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Case report

Bilateral fibroadenomas and gynecomastia in a young male: sequential or concurrent diseases: case report

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Abstract

In this case report of bilateral fibroadenomas of the breast in a 17-year-old male, we add to the relatively small number of reported cases. Initially assumed to be Highly Active Antiretroviral Treatment (HAART)-associated gynecomastia, our patient with congenital HIV, had normal hormone levels and was otherwise of normal secondary sexual development, except for an uncomplicated undescended testis. The conjunction of clinical finding, imaging and histological finding confirmed a fibroadenoma with gynecomastia. Only a small number of bilateral fibroadenomas in male have been reported in the literature. The finding of co-occurring gynecomastia strengthens the argument for gynecomastia as a necessary prerequisite for the development of fibroadenoma in male due to the quasi inexistent glandular tissue in a normal male breast (the so called sequential theory). The finding suggest that despite the scarcity of fibroadenoma in male, this condition can still be found in the spectrum of male breast pathologies.

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Introduction

A discussion on the true existence of fibroadenoma in the male spectrum of breast pathologies is ongoing. This is due to the lack of fibro-glandular tissue in the male breast. Breast tissues are identical in both sexes until puberty. The normal adult male breast is composed of subcutaneous fat, stromal elements, a small nipple-areola complex, and an underlying, poorly developed ductal system that ends blindly due to a lack of progesterone and Cooper´s ligaments [1]. During puberty, there is a temporary proliferation of breast ducts and stroma due to increasing estrogens levels, followed by involution and atrophy of ducts secondary to the significant increase in testosterone levels [2]. Because fibroadenoma is a ductal disease, the question found in literature is therefore: is fibroadenoma in males a definitive entity or a myth? [3].

Patient and observation

Clinical findings: a 17-year-old African male with perinatal HIV transmission on Highly Active Antiretroviral Treatment (HAART) since birth was referred from a primary health care center to the surgical outpatient department of Potchefstroom Hospital for suspected drug-induced gynecomastia. His initial HAART regimen was changed to the current Efavirenz containing regimen, approximately five years ago, until then he had normal breast for his age. His absolute CD4 count was 640 cells/mm^3 at presentation and he was virally suppressed. He presented with the main complaint of painless, bilateral breast enlargement with associated psychological effects, visual disturbance, and non-palpable left testis. He was of normal stature with a BMI of 16.4 kg/m^2, but with an increased arm span. A high arched palate was not noted. All vital signs were within normal parameters for age. On clinical examination, all systems were normal with normal secondary sexual characteristics. A left undescended testis with a unilateral right-sided cataract was also observed.

Bilateral gynecomastia grade III (Simon *et al*. classification) was noted with a palpable regular 6cm x 5cm mass in the left upper inner quadrant of the left breast as well as regular mass of 5cm x 4cm in the lower inner quadrant of the right breast. The appearance of both breasts was comparable to Tanner stage 4 female breasts (approximately 10cm diameter of each breast). The breast enlargement was so obvious that the patient wore oversized clothing in an effort to conceal them (Figure 1, Figure 2, Figure 3). Both lumps were elastic and nodular in nature, mobile and not attached to skin or underlying fascia. No enlarged axillary lymph nodes, skin or nipple-areola complex changes were noted. The left testis was palpable in the left inguinal region and the right testis was found to be normal. The assessment of bilateral gynecomastia with possible fibroadenoma, left undescended testis, right eye cataract in a 17-year-old HIV positive male on HAART was made.

Investigations: laboratory investigations grossly showed a normal hormonal profile, only the lactate dehydrogenase was elevated (Table 1). Computed tomography (CT) scan of the brain showed no intracranial pathology. Ultrasonography confirmed bilateral well-circumscribed hypoechoic, homogenous breast masses as described above and a unilateral undescended testis noted in the left inguinal region. The testis was normal in size, vascularity and no atrophic changes were noted. A core needle biopsy showed entrapped breast ducts. The ductal epithelium was normal in some, mildly hyperplastic in others. No evidence of malignancy was noted. Histological evaluation of an excised specimen confirmed the diagnosis with morphological and immunohistochemical results consistent with fibroadenoma and surrounding gynecomastia (Figure 4, Figure 5).

Management: our surgical approach entailed a periareolar subcutaneous nipple-sparing mastectomy with en bloc excision of the fibroadenoma and surrounding gynecomastia. To account for excessive skin tissue, we used a modified

inverted omega incision as described by Thione *et al*. [4] (Figure 6, Figure 7).

Discussion

Male breast pathology is less prevalent than female breast pathology. This difference between genders is due to morphological characteristics: the main site of origin for breast pathology is usually the terminal duct lobular unit which is rarely found in males [5]. Gynecomastia is a benign proliferation of glandular breast tissue in males and is thought to result from an increased estrogen to testosterone ratio [6]. It can be divided according to Webster *et al*. into true gynecomastia, which is due to the proliferation of ducts and periductal tissues, and pseudo gynecomastia, which is due to increased subareolar deposition of adipose tissue without enlargement of glandular breast tissue [7]. True gynecomastia is the result of a hormonal imbalance and can be attributable to changes in hormone levels, receptor defects and altered sensitivity of the breast to estrogen [8]. The endocrine imbalance can be physiological, endogenous or exogenous. Exogenous causes of endocrine imbalance leading to gynecomastia include administration of hormones, drugs with molecular structures similar to that of estrogen, or drugs that antagonize androgens [9]. In our case, the patient was initiated as per HIV protocol, on a fixed-dose combination treatment which includes Efavirenz. Efavirenz is the recommended non-nucleoside transverse transcriptase inhibitor in the standard first-line HAART regime for adults in South-Africa [10]. Three hypothesized mechanisms have been proposed for Efavirenz-associated gynecomastia [11]. Efavirenz mimics the effect of estrogen on the breast [12], breast tissue estrogen availability is increased by immune restoration [13], and elevation of the estrogen-androgen ratio by an increased area under the curve of ethinyl-estradiol by at least 37% [13]. Medication and hormonal imbalances may be the cause of proliferative changes in the male breast, like gynecomastia, lobular differentiation, and fibro-epithelial lesions such as fibroadenomas. Gynecomastia has been associated with nearly all cases of fibroadenomas in males reported in the literature. Shin *et al*. could not find any reports of fibroadenoma in male patients who did not have concurrent gynecomastia [14].

As noted, fibroadenomas in male are unexpected due to the absence of fibro-glandular tissue (lobules) and as such, are questioned in literature as an entity. Holleb *et al*. stated that no true fibroadenoma is formed in male, they further stated that fibroadenomas in male are poorly documented or appear to be nodular foci of gynecomastia [15]. Notwithstanding, fibroadenomas in male have been reported as case reports or a case series. Ansah-Boateng *et al*. described four cases of male fibroadenoma with lobular differentiation and gynecomastia [16]. Ashutosh *et al*. reported a giant fibroadenoma in a male patient who was on hormonal treatment for prostate carcinoma [17]. Bilateral drug-induced fibroadenomatoid hyperplasia in a 69-year-old male was reported by Nielsen *et al*. [18]. These handful articles illustrate the existence of reported cases of fibroadenoma in male patients. We report a complex case of bilateral fibroadenomas with gynecomastia in a young HIV patient on HAART for 17 years with a five year history of bilateral fibroadenomas and gynecomastia. There are few controversies about HAART induced gynecomastia, as this has been extensively reported in literature. HIV itself may also be implicated as the cause of proliferative changes in the male breast, like gynecomastia, lobular differentiation, and fibro-epithelial lesions, directly through hypogonadism, hyperprolactinaemia, and other HIV associated diseases; or indirectly due to medications which include antiretroviral and antifungal [19]. Although the existence of male fibroadenoma has been questioned, our clinical findings supported by ultrasound and histology results have confirmed a fibroadenoma surrounded by a gynecomastia, in a patient with a normal hormonal profile. To make sense of this observation in coherence with the current

state of knowledge, we assume that the gynecomastia is a prerequisite condition for the development of fibroadenoma in a male. This approach supports the sequential development as opposed to the concurrent development of fibroadenoma and gynecomastia in male breast. The patient had gross breast enlargement which led to low self-esteem and body dissatisfaction. As with our patient, most patients request treatment for psychological and cosmetic reasons. The goal of treating these patients is the restoration of normal anatomy and contour by resection of the abnormal tissue [20].

Conclusion

In this case report of bilateral fibroadenomas of the breast in a 17-year-old male, we add to the relatively small evidence base of this condition. Initially assumed to be HAART-associated gynecomastia, our patient with congenital HIV, had normal hormone levels and was otherwise of normal secondary sexual development, except for an uncomplicated undescended testis. The histological finding confirmed a fibroadenoma with gynecomastia. Only a small number of bilateral fibroadenomas in males have been reported in the literature. The finding of co-occurring gynecomastia strengthens the argument for gynecomastia as a necessary prerequisite for the development of fibroadenoma in male due to the quasi inexistent glandular tissue in a normal male breast (the so called sequential theory). The evident psychological impact of the unacceptable cosmetic appearance of the bilateral tumors and associated lack of self-esteem necessitates surgical management to restore normal anatomy.

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors have contributed to the conception, designing and writing of the manuscript. They all read and agreed to the final manuscript.

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Table and figures

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Figure 5: cystic and branched breast duct
Figure 6: modified inverted omega incision of the left breast
Figure 7: en bloc skin sparing excision of fibroadenoma and gynecomastia

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Table 1: hormone profile of the patient and reference range

Hormone	**Patient level**	**Normal range**
Beta-HCG	< 0 IU/L	< 5 IU/L
Lactate dehydrogenase	200 U/L	50 - 150 U/L
Testosterone	16.4 nmol/L	9 - 35 nmol/L
Alpha feto protein	1.9 ug/L	< 15ug/L
Prolactin	12.9 ug/L	2.6 - 13.1ug/L
Oestradiol	101 pg/L	73 - 173 pg/L
Progesterone	0.2 nmol/L	0.4 - 6.6 nmol/L
Lutheinizing Hormone	11.0 IU/L	0.1 - 16.4 IU/L

Figure 1: bilateral fibroadenomas with gynecomastia

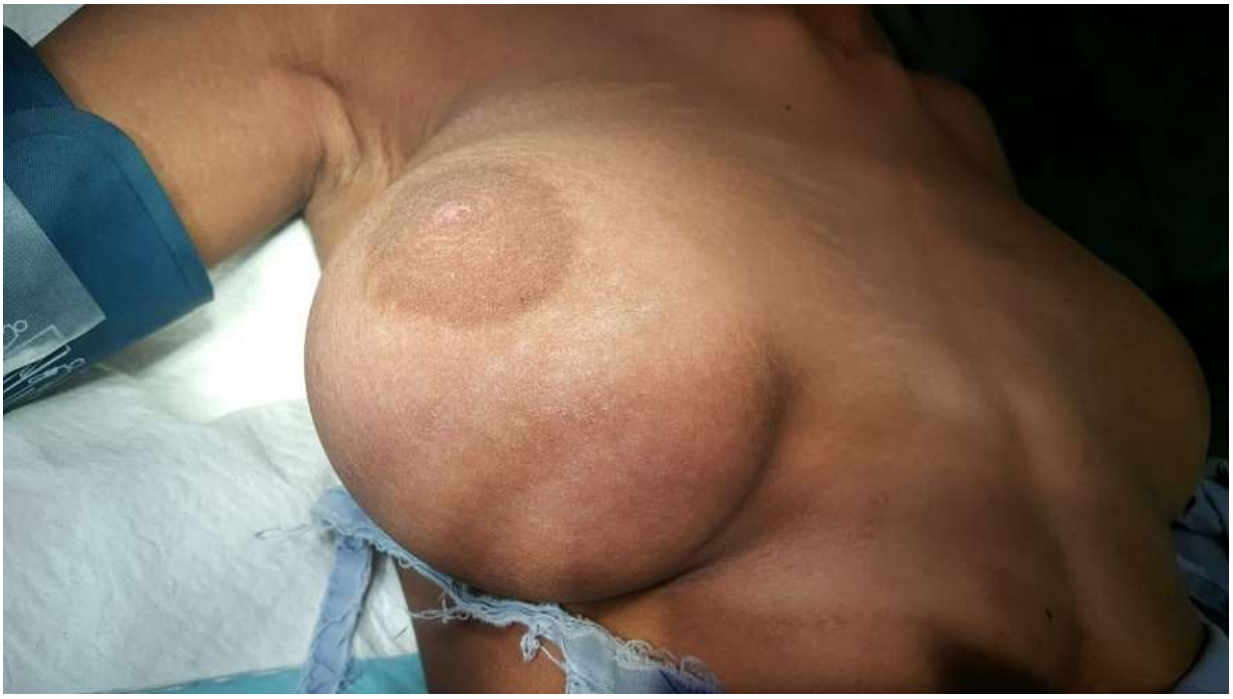

Figure 2: right breast fibroadenoma with gynecomastia

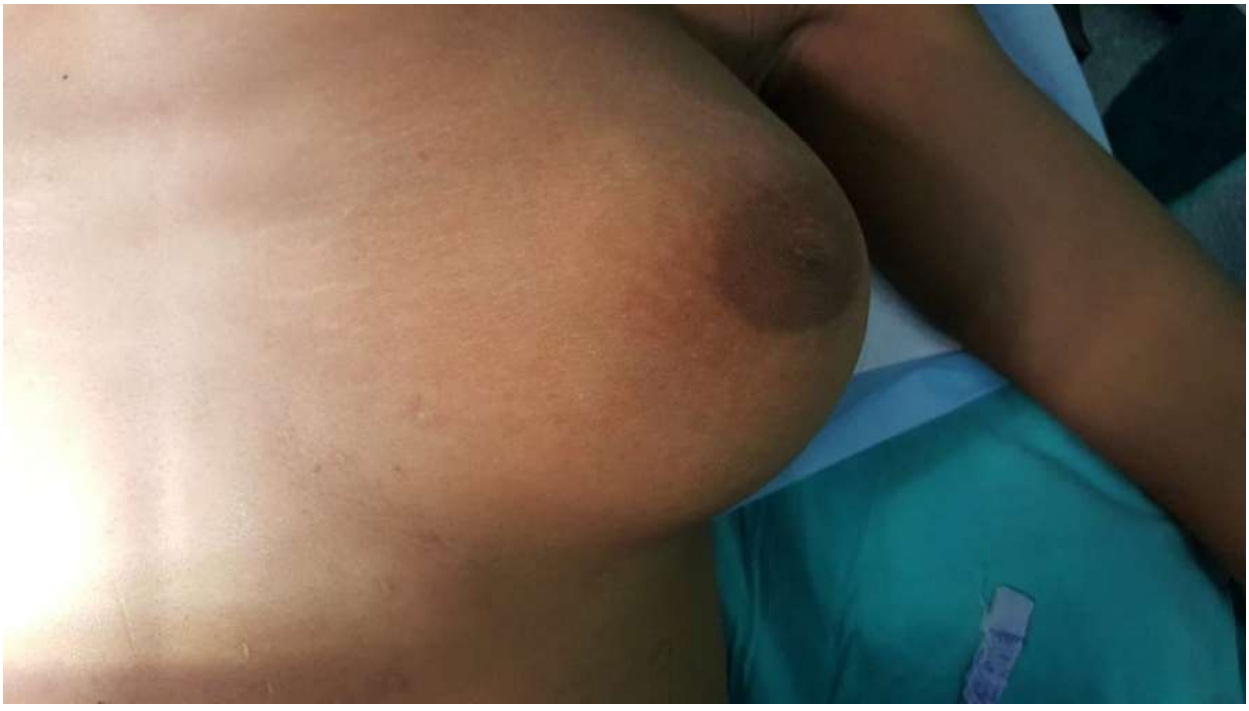

Figure 3: left breast fibroadenoma with gynecomastia

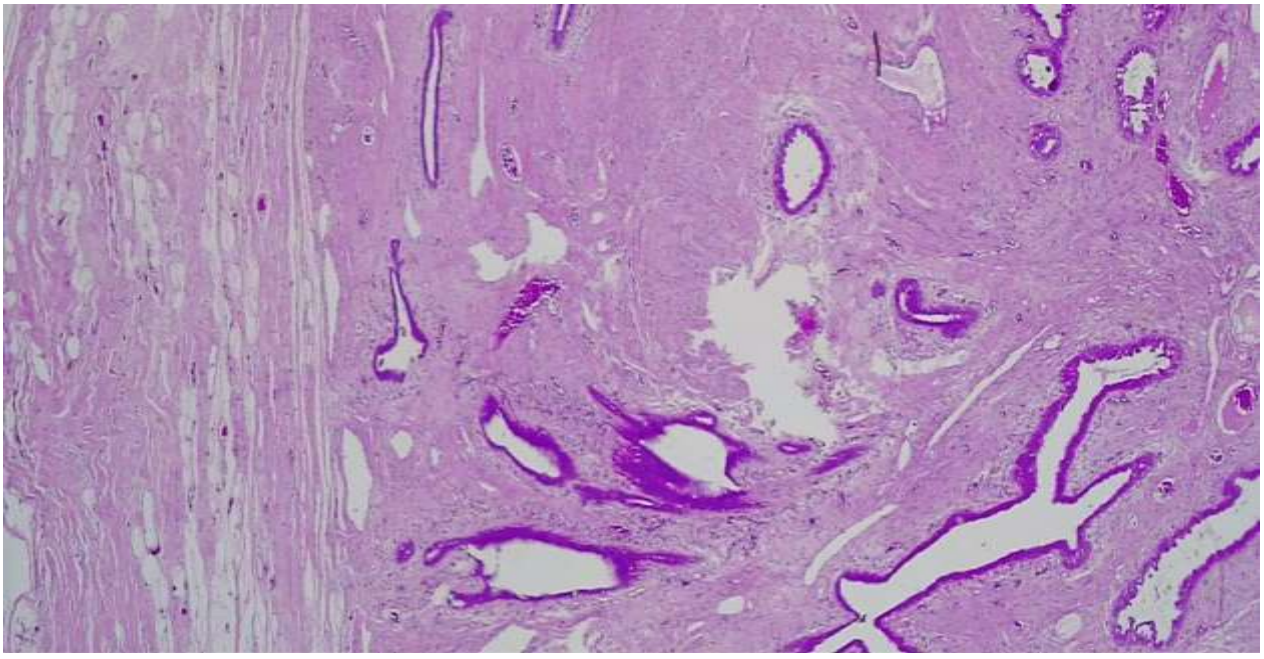

Figure 4: circumscribed edge of fibroadenoma

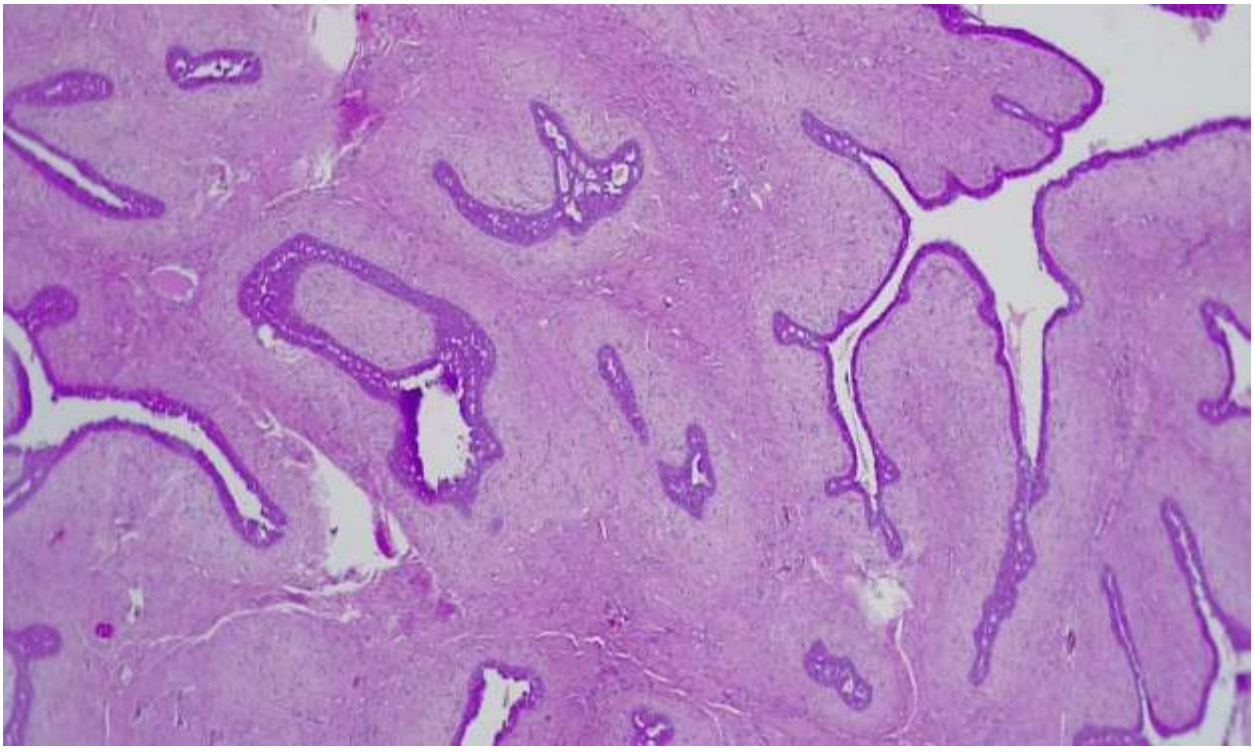

Figure 5: cystic and branched breast duct

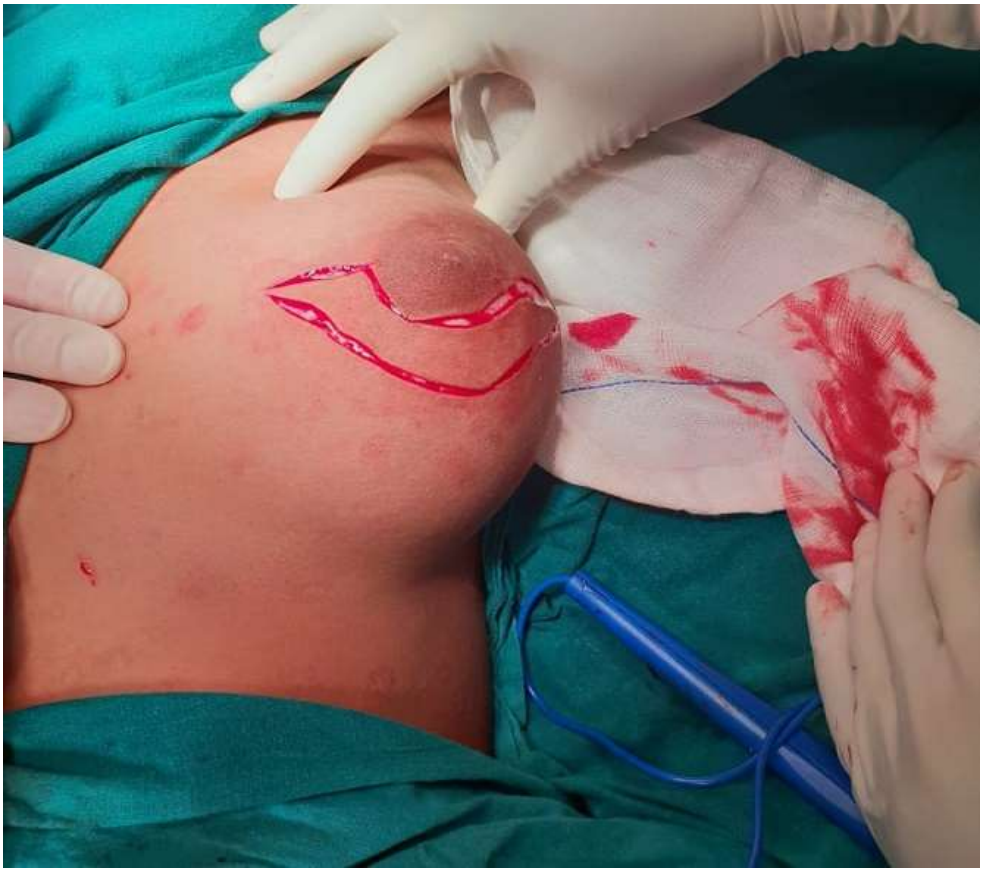

Figure 6: modified inverted omega incision of the left breast

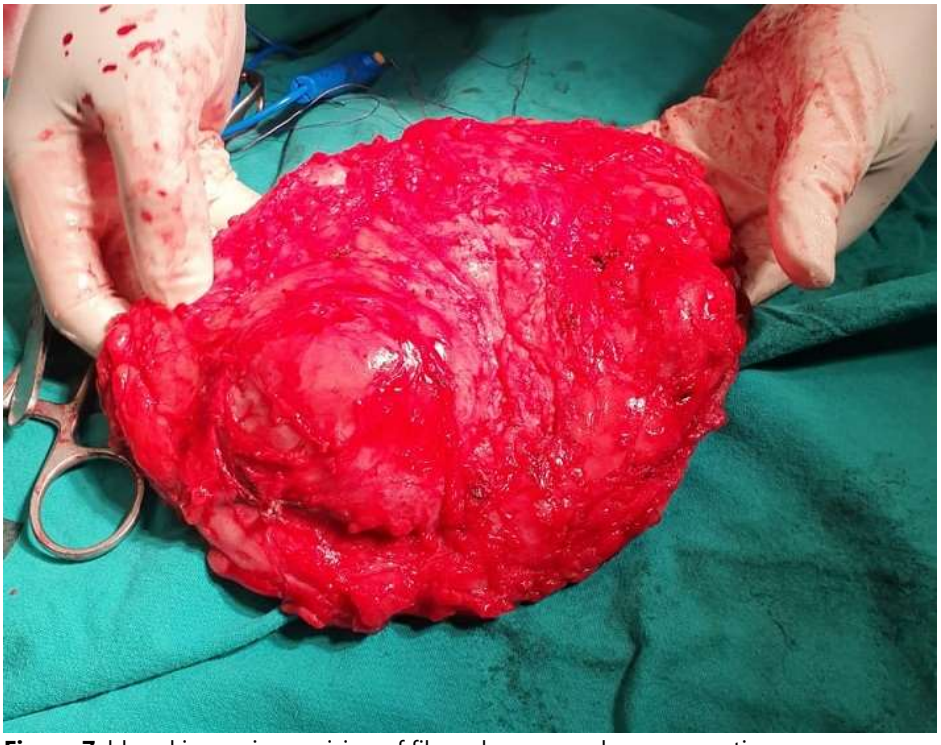

Figure 7: bloc skin sparing excision of fibroadenoma and gynecomastia