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REVIEW

Multidisciplinary Approach to Giant Malignant Recurrent Phyllodes Tumor of Breast: A Case Report and Review of the Literature

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ABSTRACT

Phyllodes tumor is a unique fibroepithelial neoplasm of the breast and accounts for roughly 0.3-0.9% of all breast malignancies. It typically appears clinically as unilateral, painless, palpable breast masses growing quickly in a short time. In cases of large tumors with skin involvement, reconstruction with autologous tissue transfer should be considered.
A 38-year-old female patient presented with a giant mass in her right breast for 2 years. Radical mastectomy was performed to the patient and the defect was covered with pedicled Latissimus dorsi musculocutaneous flap. The specimen was 33x23,5x17 cm in size and weighted 9.150 kg. Ten months after mastectomy, segmental resection of 2., 3. and 4. ribs along with recurrent tumor was performed. Thoracic wall defect was patched with Gore-Tex (2 mm) Dual MeshBiomaterial (W.L. Gore and Associates, Flagstaff, AZ, USA) to maintain chest wall stability. Pedicled transverse rectus abdominis musculocutaneous flap was harvested to cover the defect. In addition to superior epigastric vessels of pedicle, superficial inferior epigastric vein from the flap and cephalic vein from right arm were anastomosed to each other to enhance venous return in the basis of venous supercharging. The patient was symptom-free at 9-month follow-up.
In our case, we had all the factors predicting local recurrence with a continuity at the deep surgical margin, wide necrotic areas, marked pleomorphism and high mitotic rate. Several reconstructive options have been described after mastectomies. As discussed in this case, immediate breast reconstruction with flaps following a mastectomy is an option for these patients. From the case report of our study, we proposed that reliable predictive factors should be explored to identify patients at high risk of local recurrence and distant metastasis. There is urgent need to perform well-designed prospective studies for standardized multidisciplinary approach in treatment of phyllodes tumor of the breast.

Key Words: Breast tumors, breast reconstruction, pedicled flap, malignant

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INTRODUCTION

Phyllodes tumor (PT) or cystosarcoma phyllodes is a rare fibroepithelial neoplasm of the breast originating from the interlobular stroma. It represents roughly 0.3-0.9% of all breast malignancies [1]. This tumor is usually seen in women between 35-55 years of age [2].
Histological characteristics are the basis for subclassification and diagnosis. The World Health Organization (WHO) categorizes PT as benign, borderline and malignant on the basis of the degree of atypia and stromal hyperplasia [3-4]. Increased atypical proliferation and stromal overgrowth usually indicates malignant and metastatic potential [5]. 10-30% of all PTs are malignant which has tendency to give distant metastases [6-8].
It typically presents as unilateral, painless, palpable breast masses growing quickly in a short time. But 20% of PTs which identified on mammography

are nonpalpable [9]. PTs have high local recurrance rates if it is not excised with a margin of at least 1 cm and surgical excision is the mainstay of treatment for all types of PTs [7-10]. Axillary lymph node dissection is not required because metastasis to lymph nodes is very rare, even in large, malignant tumors [11-12]. The efficacy of postoperative adjuvant chemotherapy is still not clear in the management of PTs [13]. According to a study using Surveillance, Epidemiology, and End Results Program (SEER) database (1983-2013) radiotherapy does not impact cancer spesific survival of malignant PT regardless of surgery [14]. To date, there is no proven adjuvant hormonal therapy for PTs [15].

Reconstruction with implant after excision of PT has better aesthetic outcomes than autologous tissue transfer. If there is skin involvement, autologous tissue transfer should be considered [16]. Latissimus dorsi musculocutaneous (LD) flap and transverse rectus abdominis musculocutaneous (TRAM) flap are standard flaps of proven reliability for postmastectomy reconstruction. Even in cases without skin involvement, de-epithelialized flaps are useful to fill up the skin envelop [17].

In this case report, we discuss a patient who developed a giant recurrent malignant PT with chest wall invasion and local recurrence. There are a few papers related to reconstructive options following excision of giant PTs in the literature. Chest wall reconstruction following extended excision of PT along with the involved ribs to ensure negative surgical margins is rarely reported in the literature. The literature was also reviewed to expand our knowledge about this unique breast malignancy.

CASE PRESENTATION

A 38-year-old female patient was referred to our hospital in February, 2016 with a giant mass in her right breast for 2 years (Fig. 1). She has a history of small palpable, painless lump in her right breast in 2014. The patient reported significant growth without any skin changes in a short time. After she had applied to a local hospital in 2015, she underwent a core biopsy. Biopsy indicated that there was malignant mesenchymal tumor with high proliferation index in a small area with atypical nuclear structure and differential diagnosis included carcinosarcoma and PT. An incisional biopsy was performed for differential diagnosis in January, 2016. The diagnosis was spindle cell sarcoma with mitotic rates of

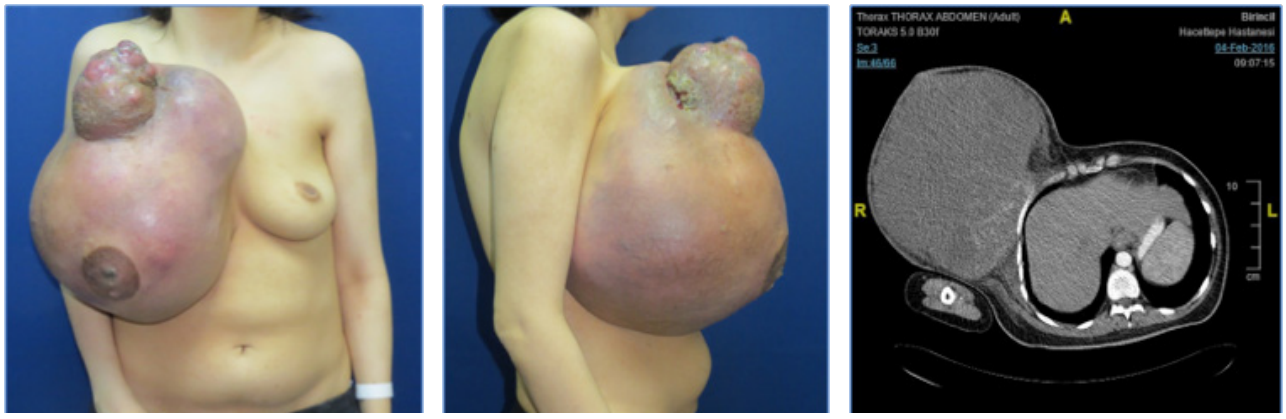


Figure 1: Preoperative images and CT scan

Physical examination revealed a huge tumor with nodular mass on its superior part with multiple invasions of the skin and areola was destructed. There were no any palpable lymph nodes and the left breast was normal. Patient's tumor marker levels were within normal range. A preoperative workup for staging was performed. There was no distant metastasis on computed tomography scans. On PET-CT scans there was no fluorodeoxyglucose metabolism except from tumor area in right breast. Pectoralis major muscle invasion was detected on CT images which is reported in only 2.4% of PT cases in the literature [3].

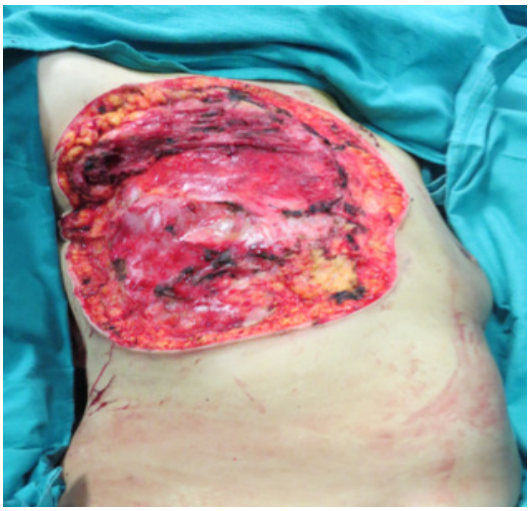


Figure 2: Intraoperative image after tumor resection

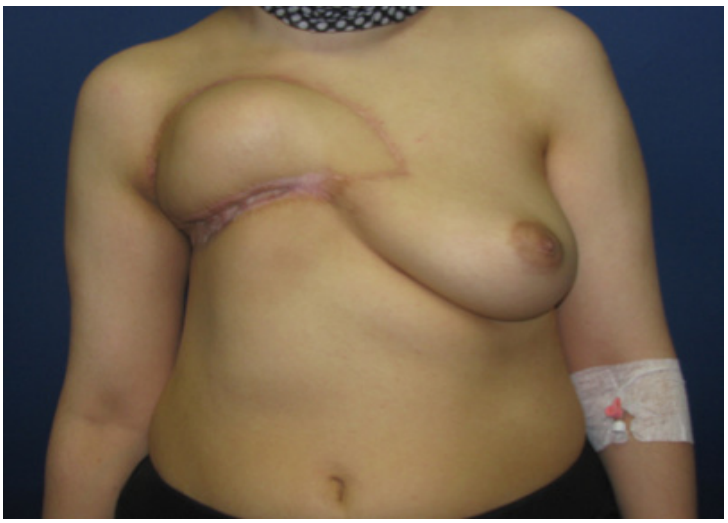


Figure 3: Postoperative image after reconstruction

Radical mastectomy was performed (Figure 2) to the patient without axillary lymph node dissection and the defect was covered with pedicled LD flap plus split-thickness skin graft taken from right thigh on February, 2016 (Figure 3). The specimen was sent to pathology. It was 33x23,5x17 cm and weighted 9.150 kg. Diagnosis of malignant PT was confirmed by microscopic examination (Figure 4). The malignant areas consist of wide necrotic and multiple chondromyxoid differentiation areas with cellular pleomorphism. Tumor has high mitotic rate of >50/10 HPF. Tumor invaded fascia at surgical margin. Patient had radiotherapy for 33 days

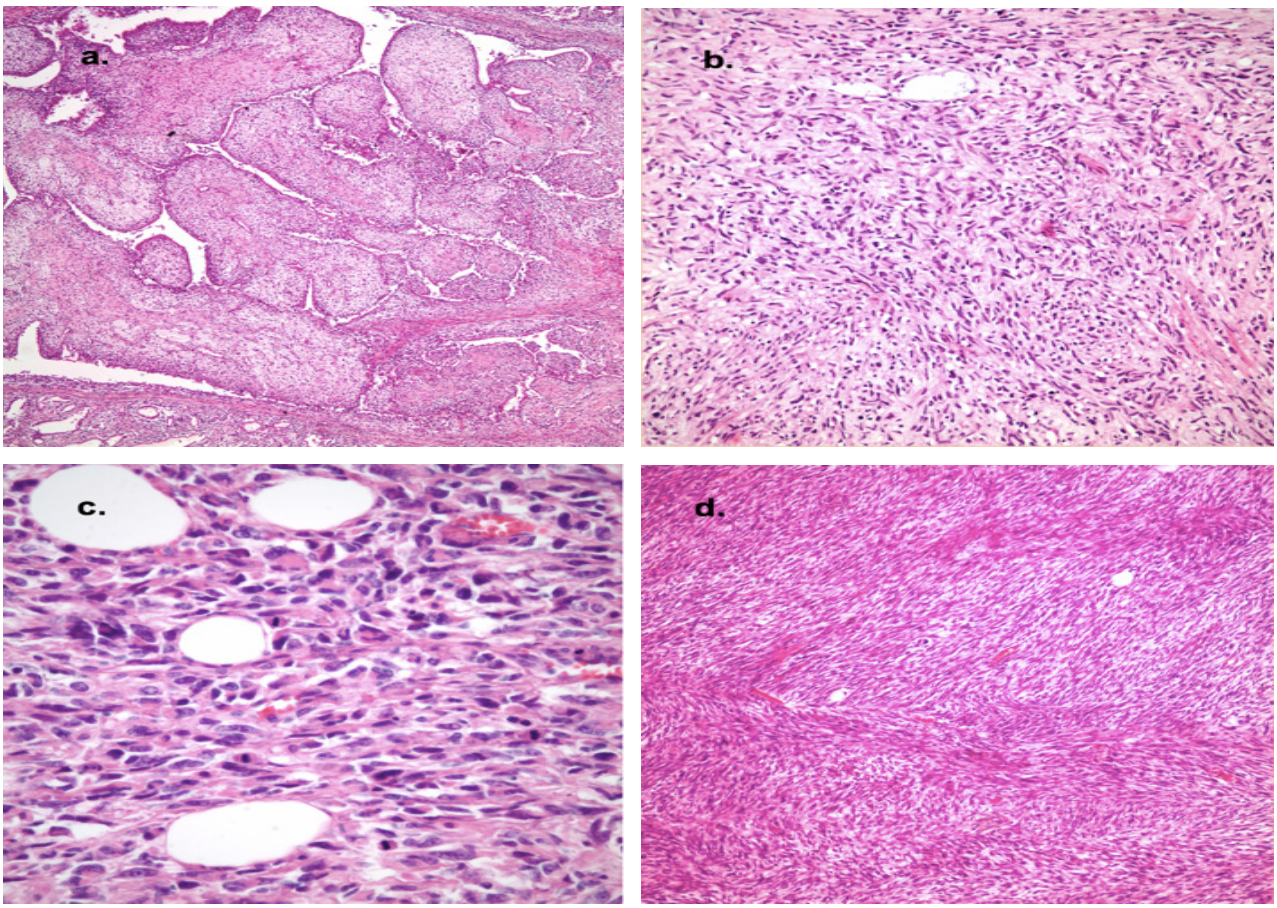


Figure 4: Pathology images

a. Leaf-like structures characteristic of phyllodes tumor, caused by stromal overgrowth
b. Low-intermediate grade sarcoma with increased cellularity and mild cytological atypia
c. High grade sarcoma featuring severe cytological atypia and abundant mitotic figures
d. Storiform and "herring-bone" like pattern, reminiscent of fibrosarcoma

Patient noticed a palpable nodular mass beneath the flap on November, 2016. Ultrasonographic examination, CT scans and MRI showed 11.7x4x3.5 cm recurrent tumor extending to the intercostal adipose tissue with pectoralis minor muscle invasion (Figure 5). Bone scintigraphy showed a focal activity at 3rd costochondral joint which was compatible with local recurrence of the primary tumor.

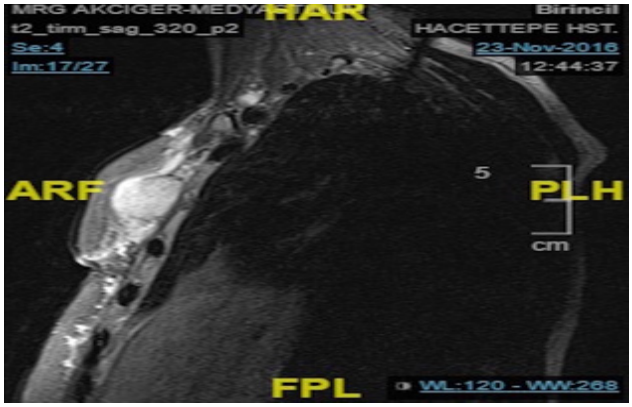
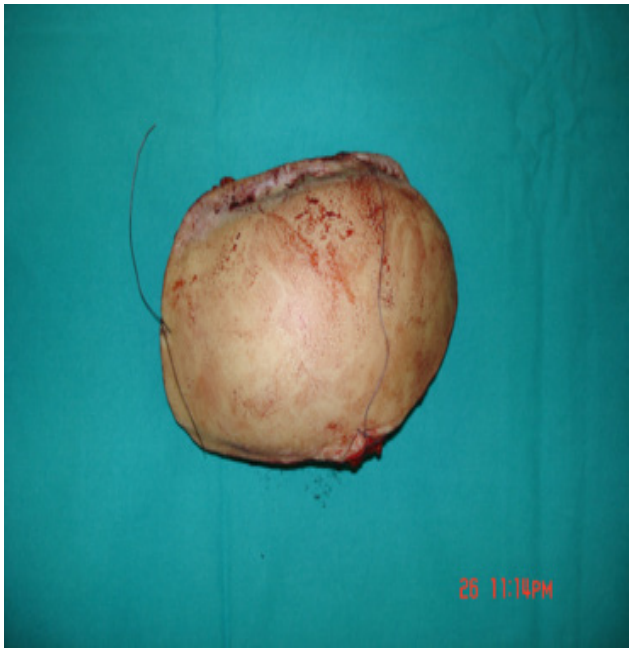


Figure 5: Recurrent tumor beneath the flap. MRI

Segmental resection of 2., 3. and 4. ribs along with recurrent tumor was performed with safety margin of 2 centimeters by thoracic surgery team on December, 2016 (Fig. 6). 32F chest tube was inserted. Thoracic wall defect was patched with Gore-Tex (2 mm) Dual MeshBiomaterial (W.L. Gore and Associates, Flagstaff, AZ, USA) to maintain chest wall stability and prevent lung herniation (Figure 7). Pedicled TRAM flap was harvested from left side of the patient to cover the defect. In addition to superior epigastric vessels of pedicle, superficial inferior epigastric vein from the flap and cephalic vein from right arm were anastomosed to each other to enhance venous return in the basis of venous supercharging. 2 Jackson-Pratt drains were placed beneath the donor site and other two were placed underneath the flap (Fig. 8). Her drains were pulled out and patient was discharged on January, 2017.



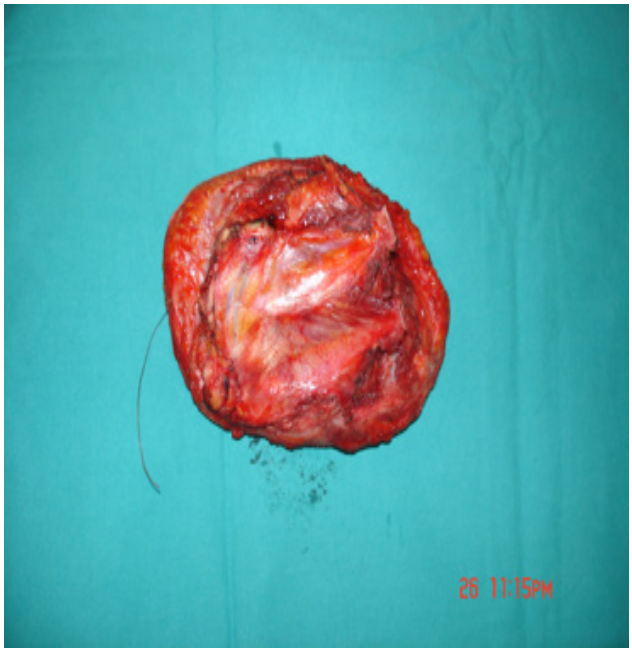


Figure 6: Resection of recurrent tumor beneath the LAD flap along with ribs

One week after hospital discharge, breathing difficulty with shortness of breath and pleural effusion of right lung was encountered on patient's postoperative twentieth day. Effusion was drained using a pigtail catheter by interventional radiology. After complete regression of pleural effusion patient was discharged. In the end, the patient was symptom-free at 9-month follow-up.

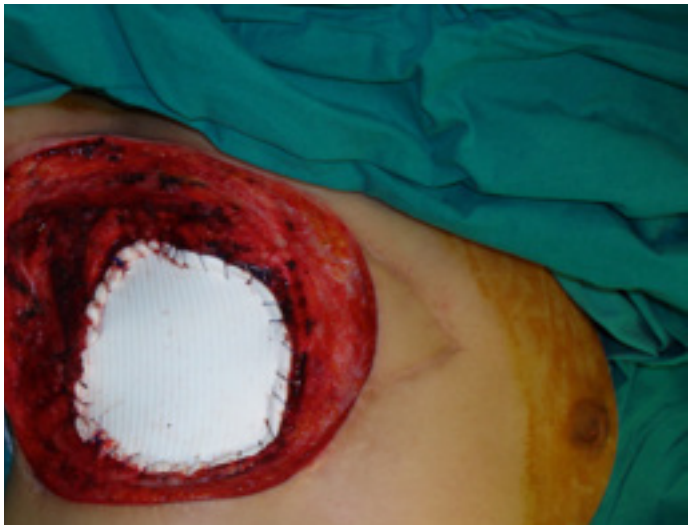


Figure 7: Chest wall reconstruction after rib excision

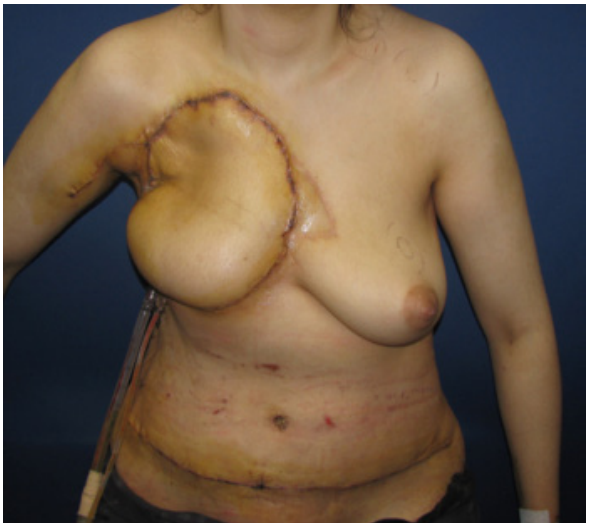


Figure 8: Postoperative image after reconstruction with venous supercharged TRAM flap

DISCUSSION

Chelius was the first who described the PT in 1827, however, Johannes Mull used the term cystosarcoma phyllodes for the first time in 1838. He described this tumor as a large neoplasia with a cystic lobulated structure and rapid growth. Phyllon is the Greek word for leaf, and these biphasic breast tumor has leaf-like projections when viewed histologically and displays combination of cystlike spaces and hypercellular stroma [18-19].

Benign forms may present similar to fibroadenoma. There is no proven relationship between fibroadenomas and PT but in the literature, few cases report that it is possible to transform into a PT from fibroadenomas [20-21]. If there are indications, core needle biopsy is recommended for differential diagnosis. Mammography or ultrasound is not useful in the diagnosis because we cannot get any pathognomonic features by using these. Because of the tumor heterogeneity if there is any remaining clinical suspicion after core needle biopsy excisional biopsy is indicated [9-22].

PTs' size typically varies from 1-45 cm [23]. Salvadori et al. reported no correlation between tumor size and malignant potential [24]. In contrast to that, Ramakant et al. suggested, giant PTs' (>10 cm) malignant potential and local recurrence rates are higher than smaller tumors. So, these tumors require more aggressive treatments and wider surgical resections [25]. In a study, PTs adequately excised with margins not wider than 1 mm have low recurrence rates despite traditional 1-cm wide margin concept [26]. Recurrence rates of phyllodes tumors of the breast range from 15 to 20%. The factor closely associated to local recurrence, more than histological characteristics, is the presence of malignant tumor at the surgical margin [27]. In our case, we had all the factors predicting local recurrence with a continuity at the deep surgical margin, wide necrotic areas, marked pleomorphism and a mitotic rate of >50/10 HPF. It is also reported that stromal overgrowth, infiltrating tumor margins and mitotic activity are all associated with distant metastases [11]. Metastasis could be found almost everywhere in the body. Metastatic lesions are lack of epithelial cells and resemble sarcomatous components of the original PT [28-29]. Grimes et al, also noted that 87.5% of PTs with mitosis greater than 15/10 HPF eventually give rise to metastasis [30]. Local recurrence is also a predicting factor for metastasis. Most of distant metastasis of PT occur after local recurrence [28]. Progression to distant metastasis is the main prognostic factor which reduces survival to 1-24 months [3-31]. Guerrero et al. suggested, if there are recurrences, bone metastasis or surgical margin free of tumor is not obtainable radiotherapy is needed [15]. But the use of chemotherapy and radiotherapy in malignant tumors is still controversial. Mastectomy is performed for large tumors (>10cm), recurrent tumors and for patients having tumors of <10cm with small breast [32]. Several reconstructive options have been described after mastectomies. As discussed in this case, immediate breast reconstruction with flaps following a mastectomy is an option for these patients. In addition to that, application of

vacuum-assisted closure after mastectomy to temporize the wound coverage until the determination of negative surgical margins by the pathology report is an alternative surgical approach. After the determination of full tumor resection, definitive reconstructive surgery is performed [33].

In our case, we presented a giant malignant PT with chest wall invasion and local recurrence. There is urgent need for reliable predictive factors to identify patients at high risk of local recurrence and distant metastasis. To date, although PTs have poor prognosis, there is no established consensus regarding the multidisciplinary treatment strategies for PTs. Multicenter well-designed prospective studies should be conducted for multidisciplinary treatment algorithms.

In conclusion, our patient presented with an agressive recurrent giant form of phyllodes tumor. Unfavourable prognostic criteria and inadequate surgical margins may lead to local recurrence as in our case. PT of breast is a rare entity with distinct clinicopathological features. There is no standardized optimal type of surgery and treatment algorithm. In the future, multicenter clinical studies should be performed for standardized multidisciplinary approach to malign PT of the breast

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 if requested.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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