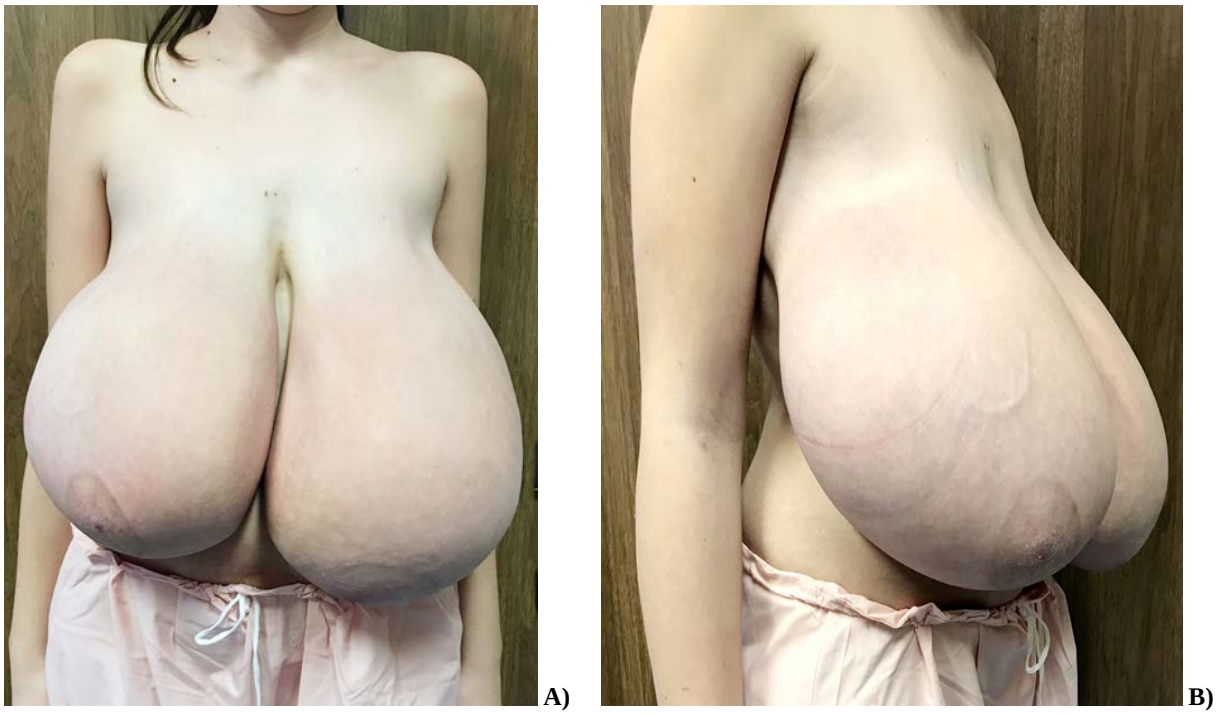
Ultrasound (US) of the breasts described that both of the breasts were extreme in volume, with a glandular parenchymal structure. Bilaterally, in the parenchyma, there were multiple large hypoechogenic lesions with a detectable Cd signal. The largest one is located in the left breast at the fusion of the upper quadrants towards the left upper quadrant (LUQ), spanning a longitudinal diameter of 10 cm. US-guided core biopsy was performed, and one sample was obtained and sent for pathology analysis. In the right breast in the upper right quadrant (URQ), the largest focal lesions spanned a diameter of 6 cm. Two core biopsy samples were obtained and sent for pathology analysis and report. The breast parenchyma was diffusely oedematous. There were no pathologically altered lymph nodes (LN) in the axillae. The pathology report stated that the samples were made up of focally multiplied connective tissue, which incorporated ducts and lobules of the breasts, coated in a uniform epithelium. Multiple microcalcifications were noted. There was no tumorous tissue in the samples.

Based on the medical exam and a detailed radiological and endocrinologic exam of the patient, a uniform decision was reached by the council of specialists for a bilateral subcutaneous mastectomy with a primary reconstruction with implants. The patient gave full and informed consent for the surgical intervention.

The tissue removed from the right breast weighed 6,300 g, and the left 6,800 g (Figures 2A and 2B).

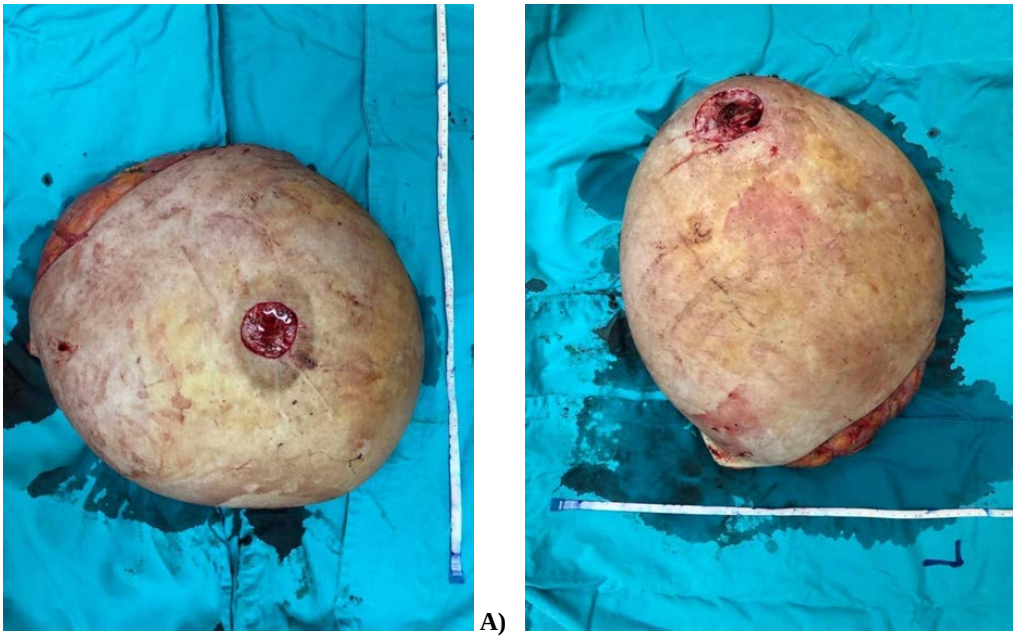
In the immediate postoperative period, the patient was not anemic, and no other frequently associated postoperative complications presented.

The pathology report defined the benign tissue sample as a secondary extensive proliferation of the glandular and stromal tissue. There was no chronic inflammatory cell infiltration nor histopathological confirmation of malignancy. Testing for ER and PR receptors was negative, which allowed for the omission of using tamoxifen in the postoperative period.



A) **B)**

Fig. 1 A) and B) – Slightly asymmetric hypertrophy of both breasts in a 19-year-old patient with a larger left breast. In both breasts, the nipples are deformed, atrophied, and inflamed. The skin overlying both breasts is distended and dark red with a visible dilated venous presentation.



A) **B)**

Fig. 2 – Tissue removed from the breasts of the first presented patient: A) from the right breast, weighing 6,300 g and B) from the left, weighing 6,800 g.

Case 2

A 16-year-old Caucasian nulliparous female patient presented with extreme asymmetric bilateral JG. The patient stated that further growth of already-developed breasts was noticed. In the beginning, the enlargement was asymmetric and moderate; however, ten months ago marked the onset of extreme breast growth, with considerably pronounced growth of the left breast.

The patient stated that the onset of menarche was at the age of 11 and that it was since followed by regular menstrual cycles lasting 28 days. The patient denied chronic illnesses, medication use, and allergies to food and medications. She negated positive family history of gigantomastia or macromastia; however, she stated that her mother had a fibroadenoma of the breast.

When we encountered the patient, she noted and presented previous medical documentation stating that she had previously had two partial resections of the left breast with seven months in between. Following each of the resections, the enlargement continued at a rapid pace.

The patient stated that before the onset of the described breast growth, her breasts were a C-cup in bra size and that in the course of 22 months, the breasts enlarged to the presenting size. At the start of the clinical course of enlargement, the left breast began to enlarge and was erythematous in presentation. The patient was put on triple antibiotic therapy for mastitis. This problem recurred multiple times, and each time, the patient was put on the same antibiotic therapy, which alleviated the symptoms short term. That was followed by a subsequent enlargement of the right breast. The enlarged breasts posed as both a physical burden causing back pain, frequent mastitis, and restriction in everyday activities, and a psychological burden including but not limited to social isolation and withdrawal from peer groups.

Upon examination, it was noted that there was an extreme asymmetric hypertrophy of both breasts, with a significantly larger left breast, which in the upright standing position reached below the umbilicus. The skin overlying both breasts was intact, without ulcerations, strained, dark red with a visually evident and dilated venous presentation. In both breasts, it was noted that the nipples were deformed, atrophied, and inflamed (Figures 3A and 3B). On palpation, the breasts were hard and nodular. The distance between the midline and the nipple was 37 cm on the right breast and 58 cm on the left.

Hormonal levels of ER, PR, testosterone, prolactin, LH, FSH, as well as tumor marker analysis for CA-125, all came back within the normal physiological ranges. The patient was tested for systemic lupus, diabetes mellitus, and diseases of the thyroid gland. All test results were negative.

US of the breasts stated that the breasts were voluminous, with the left breast being substantially more voluminous than the right. The breasts were of a glandular composition, hypoechogenic. The left breast showed hypertrophy with numerous hypoechogenic zones clearly demarcated from the surrounding tissue between the connective tissue septa, which could differentially be diagnosed most likely with gigantocellular fibroadenoma, the largest zone spanning up to 2.5 cm. In the right breast in the LUQ, a hypoechogenic solid lesion spanning 2 cm and, next to it, a smaller one spanning 0.8 cm were present. At the fusion with the right quadrant, two hypoechogenic solid lesions spanning 2.1 cm and 1.8 cm, respectively, were noted. Ductal (canals) had a width of up to 3 mm, without clear differentiation of intraluminal proliferation. There were no enlarged or pathologically differentiated LN in the axillae.

Magnetic resonance imaging (MRI) of the breasts was performed with and without contrast. It stated that the structure of the breasts was fibroglandular. Bilaterally there were no suspicious tumorous lesions, nor was there a pathological post-contrast increase in signal intensity. The left breast showed a significantly increased cutaneous thickness. No morphological or dynamic MRI signs of malignancy were noted. Biopsy samples taken from the breasts came back with a diagnosis of multiple giant fibroadenomas.

Based on the medical exam, pediatrician consultation, and a detailed radiological and endocrinologic exam of the patient, a uniform decision was reached by the council of specialists for a bilateral subcutaneous mastectomy with a primary reconstruction with implants. Due to the patient's age, her parents gave full and informed consent for the surgical intervention.

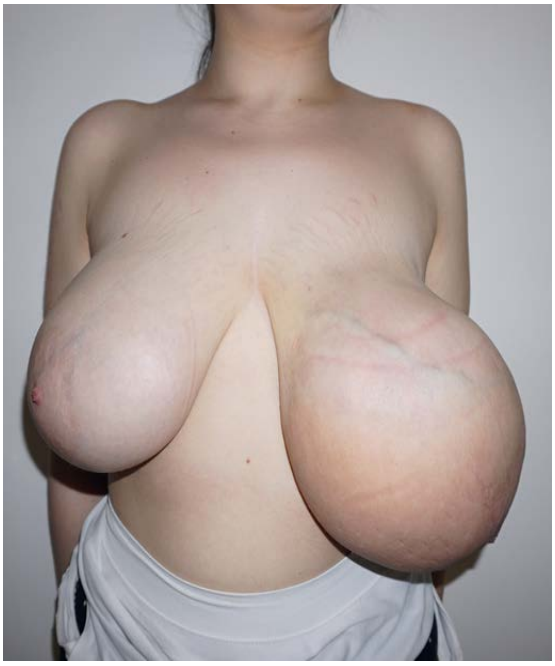
The tissue removed from the right breast weighed 2,600 g, and from the left, 4,100 g (Figures 4A and 4B).

In the immediate postoperative period, the patient was not anemic, and no other frequently noted postoperative complications presented (Figures 5A and 5B).

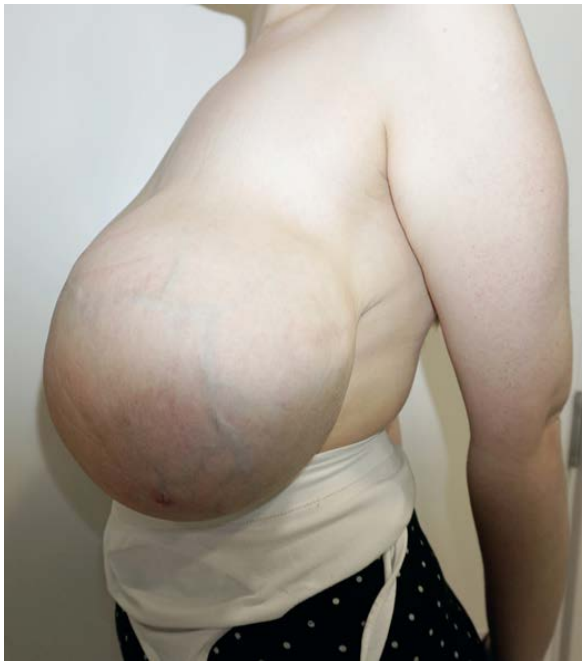
The pathology report defined the benign tissue sample as the secondary extensive proliferation of glandular and stromal tissue. There was no chronic inflammatory cell infiltration nor histopathological confirmation of malignancy. Testing for ER and PR receptors was negative, which allowed for the omission of using tamoxifen in the postoperative period.

Our surgical technique included a subcutaneous mastectomy with nipple reconstruction as free transplants (Figures 6A and 6B).

The patients were satisfied with the esthetic outcome of their individual surgery (Figures 7 and 8).

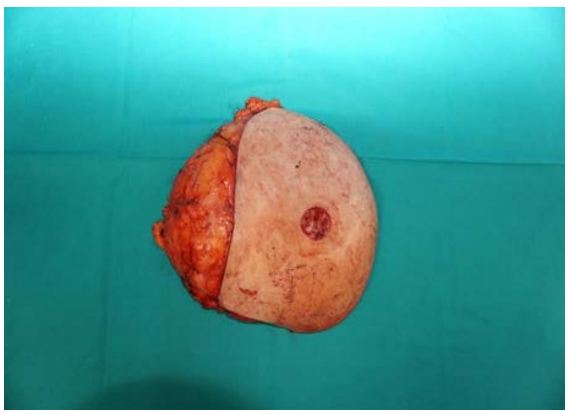


A)

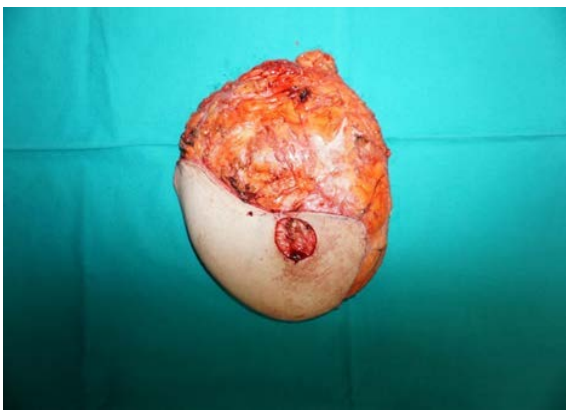


B)

Fig. 3 A) and B) – Extremely asymmetric hypertrophy of both breasts in a 16 year-old-patient. Skin overlying both breasts is dark red with evident and dilated venous presentation. Nipples are deformed, atrophied, and inflamed.

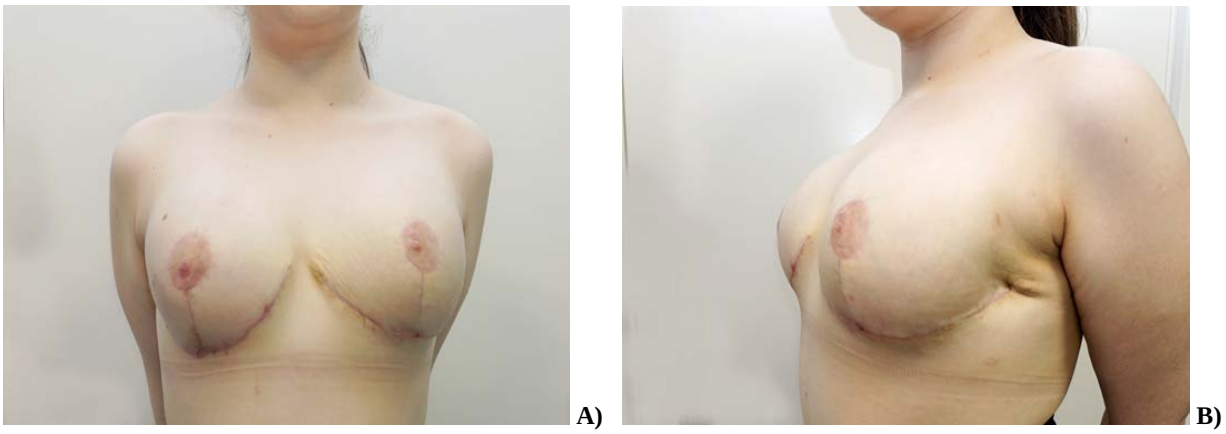


A)



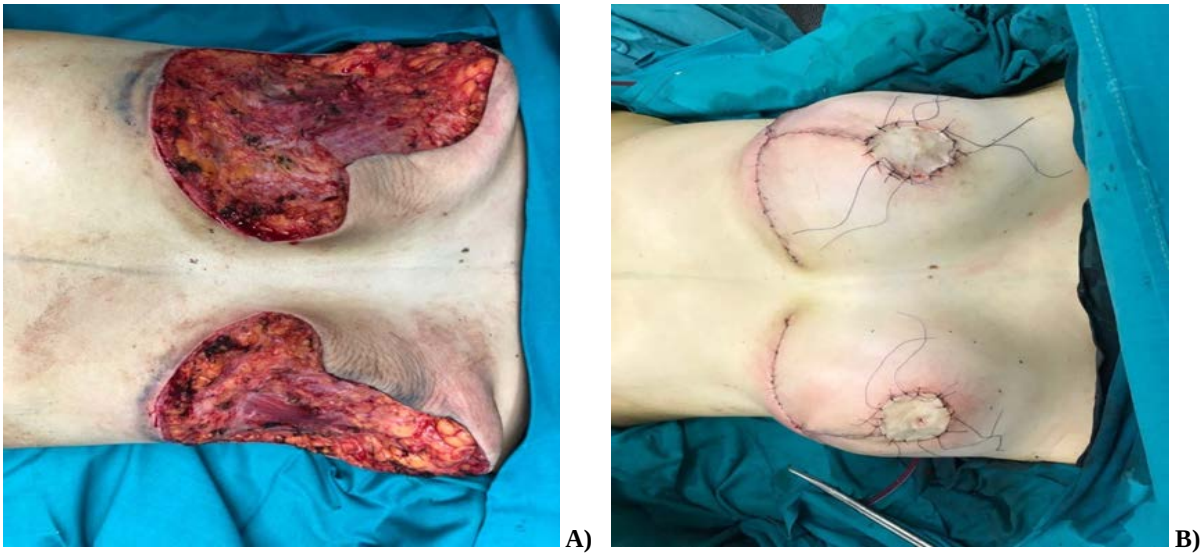
B)

Fig. 4 – Tissue removed during mastectomy from the breasts of the second presented patient: A) from the right breast, weighing 2,600 g and B) from the left, weighing 4,100 g.



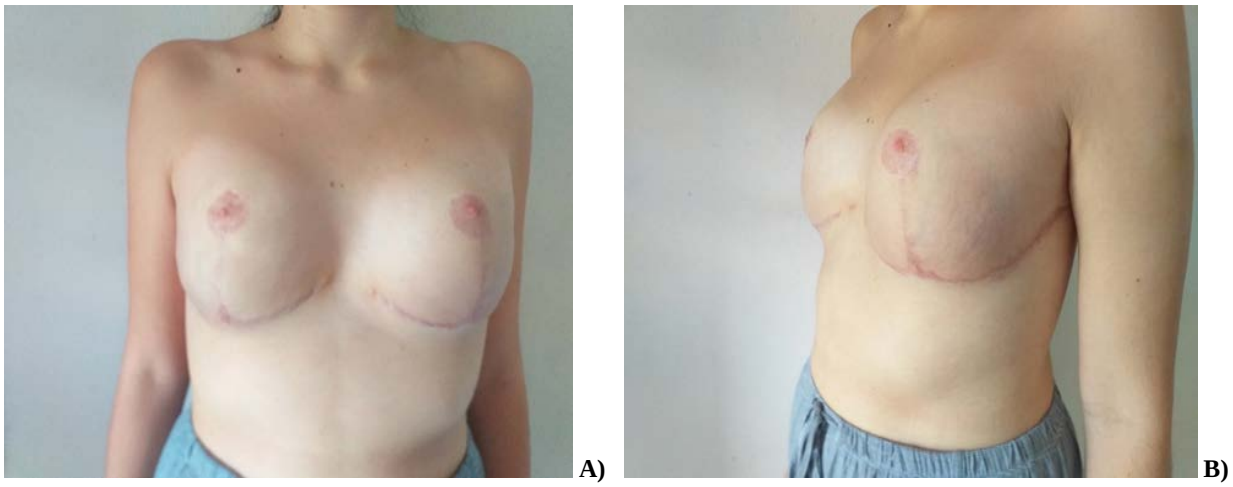
A) B)

Fig. 5 A) and B) – Appearance of the patient in the immediate postoperative period: she was not anemic and no complications presented.



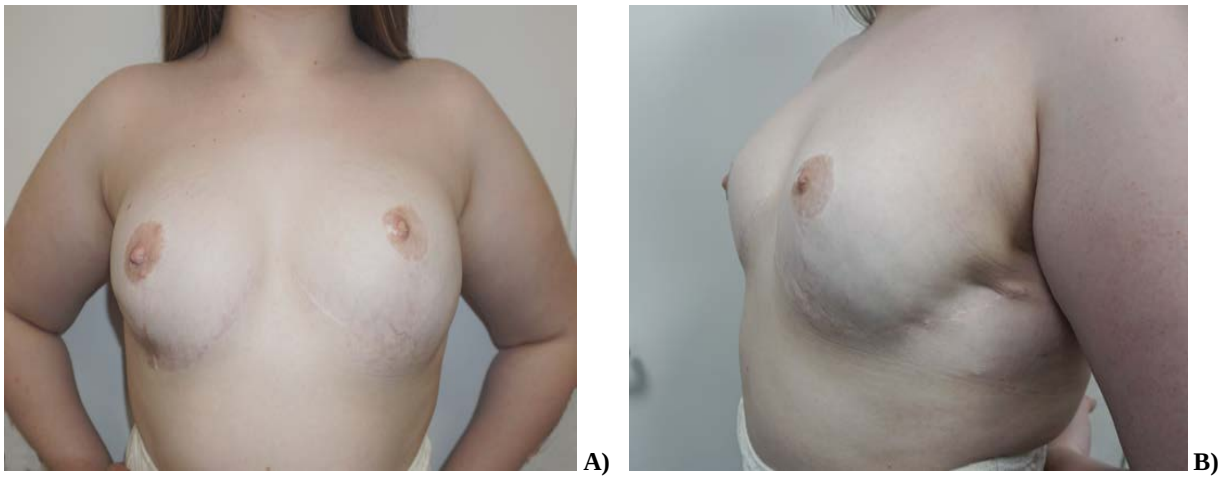
A) B)

Fig. 6 A) and B) – Appearance of the patient on whom the surgical technique was performed including a subcutaneous mastectomy with nipple reconstruction as free transplants.



A) B)

Fig. 7 A) and B) – Aesthetic outcome in the first operated patient.



A) B)

Fig. 8 A) and B) – Aesthetic outcome in the second operated patient.

Discussion

The exact etiology of JG is not fully understood. Contemporary theories describe the sensitivity of the receptors in the breasts to normal levels of circulating ER, increased local or generalized levels of ER, or expression of the PR receptors, including some congenital and autoimmune diseases.

Recently, genetic background to phosphatase and tensin homolog tumor-suppressor (*PTEN*) gene has been assigned. In 2002, Li et al. [16] demonstrated using live mice experiments that mutation and deletion of the *PTEN* gene are connected to increased lobuloalveolar and ductal growth, delayed involution, and hyperproliferation of the epithelium of the breast glandular tissue; however, the clinical analyses have not confirmed this [17].

Our patients had specific and prominent clinical presentations of JG. They did not have positive family histories or any correlation with chronic and autoimmune diseases. Analysis of the *PTEN* gene mutation was not performed as there is still a significant lack of validated and current guidelines and recommendations for *PTEN* testing [18]. Both presented patients had normal endocrinological status both pre- and postoperatively.

The clinical characteristics of JG in the presented patients were similar compared to other types of gigantomastia. Their physical, psychological, and social consequences included bodily symptoms of back and neck pain and avoiding socialization due to extreme breast size. The patients also presented with chronic intertrigo resistant to topical therapy underneath the breasts, grooving on the shoulders from excess weight supported by the brassiere, and numbness and tingling sensation in the arms and fingers. The patient's body mass index (BMI) was in the overweight range due to the enormous weight occupied by the enlarged breasts.

We applied the Mosteller formula: body surface area (m^2) = [height (cm) × weight (kg)] / 3,600)½ [19], which calculates the patient's body surface area and takes into account their presenting height and weight preoperatively. The Schnur Sliding Scale (SSS) uses the Mosteller formula to break down the body surface area and give us the exact amount of minimal breast tissue to remove. The patient from the first case was 180 cm tall and weighed 86 kg with a BMI of 26.5. The Mosteller formula for her calculated that her body surface area (BSA) was 2.11 m^2. SSS defined the minimal amount of breast tissue to be removed at 750 g per breast. The patient from the second case was 170 cm tall and weighed 74 kg with a BMI of 25.6. The Mosteller formula for her calculated that her BSA was 1.87 m^2. SSS defined the minimal amount of breast tissue to be removed at 482 g per breast.

Prior to consulting plastic surgery specialists, the patients had undergone routine diagnostic procedures, including biopsies, under the care and referral of oncologists and presented the stated medical documentation. Histological analysis of the specimen is the only definitive means of establishing a proper diagnosis, where the normal glandular-alveolar development of the normal breast tissue is significantly surpassed by ductal proliferation and stromal alteration that presents with this diagnosis.

In the differential diagnosis of JG, we have to exclude benign changes such as giant fibroadenomas and phyllodes tumors, malignant tumors such as lymphomas and sarcomas, pseudo-gigantomastia associated with obesity, and breast hypertrophy due to various endocrine disorders [20].

JG can be treated in four ways: surgical management, pharmacological therapy given preoperatively or postoperatively, and sole pharmaceutical management.

In the case of surgical management, the choices are subcutaneous mastectomy and primary reconstruction with implants, and various techniques of reduction mammoplasty. The nipples can be reconstructed on a vascular pedicle or as free transplants.

Our surgical technique included a subcutaneous mastectomy with nipple reconstruction as free transplants, which was based on research by Hoppe et al. [21], who claimed a significant correlation ($p < 0.01$) and coefficient quota 7.0 for the probability of a recurrence using reduction mammoplasty compared to mastectomy [21] and the research by Fiumara et al. [22], who published statistical proof that reconstruction of the nipples as free transplants leads to a reduction in the possibility of recurrence compared to those reconstructed on a vascular pedicle ($p = 0.005$). We adapted our surgical tech-

nique and avoided inferior de-epithelialization of the flap and serratus muscle flap due to the characteristics of polyurethane implants that we used.

Tamoxifen is a selective ER modulator used as the first line in medicament treatment as a conservative treatment in juvenile hypertrophy of the breasts [23]. Conservative treatment shows the possibility of stopping progression and causing slight regression of the disease; however, it is incapable of restoring the breasts to their original size if not used in conjunction with other treatment options. It is stated that tamoxifen is given as a means to decrease the recurrence of disease in breast reduction [24]. There is little evidence of the efficacy of tamoxifen; its long-term effects, as well as its safety, are unknown. The known side effects are an increased risk of endometrial cancer, thromboembolism, hot flashes, and a decrease in bone density [2, 21, 25]. Due to the complete removal of all glandular tissue in the breasts, negative ER and PR tissue receptors, there was no need to treat our patients with tamoxifen postoperatively.

Both patients wore compressive bras for a month following the surgery, and they were advised to keep wearing a bra daily as part of their everyday attire. Two weeks following the surgery, the patients presented their breasts with healed nipples, minimal scarring, and no wound infection or ulceration. At the same appointment, the sutures were removed, and the patients were told to hydrate their scars and to start applying topical scar treatment ointment to improve the appearance of their operative scars. The patients were asked to refrain from physical activity for the first postoperative month and to sleep on their backs. At the one-month mark, the patients were showcased how to massage their breasts to help with the adaption of the tissue and its placement over the implant. Three months following the surgery, the entire reconstruction was very satisfactory in appearance. Surgical management had an enormously positive influence on the physical and psychological status of the patients, and with time they could return to their everyday activities.

Complications following mastectomy have been described in the literature as early and late surgical complications, as well as local and systemic complications. They comprise bleeding, swelling, hematomas, seromas, disruption of the wound, dermatitis, nipple graft complications, lymphedema, scar and nipple discoloration, wound infection, etc. [26].

We followed the patients for the first two years with the following appointment schedule – two weeks postoperatively, one month, three months, six months, one year, and two years, respectively. Postoperative US was done at six-month intervals, which evaluated the implant placement and the continuity of the physical state of the implant.

In both cases, the patients were satisfied with the esthetic outcome, of their individual surgery.

Conclusion

Bilateral subcutaneous mastectomy with the primary reconstruction of the breasts using polyurethane implants and reconstruction of the nipple by the free nipple graft technique can be recommended for the successful management of JG with a very satisfying esthetic result.

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Received on April 23, 2020
Revised on March 7, 2022
Accepted March 14, 2022
Online First March 2022