



## Case report

## Preoperative embolization of a giant benign phyllodes tumor: A case report and review of literature

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## ABSTRACT

**Introduction and importance:** Phyllodes tumors (PT) account for less than 1% of all breast tumors. Giant PTs can lead to breast disfigurement, tumoral ulceration, and bleeding. Outright surgical excision can be challenging or unsafe. Preoperative transarterial embolization (TAE) has a role but data on its use in the management of PT is limited.

**Case presentation:** A 43-year-old female presented with a 28 cm fungating, necrotic, benign PT on her left breast that eventually developed tumoral bleeding leading to hemodynamic instability. Preoperative TAE controlled the bleeding and allowed the safe performance of mastectomy. A literature review of preoperative TAE of PTs is also presented including the addition of a chemotherapeutic agent in malignant types.

**Clinical discussion:** PTs are rare and comprise only 2.5% of all fibroepithelial breast lesions. Tumoral bleeding causing severe anemia is one of the most common presentations of massive ( $\geq 20$  cm) PTs, especially when neglected. Indications for preoperative TAE include (1) to halt rapid tumor growth, (2) to control active/persistent tumoral bleeding, and (3) to shrink the tumor size and allow successful resection with negative margins, and avoidance of skin grafting. Post-TAE side effects include fever, chest pain, gradual/expanding tumor necrosis, decrease in tumor weight, and diminished tumoral abscess/discharge, and loss of tumoral vessel elasticity.

**Conclusion:** Neglected PTs can reach an alarming size. Preoperative TAE is a safe and effective method of controlling life-threatening tumoral hemorrhage and decreasing the size of PTs thereby allowing definitive resection while avoiding skin grafting and/or flap reconstruction.

## 1. Introduction

Phyllodes tumors (PT) of the breast are rare fibroepithelial neoplasms accounting for less than 1% of all breast tumors. The classification of PTs includes benign, borderline, and malignant entities based on their stromal cellularity and atypia, mitotic activity, stromal overgrowth, and characteristics of tumor border on histology [1]. The most common subtype is the benign PT comprising up to 64% of all tumors. Overall, these tumors have an unpredictable nature that even the benign type, although rare, does locally recur and metastasize distantly [2]. Most PTs present as a benign, painless breast mass, occasionally longstanding, that eventually increase massively in size [2,3].

Reported cases (neglected) of PT can go up to 50 cm in size, leading to breast disfigurement such as stretching and discoloration of the skin,

distention of subdermal vessels, tumoral ulceration, and bleeding/anemia [2–4]. Giant and bleeding tumors, especially when severe, present a management dilemma that outright surgical excision can lead to a large skin defect post-mastectomy and catastrophic intraoperative bleeding [5,6]. Other authors have reported their experience with using preoperative angioembolization in malignant PTs to reduce tumor size and blood loss during surgery [5–7]. However, only one reported case of benign PT has utilized embolization before surgery [8]. We aim to (1) report another case of a benign PT with skin ulceration and spontaneous bleeding managed with preoperative transarterial embolization (TAE), and (2) review the literature on the utility of TAE for the management of PT of the breast. This case report is presented in line with the SCARE criteria [9].

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## 2. Presentation of case

A 43-year-old Filipino female presented with a rapidly growing left breast mass noted 13 months before the consultation. There were no associated medical comorbidities, hereditary disease, personal history of malignancy, nor a history of weight loss. She noted an egg-sized mass on her left breast, which rapidly enlarged to occupy the whole breast over five months, prompting her to seek a consult with a general surgeon and a subsequent referral to a medical oncologist. The doctors advised computed tomography (CT) scan of the chest and core needle biopsy (CNB). However, because of a government-enforced community lock-down/quarantine due to the COVID-19 pandemic, she was unable to comply. Instead, she resorted to natural/herbal medicine and faith healing, recalling the application of a “miracle oil” on the affected breast during this time. However, the mass continued to increase in size with thinning of breast skin that subsequently resulted in ulceration. There was an episode of significant spontaneous bleed, thus prompting a follow-up consultation with her breast surgeon.

When seen at the clinic, the patient had a huge left breast mass approximately 28 cm in its widest diameter, occupying the entire left chest with engorgement of superficial veins and a large central area of ulceration with overlying necrosis but no active bleeding (Fig. 1). The mass was firm to hard on its base with small fluctuant areas on all breast quadrants, non-tender, mobile, and not attached to the chest wall. Several enlarged lymph nodes were noted on the ipsilateral axilla with moderate edema of the left arm. The patient was pale and tachycardic at 124 beats per minute (bpm). Thus, admission was advised for transfusion and possible surgery. A CNB was done before admission, which showed a fibroadenoma.

Upon hospital admission, a complete blood count showed a hemoglobin (Hgb) of 4.3 g/dL, serum albumin of 2.2 g/dL, with normal bleeding parameters. Nutritional supplements were started, and four units of packed red blood cells (pRBC) were transfused, which raised the Hgb level to 9.2 g/dL. There was progressing congestion of the left breast mass, with the patient claiming increasing heaviness of the breast with a significant increase in size in just a few days.

Additional units of pRBCs were requested for possible surgery, but all



**Fig. 1.** A huge breast mass occupying the entire left chest with dilated subdermal vessels and tumor necrosis.

the blood products obtained were incompatible. The patient was referred to a hematologist, who then started the patient on steroids with an initial impression of acute hemolytic transfusion reaction vs. acute hemolytic anemia. Surgery was deferred. The patient was discharged with a plan to continue nutritional build-up and surgery re-scheduled when matched blood products would become available. A low-dose oral steroid was continued.

The patient was re-admitted after 12 days presenting with tachycardia (124 bpm), lightheadedness, and bipedal edema. Repeat blood tests showed Hgb maintained at 9.2 g/dL but serum albumin level has decreased to 1.9 g/dL. Supplemental parenteral nutrition and albumin infusion were initiated along with the oral nutritional supplements. Contrast-enhanced computed tomography (CT) scan of the chest showed a large (26 × 28 × 27 cm) lobulated soft tissue mass arising from the left breast with a few small to borderline (up to 1 cm) left supraclavicular and axillary lymph nodes. 2D-echocardiography was performed, which ruled out any cardiac pathology showing an estimated ejection fraction of 74%. Persistent tachycardia was attributed to the systemic response brought about by the chronic illness, and the patient was started on Ivabradine, which resulted in the normalization of the heart rate.

While awaiting cardio-pulmonary clearance, the patient had another episode of excessive tumoral bleeding from two different points on the mass associated with tachycardia and hypotension at 70/40 mm Hg. The Hgb level further decreased to 7.4 g/dL. The patient responded to the initial fluid resuscitation and was subsequently referred to an interventional radiologist for an emergency angioembolization.

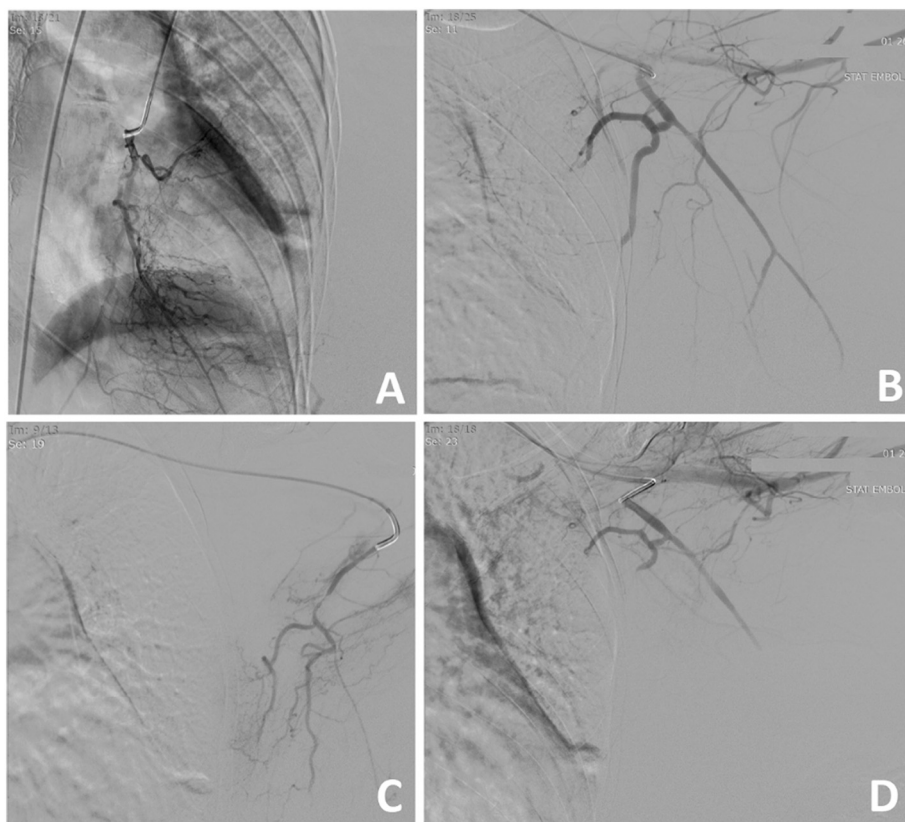
Angiogram confirmed several feeding vessels to the breast mass, including a tortuous and ectatic left internal mammary, lateral thoracic, and thoracoacromial arteries (Fig. 2A–C). Trans-arterial embolization was carried out using PVA 250–355 μm. Post-embolization angiogram showed almost complete occlusion of the arterial feeders with preserved non-target vessels (Fig. 2D). External tumor bleeding stopped, and the patient remained normotensive. There was a slow progression of necrosis, diminished engorged vessels, and lesser congestion on the affected breast without pain (Fig. 3A). Three units of pRBCs were then transfused before surgery.

Two days after angioembolization, the patient underwent total mastectomy with primary closure of the mastectomy defect and placement of a silastic drain (Fig. 3B). The procedure was performed by a senior breast surgeon. The patient tolerated the entire duration of the procedure with minimal blood loss (<100 mL) and without intraoperative complications. Grossly, the specimen weighed 12 kg, measuring 25 × 32 × 23 cm. Final biopsy was benign PT (Fig. 4). Postoperative Hgb level was 6.6 g/dL; thus, two more units of pRBCs were transfused. The patient was discharged after three days with an uneventful postoperative course. Removal of the silastic drain was done at the outpatient clinic on the 7th postoperative day. There was no necrosis or signs of infection on the postoperative site (Fig. 5A). The patient was delighted with the surgical outcome and stated that she could immediately resume daily living activities and return to work, significantly improving her quality of life. No tumor recurrence was noted at 6 months follow-up (Fig. 5B).

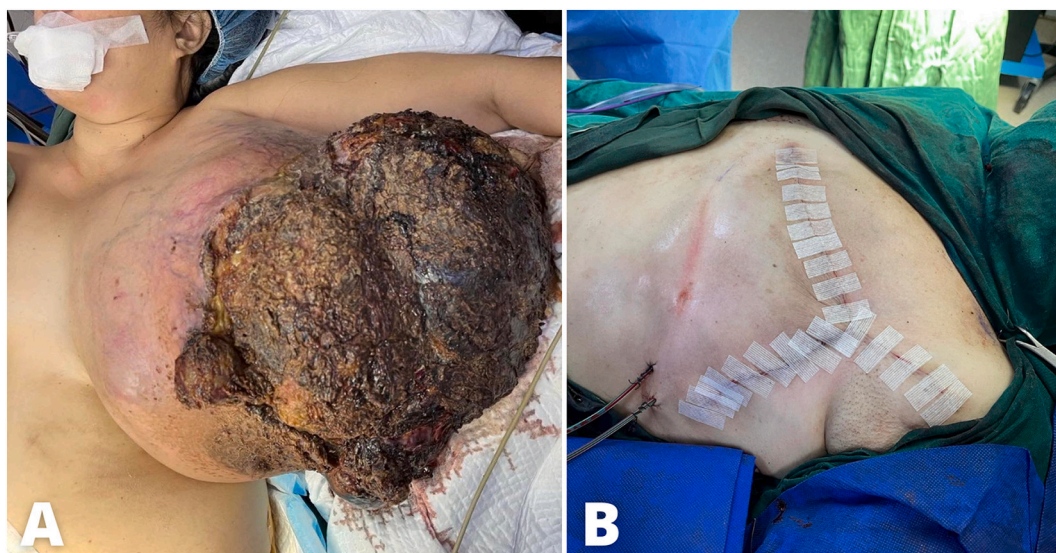
## 3. Discussion

Fibroepithelial lesions of the breast have a broad and varied biologic behavior consisting of PTs, benign fibroadenoma (most common), and variants of fibroadenomas [10]. PTs are rare and comprise only 2.5% of all fibroepithelial breast lesions, occurring predominantly in middle-aged women (average 40 to 50 years). However, they are reported more frequently at a younger age among Asian women [3,11]. In a single-center experience from 1952 to 2013 with 340 patients diagnosed with PT, the prevalence of benign PT was 55%, while borderline and malignant PTs were 11.8% and 33.2%, respectively [12].

The National Comprehensive Cancer Network (NCCN) guidelines recommend breast ultrasound and mammography (for ≥30 years) as



**Fig. 2.** Preoperative transarterial embolization of a phyllodes tumor. Femoral artery was cannulated then angiogram showed feeding vessels supplying the tumor: branches of internal mammary artery (A), thoracoacromial artery (B), and lateral thoracic artery (C). Post-embolization showed complete occlusion of the arterial feeders (D).

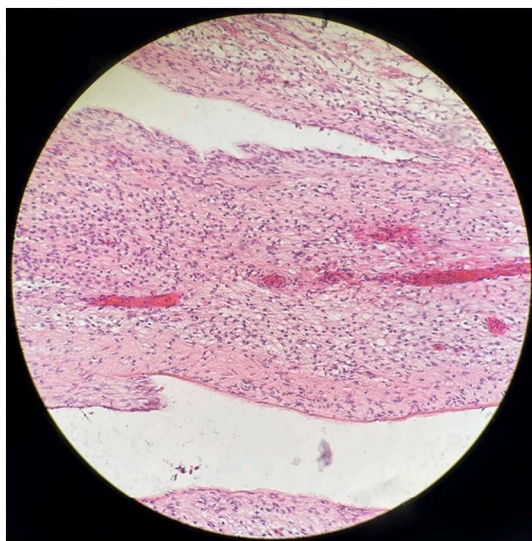


**Fig. 3.** The engorged subdermal blood vessels were significantly reduced after preoperative embolization (A). Total mastectomy of a phyllodes tumor with successful primary closure of the mastectomy defect (B).

initial diagnostic work-up for patients with clinical suspicion of PT. Although certain radiologic features may suggest PTs, distinguishing them from fibroadenomas can be challenging [13]. Furthermore, in patients presenting with a giant and painful breast mass, the imaging studies mentioned earlier may be of limited use. Thus, CT scan and magnetic resonance imaging (MRI) are occasionally employed [5–8,14,15]. Typically, it will show a heterogeneous, enhancing mass on

these imaging studies, and pectoralis muscle invasion almost always suggests malignancy [7,8,14,15]. Although some evidence has suggested that MRI may have a high concordance with the pathologic type of PT, its role in the diagnosis is still under argument [2].

Preoperative CNB can establish a pathologic diagnosis. However, differentiating PTs from cellular fibroadenomas can also pose a diagnostic challenge, especially when samples are limited. Thus, excisional



**Fig. 4.** Microscopic examination shows proliferating ducts forming elongated branching cleft cells lined by layers of myoepithelial and secretory cuboidal epithelial cells with focal multilayering. The stroma is fairly cellular composed of bland, spindle cells with mild to moderate atypia. Mitotic figures are 2–4 per 10 HPF. The tumor does not exhibit infiltrative borders and lacks stromal overgrowth consistent with a benign phyllodes tumor.

biopsy often is required for a definitive pathologic classification [2,3,10]. The histologic features of benign PT include mild stromal hypercellularity, mitosis of  $\leq 4$  per high power field (HPF), absent stromal overgrowth, mild to no atypia, and circumscribed tumor borders. Borderline PTs may show focal infiltration and stromal overgrowth, moderate cellularity, mitosis of 5–9 per HPF, and moderate stromal cell atypia. Malignant PTs have infiltrative borders, stromal overgrowth, malignant heterologous elements, marked and diffuse stromal cellularity, and atypia, with a mitotic activity of  $>10$  per HPF [9,16].

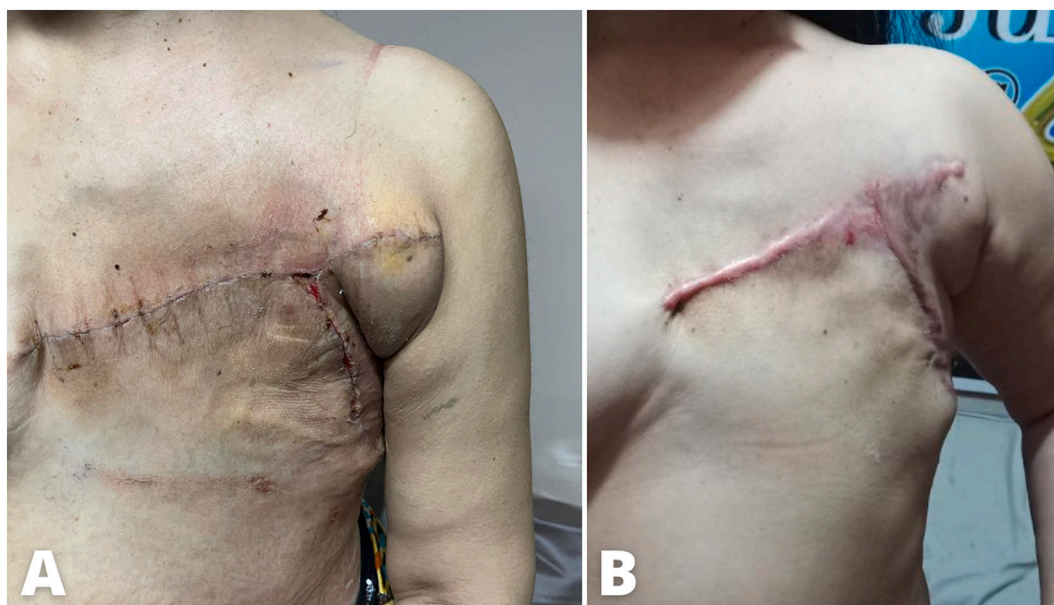
The patient had persistent tachycardia despite improvement in Hgb levels with preoperative blood transfusion and normal 2D-echocardiography and hypoalbuminemia without a history of weight loss. Samiian

et al. [17] reported a case of malignant PT (29 cm) with a high protein content of the cystic component that also presented with anemia (Hgb 7.2 mg/dL) and hypoalbuminemia (serum albumin 1.6 g/dL). They noted abrupt normalization of albumin levels after wide excision of the tumor. The mechanism of PT-induced hypoalbuminemia without cachexia is not well-understood. It could be attributed to either sequestration and degradation of albumin in the tumor tissue or de novo synthesis of albumin in the tumor siphoned from the systemic amino acid precursors [17]. Aside from chronic anemia/blood loss, tachycardia may also be attributed to “hypermetabolism” from a giant PT [15].

Tumoral bleeding causing severe anemia is one of the most common presentations of super-giant ( $\geq 20$  cm) PTs, especially when neglected [4]. Tumors of this size often present with skin ulceration and necrosis, friable tumor/tissue that easily bleeds, dilated/engorged subdermal vessels, palpable thrill, and is hypervascular on imaging tests. These characteristics, compounded by decreased Hgb/persistent bleeding, and the likelihood of a wide post-mastectomy defect, make outright surgery unsafe and impractical [4,6,8,14,15].

TAE with or without a chemotherapeutic agent has been a long-accepted minimally invasive method of treating varying clinical presentations of cancer. The arrest of life-threatening tumoral hemorrhage and tumor necrosis leading to size reduction is achieved by deliberately occluding the vessel(s) supplying the primary tumor of interest using various embolization agents [18]. However, data on its use in the management of PTs is limited.

We searched PUBMED and GOOGLE SCHOLAR for keywords “phyllodes tumor” AND “breast” AND “embolization” and found a total of 6 reported cases (Table 1). All patients (female) presented with a mean tumor size of 22.8 cm (range 7–35). Five out of the 6 cases had a final pathologic diagnosis of malignant PT. The smallest case (7 cm) was a benign PT presented as a smooth breast mass with a palpable thrill and prominent vascularity on doppler scan and MR angiography. Preoperative TAE was performed due to the “hypervascular nature” of the tumor and to minimize intraoperative bleeding [8]. Additional indications for preoperative TAE of PTs as reported by other authors include (1) to halt rapid tumor growth, (2) to control active/persistent tumoral bleeding, and (3) to shrink the tumor size and allow successful resection with negative margins, and avoidance of skin grafting [5–7,14,15]. Two cases of malignant PT involved multiple cycles of TAE with an addition of a chemotherapeutic agent (epirubicin) at different intervals leading to a



**Fig. 5.** The surgical site on the 7th postoperative day (A) and 6th month follow-up (B). There were no noted skin necrosis, surgical site infection, seroma formation, or tumor recurrence.

**Table 1**  
Cases of phyllodes tumors of the breast managed with preoperative embolization ± chemotherapy.

Author, year	Age	Size (cm)	Classification of PT	Indication(s) for preoperative embolization	Agent(s) used during embolization	Interval to surgery	Definitive therapy	Outcome
Kataoka et al. 1998 [6]	54	35	Malignant	Persistent bleeding	Gelfoam	NM	TM + ALN sampling	16 months - DF
Leung et al. 2004 [8]	55	7	Benign	"Hypervascular nature"; to ↓ intraop blood loss	Gelfoam, particles, coils	23 days	Lumpectomy + re-excision <sup>b</sup>	12 months - DF
Takenaka et al. 2011 [7]	57	21.5	Malignant	To ↓ intraop blood loss	NM	NM	MRM + partial pectoralis excision	17 months - DF
Hashimoto et al. 2016 [4]	37	19	Malignant	To ↓ tumor size	Embosphere <sup>c</sup> microspheres + epirubicin (3 cycles)	14 days <sup>a</sup>	TM	6 months - DF
Kuo et al. 2019 [14]	51	30	Malignant	To ↓ tumor size	Embozene <sup>c</sup> microspheres + epirubicin (4 cycles)	NM	TM + adjuvant RT	Chest wall recurrence - 2 months
Tian et al. 2021 [15]	41	24	Malignant	To halt/↓ tumor growth and bleeding; to ↓ intraop blood loss; to improve success rate of operation	Gelfoam	3 days	TM + level 1 ALND + adjuvant ChemoRT	14 months - DF
Our case	43	32	Benign	Persistent bleeding; hypotension	PVA	2 days	TM	6 months - DF

NM: not mentioned; PVA: polyvinyl alcohol; PT: phyllodes tumor; TM: total mastectomy; ALN: axillary lymph node; MRM: modified radical mastectomy; ALND: axillary lymph node dissection; DF: disease free; RT: radiation therapy.

<sup>a</sup> From last cycle of embolization.

<sup>b</sup> Due to positive margins.

<sup>c</sup> With chemotherapeutic agent.

45% and 74.9% tumor reduction, respectively [5,14].

The majority of the tumors were commonly supplied by the internal mammary and lateral thoracic artery. One case reported an abnormal branch coming from the humeral artery [5]. Embolization agents used include gelfoam, microspheres, particles, and coils. Patient-reported effects post-TAE ± chemotherapy include fever and chest pain that resolved within two days, gradual/expanding tumor necrosis, decrease in tumor weight, and diminished tumoral abscess/discharge. Surgeons have reported a loss of tumoral vessel elasticity intraoperatively, allowing easy hemostasis with almost negligible blood loss [5,14,15]. There is no clear consensus on the ideal time/interval to perform surgery after TAE in PTs. In 2 cases with TAE alone, surgery was successfully carried out after an interval of 3 and 23 days, respectively while, Hashimoto et al. performed total mastectomy two weeks after the last cycle of TAE with epirubicin [5,8,14]. One case of malignant PT who refused adjuvant radiation therapy (RT) developed chest wall recurrence two months postoperatively, while the rest were disease-free at a mean follow-up of 13 months (range 6–17).

The NCCN guidelines recommend an excisional biopsy (without the intent of obtaining surgical margins) as minimum surgical therapy for benign PT. In contrast, wide excision with a ≥1 cm margin is a standard approach for borderline and malignant PTs [19]. Recent studies have not shown a direct relationship between margin width and local recurrence. However, a positive surgical margin remains an independent prognostic factor in local and distant recurrences [2,16]. The majority of large PTs (>5 cm) may require advanced oncoplastic techniques or total mastectomy. Secondly, a large post-mastectomy defect is challenging and often requires skin grafting and local or free flap reconstruction when primary closure is not feasible [16,20]. Moreover, patients presenting with persistent tumoral bleeding with hemodynamic instability preclude safe surgery. Axillary lymph node sampling/dissection is unnecessary in all types of PT since the route of spread is hematogenous unless there is clinical or histopathologic evidence of nodal disease [16].

As mentioned earlier, the addition of epirubicin during TAE has provided a substantial decrease (up to 74.9%) in tumor size. However, there is no clear evidence assessing the efficacy of chemotherapy in the management of PTs [2,19]. Whether the effect on tumor shrinkage was mainly due to vessel embolization or chemotherapeutic agent could not be established. The recurrence rates for PT are as follows, 8–10% for benign, 13%–14%, and 18% for borderline and malignant types. Adjuvant RT has shown decreased locoregional recurrence rates, and it is increasingly utilized in the treatment of borderline and malignant PTs.

However, there are no prospective randomized studies published yet to support its use, and thus is considered on a case-to-case basis [16,19]. Recurrences generally present within the first three years; thus, follow-up clinical assessment should be done every six months with annual ultrasonography and mammogram when indicated [2].

The diagnostic impression on the initial consultation at the clinic was a benign PT. Clinical assessment showed a movable mass with no potential attachment to the pectoralis muscle; thus, a CT scan was not initially requested and only contralateral mammography was advised. An upfront consultation with a plastic surgeon was done to allow preoperative evaluation, planning, and thorough discussion of wound closure options after tumor extirpation. CNB revealed a fibroadenoma with a final histopathologic report of benign PT. Despite its limited clinical significance as a preoperative diagnostic tool for PT, with the majority being reported as a fibroadenoma, a preoperative CNB is vital to rule out malignancy. Persistent tachycardia despite correction of the anemia prompted a referral to a cardiologist and subsequent initiation of Ivabradine, an HCN channel blocker which brought about the normalization of the heart rate. Preoperative embolization significantly reduced the engorgement of the blood vessels. With an intraoperative blood loss below 100 mL, the patient remained hemodynamically stable, without necessitating intraoperative blood transfusion. The low serum albumin and bipedal edema progressively resolved over 4–6 weeks. Surgical margins were clear thus radiation treatment was not recommended. The patient was advised to have a clinical breast examination every 6 months for 3 years then yearly thereafter along with annual mammography.

#### 4. Conclusion

PTs of the breast, especially when neglected, can grow to an alarming size. Management of such patients also presenting with persistent bleeding or hemodynamic instability is challenging. Preoperative TAE is a safe and effective method of controlling tumoral bleeding, allowing safe definitive surgical resection of giant PTs. This case highlights the importance of a multidisciplinary approach in managing breast tumors. Involving a team composed of a breast surgeon, plastic surgeon, anesthesiologist, cardiologist, and interventional radiologist enabled a successful outcome.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Ethical approval

Ethics approval is not needed for Case Reports in our institution.

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## CRediT authorship contribution statement

Dr. Ralph Victor Yap: Study concept, data collection, writing the paper, and making the revision of the manuscript.

Dr. Frances Marion De La Serna: Reviewing, making revision of the manuscript, and validating the manuscript's credibility.

Dr. Ma. Arlene Cala-Or: Reviewing, making revision of the manuscript, and validating the manuscript's credibility.

Dr. Aireen Grace Castillon: Study concept, data collection, reviewing and validating the manuscript's credibility.

## Declaration of competing interest

None.

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