

Coexistence of a Malignant Phyllodes Tumor of the Breast with Heterologous Elements (Osteosarcoma and Chondrosarcoma) and Invasive Ductal Carcinoma: Case Report and Review of the Literature

Nicolas Ashjian¹, Cynthia Mehrabi¹, Lawrence Willes², Lana Louie³ and Brian Dickinson^{1*}

¹Plastic and Reconstructive Surgery, 351 Hospital Road Suite 415, Newport Beach, CA, USA

²Adventist Health Glendale, 1509 Wilson Terrace, Glendale, CA, USA

³Breast Surgery, 18370 Burbank Blvd. Suite 607, Tarzana, CA, USA

*Corresponding author: Brian Dickinson, Plastic and Reconstructive Surgery (Private Practice), 351 Hospital Road Suite 415, Newport Beach, CA, USA. E-mail: drdickinson@drbriandickinson.com

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Abstract

Malignant phyllodes tumor (MPT) is a rare lesion in the female breast, representing less than 1% of all breast tumors. There have been case reports of coexistent breast carcinoma (both ductal and lobular carcinomas) with MPT. This coexistence has been shown to be associated with the malignant category of phyllodes tumors. Rarely, is breast carcinoma diagnosed preoperatively in the setting of MPT. We report a case of regionally metastatic MPT with heterologous components of osteosarcoma and chondrosarcoma with an incidental finding of an internal mammary lymph node positive for invasive ductal carcinoma while the axillary lymph nodes are positive for the sarcoma. This case is presented along with a literature review. The multidisciplinary breast care team must be aware of the coexistence of carcinoma and MPTs and consider a thoughtful treatment plan for extirpation and reconstruction with potential need for radiation and systemic therapy.

Keywords: Breast cancer; Phyllodes tumor; Breast cancer staging

Introduction

Malignant phyllodes tumors (MPTs) are rare biphasic breast tumors (composed of both epithelial and stromal components) accounting for less than 1% of primary breast malignancies [1]. Phyllodes tumor (PT) of the breast are classified into benign, borderline, and malignant categories based on histopathological features defined by the World Health Organization (WHO). These criteria focus on stromal characteristics and tumor behavior, with classification impacting treatment and prognosis [2]. The classification is based on five primary features: 1) stromal cellularity, 2) stromal atypia, 3) mitotic activity, 4) tumor borders, and 5) stromal overgrowth. They are benign in 60-75%, borderline in 15-26% and malignant in 8-20% of cases [3].

When the stromal component contains heterologous differentiation, such as liposarcomatous, chondrosarcomatous, and/or osteosarcomatous differentiation, this automatically classifies the PT as malignant (with the exception of well-differentiated liposarcoma). Malignant phyllodes tumors (MPTs) with osteosarcomatous differentiation account for about 1.3% of all PTs of the breast [4]. MPTs with osteosarcomatous or chondrosarcomatous differentiation are rare aggressive variants with unfavorable prognostic significance for recurrence, metastasis, and mortality. Any PT with a size greater than 10 cm is considered a 'giant PT,' and has a higher propensity for local recurrence [5].

Invasive ductal carcinoma (IDC) arises from the epithelial components of the breast and accounts for 80% of all breast cancers. The coexistence of PT with breast carcinoma, either in situ or invasive, is uncommon, with reported incidence rates ranging from 1.1% to 13.7% [6-8]. We describe the case of an IDC coexisting with an ipsilateral high-grade MPT containing both osteosarcomatous and chondrosarcomatous differentiation in a patient with a MET germline mutation-of unknown significance. Our case highlights the importance of increased vigilance in assessing MPTs for concurrent carcinomatous involvement and regional lymph node metastasis. It illustrates the challenge of treating patients with these distinct yet intertwining breast malignancies. While the mainstay of treatment of MPTs is wide local excision, there is no standard role for lymph node dissection, radiation, or chemotherapy. The treatment of IDC includes the routine combination of mastectomy or partial mastectomy, lymph node evaluation, endocrine therapy, chemotherapy, and radiotherapy. There are no uniform guidelines for the management of concurrent MPT with invasive carcinoma.

Case Presentation

The patient is a 55-year-old nulliparous woman with a maternal history of breast cancer who presented with a progressively increasing left breast mass. She first noticed the lesion getting larger in September 2024. In November 2024, the patient underwent a core-needle biopsy which revealed a fibroepithelial lesion with marked stromal hypercellularity and moderate atypia. An ultrasound showed a 9.5 cm lobulated coarsely calcified mass occupying most of the left breast. The MRI revealed an 11 cm mass in the left breast with no evidence of axillary lymphatic involvement (Figure 1). The lesion did extend to and involve the pectoralis major muscle in addition to the nipple-areolar complex. The right breast was negative for any evidence of disease. The patient declined plastic surgery consultation and was interested in proceeding with a mastectomy. In December 2024, the patient underwent a left mastectomy with axillary lymph node biopsy with no reconstruction. Her final pathology revealed a 14.0 cm malignant phyllodes tumor with heterologous chondrosarcoma and osteosarcoma elements (marked stromal cellularity, moderate atypia, 30 mitoses per 10 HPFs) (Figure 2). All her margins were negative for disease with the closest margin of 3 mm. Two of the three axillary sentinel lymph nodes were positive for macro-metastatic MPT (sarcoma) disease (Figure 3). She underwent a left axillary dissection in January which removed 8 additional lymph nodes all negative for disease. She declined genetic testing preoperatively but after her mastectomy, a genetic test revealed a MET mutation-of unknown significance. Within 3 weeks from her mastectomy, a solid mass developed superior and lateral to her transverse mastectomy incision. Ultrasound examination of the mass revealed a 3.1 cm irregular mass (Figure 4). The mass was solid, immobile, and adherent to the overlying skin, but not the pectoralis muscle (Figure 5). In February 2025, she underwent a wide local excision of the recurrence and surrounding skin with an immediate left deep inferior epigastric artery free flap reconstruction of the chest wall. The internal mammary vessels were used as the recipient vessels. (Figure 6). The re-excision revealed a high-grade sarcoma consistent with recurrent malignant phyllodes tumor (4.8 cm) involving the dermis, and focally the skeletal muscle (Figure 7).

A final deep margin consisting of pectoralis major muscle was negative. An additional left axillary lymph node was negative for malignancy; however, the left internal mammary lymph node was positive for invasive ductal carcinoma (ER+, PR+, and HER2 positive) (Figure 8). A metastatic workup was negative. She received radiotherapy of 27 treatments in the cumulative amount of 5000 cGy to the chest wall and draining lymphatic basins with a 1000 cGy boost to the area of recurrence. Medical oncology placed her on a regimen of Pazopanib. At the completion of Pazopanib, she will continue with 1 year of trastuzumab and endocrine therapy. After 7 months of follow-up the patient is recurrence free.

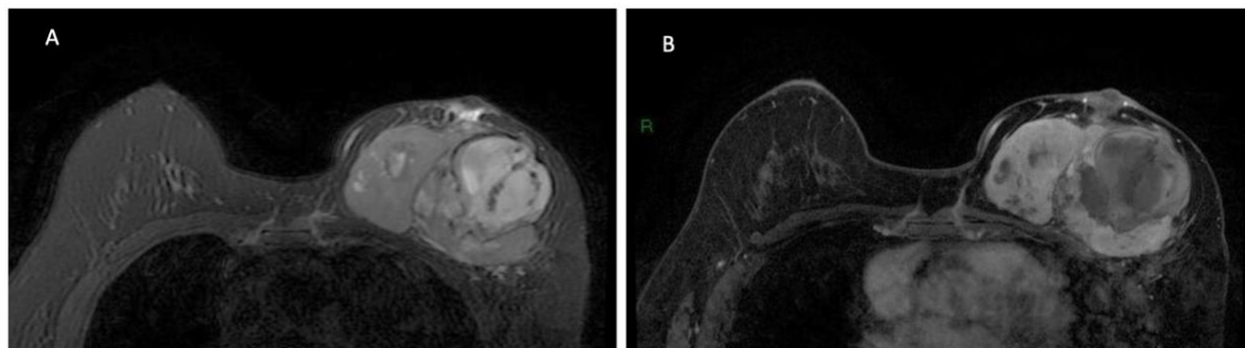


Figure 1: Preoperative MRI of Left MPT. A) Axial T2 fat sat MRI showing 11 cm lobulated heterogeneously enhancing mass with extensive necrosis. B) Axial post contrast T1 fat sat MRI showing mass invading lower pectoralis major muscle as well as the nipple-areola complex. Areas of necrosis visualized.

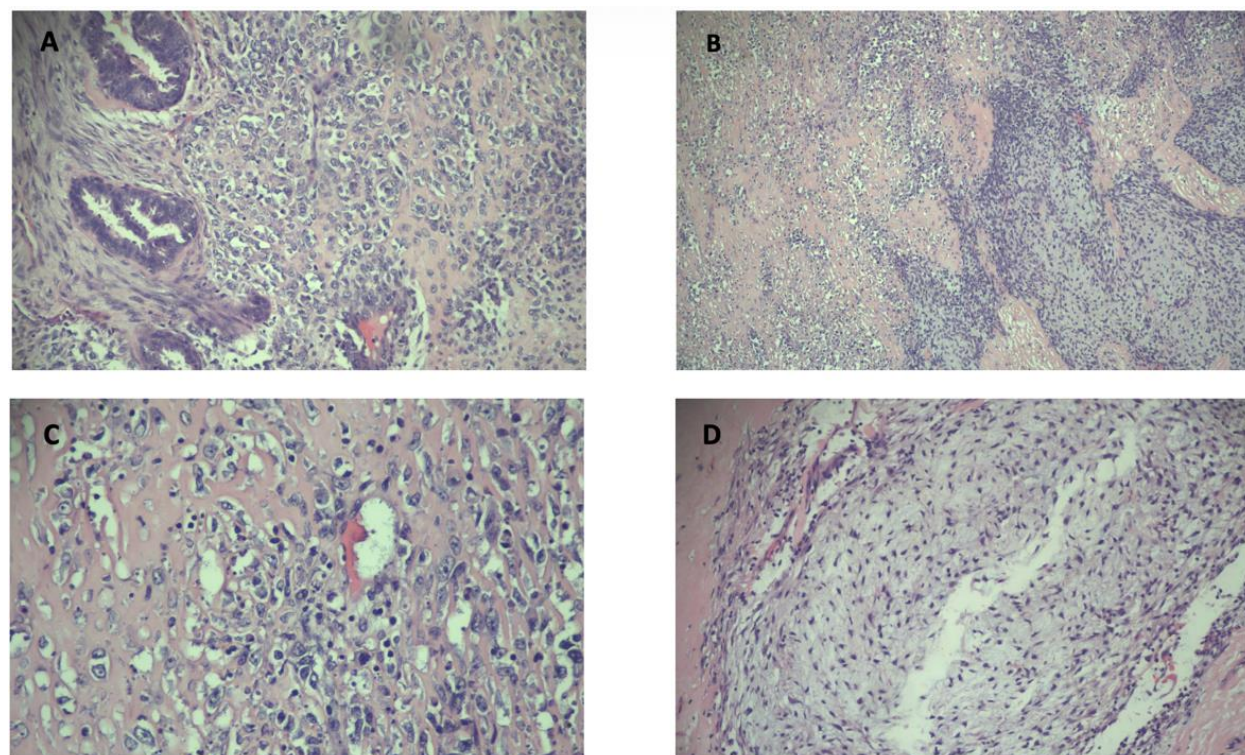


Figure 2: Pathology of MPT after initial mastectomy. A) High power showing mesenchymal epithelial biphasic aspect with a malignant stromal component around epithelial elements. B) Low magnification showing malignant stroma with heterologous differentiation (osteosarcoma and chondrosarcoma). C) Between the malignant cells are areas of eosinophilic amorphous extracellular matrix, consistent with osteoid. This is suggestive of osteosarcoma heterologous elements. D) Slide demonstrates chondrosarcomatous elements of the MPT with pale blue/light purple hyaline chondromyxoid extracellular matrix (relatively hypocellular) characteristic of cartilage.

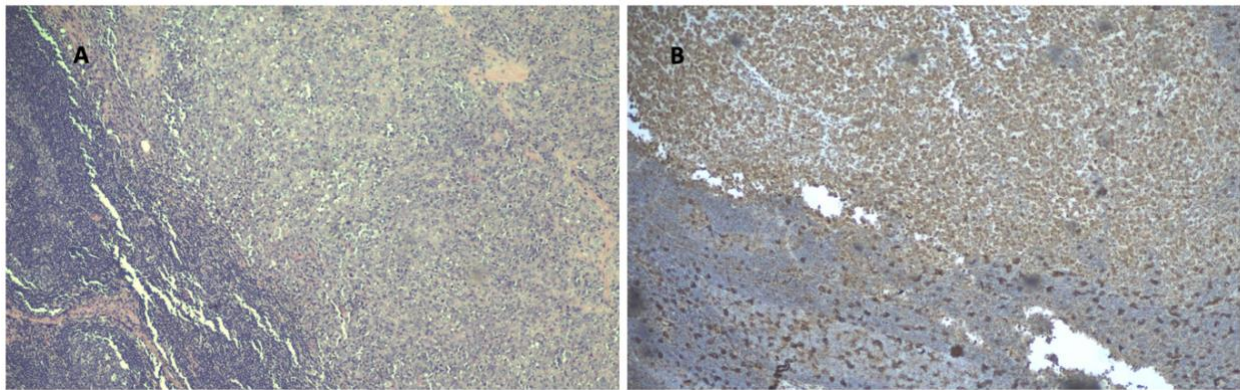


Figure 3: Axillary lymph node biopsy from initial mastectomy. A) Image showing metastatic sarcoma to the axillary lymph node with the normal lymph node architecture replaced by dense, hypercellular areas of atypical spindle to epithelioid cells. The metastatic component is entirely stromal in nature. B) Image shows positive vimentin immunohistochemical staining confirming the mesenchymal origin (sarcoma) of the metastatic tumor cells.

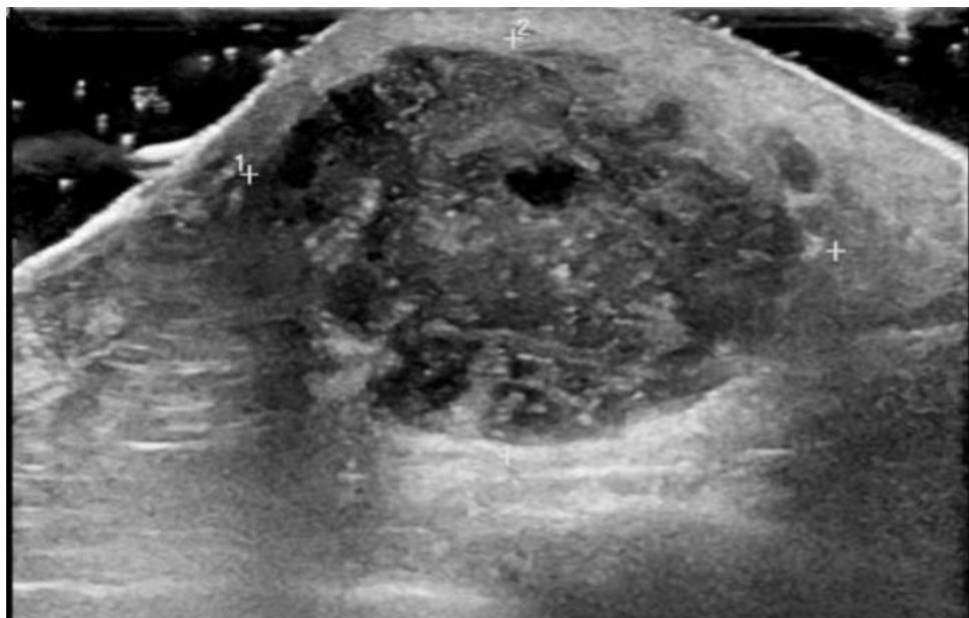


Figure 4: Ultrasound examination of the recurrent MPT on upper outer aspect of mastectomy incision. Image demonstrating a 3.1 cm irregular hypoechoic mass with internal vascularity.



Figure 5: Recurrent MPT several weeks after mastectomy in the lateral aspect of the transverse mastectomy scar.



Figure 6: Left chest wall reconstruction after wide excision of recurrent MPT with a deep inferior epigastric artery perforator flap. The recipient vessels were the left internal mammary vessels after resection of the 3rd costal cartilage.

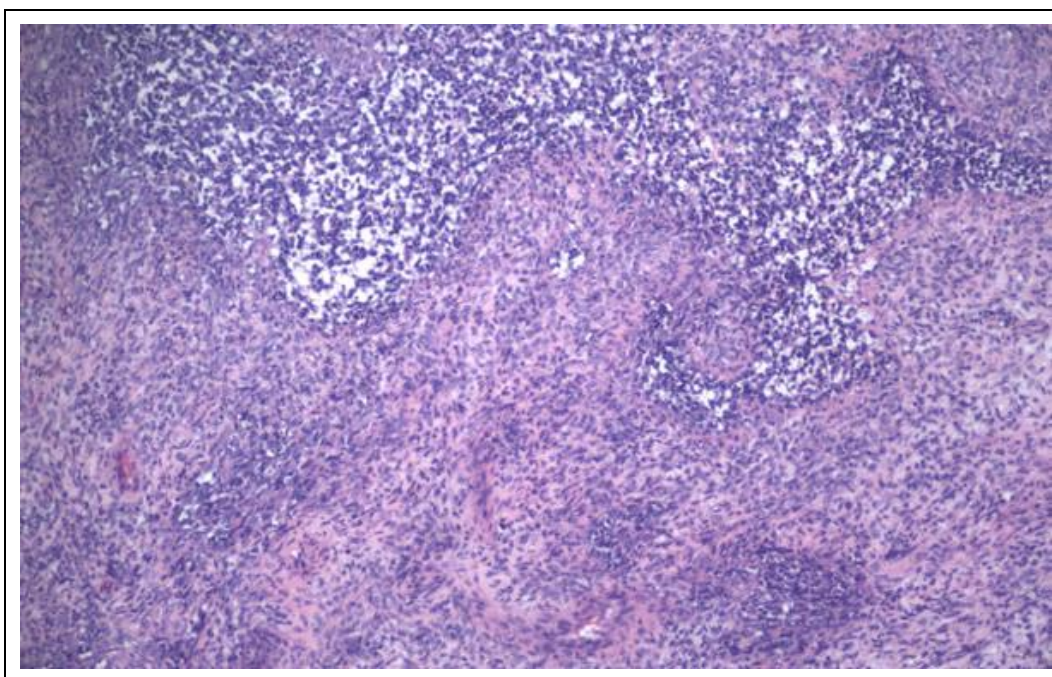


Figure 7: Pathology after wide excision of recurrent MPT. Image shows highly cellular lesion with a dense proliferation of spindle to epithelioid-shaped stromal cells, consistent with the sarcomatous component of MPT. There is marked nuclear atypia, with enlarged, hyperchromatic and pleomorphic nuclei. Overall architecture is disorganized with absent epithelial component.

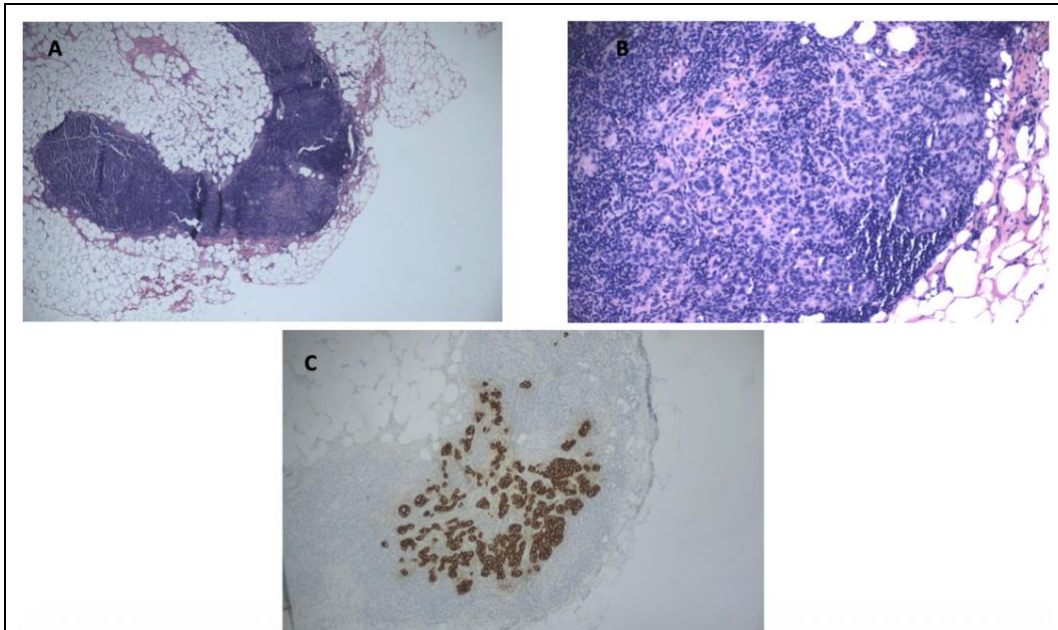


Figure 8: Left internal mammary lymph node. A) Low power showing section of IM node with small (micrometastatic) foci of metastatic carcinoma. Largest focus of carcinoma measured 1.07mm. B) On higher magnification, typical features of ductal carcinoma with irregular cell arrangements forming small groups and occasional glands with moderately pleomorphic nuclei. C) Pan-cytokeratin immunostaining demonstrates high sensitivity for epithelial tumors. The well-defined staining pattern confirms the epithelial nature of the metastatic cells within the internal mammary lymph node.

Discussion

To our knowledge, this is the first report of a concurrent ipsilateral IDC and MPT with osteosarcoma and chondrosarcomatous differentiation. The breast carcinoma was found as an incidental finding during the biopsy of an internal mammary lymph node while the recipient internal mammary vessels were being prepared for deep inferior epigastric artery perforator (DIEP) free flap reconstruction. While epithelial proliferation is a common feature of PTs, epithelial malignancy is rare. Concurrent presentation of MPTs and ductal carcinoma is even more rare, with management and outcome data limited to case reports [9-14]. In our case, the MPT component is classified as Stage IV (T3N1MX) and the breast carcinoma component is classified as Stage IB (T0N1bM0).

MPTs are identified when the tumor exhibits marked stromal nuclear pleomorphism, stromal overgrowth with infiltrating borders, severe nuclear atypia, and increased mitotic activity (> 10 mitoses per high-power fields) [1]. The presence of malignant heterologous components such as osteosarcoma, chondrosarcoma, and liposarcoma are occasionally observed. In such cases, the differential diagnosis of metaplastic carcinoma, primary osteosarcoma, or myositis ossificans must be made [15]. Osteosarcoma only differentiation account for 1.3% of MPTs [4]. These tumors are potentially more aggressive (especially when surpassing 5 cm) and have a greater potential to metastasize to the lung, brain, bone, and contralateral breast [16].

While epithelial proliferation is common in PTs, epithelial malignancy is rare. Breast cancer may coexist with MPTs in two situations: within the MPT of the ipsilateral breast or separate from the MPT in the ipsilateral breast. While the etiology of carcinoma arising away from the PT may be coincidental, the underlying etiology of a carcinoma arising within a PT or MPT may be multifactorial [17]. In our case, we did not identify the ductal carcinoma in the breast pre- or post-surgical, which effectively establishes a diagnosis of unknown primary invasive ductal carcinoma. Therefore, determining if the carcinoma was contained within the MPT or in the surrounding breast parenchyma was not possible. In a review, Cook et al. identified a total of 98 cases of in-situ or invasive carcinoma within PTs. Cases of synchronous carcinoma in the ipsilateral or contralateral breast were excluded [8]. They found that MPTs correlated with a higher likelihood of epithelial malignancy, suggesting that malignant stroma may have a role in the malignant transformation of the epithelium. They found that a greater proportion of carcinomas within MPTs and borderline PTs were invasive compared to benign PTs. Of the 40 carcinomas within MPTs, 20 were invasive versus in-s(50%) compared to 7 of the 16 within borderline (44%) and 12 of 34 within benign tumors (35%). Previous molecular studies have postulated a pathophysiological relationship between the epithelium and stroma of PTs [18-20].

Preoperative determination of coexistent breast carcinoma within or adjacent to a PT is essential to help plan surgical intervention. For example, while sentinel lymph node evaluation does not have a routine role in the surgical treatment of MPTs, it does have a role in the treatment of invasive breast carcinoma. However, if breast carcinoma coexists within or close to a PT, preoperative assessment is difficult because the PT might obscure the carcinoma presentation on either clinical breast exam or imaging. In a series by Gemci et al., none of the 4 coexistent breast carcinomas were diagnosed by preoperative core biopsies [6]. A comprehensive workup includes mammography, MRI, core needle biopsy, and genetic evaluation in patients with a family history of breast cancer or multisite malignancies in multiple family members.

The management of MPTs is primarily surgical excision. Both breast-conserving surgery (BCS) and mastectomy are feasible options which primarily depend on the overall size of the lesion in relation to the overall breast volume. Margins of 1 cm are generally accepted [21,22] Su et al. reviewed a total of 134 cases of borderline and malignant phyllodes tumors. With 66-month follow-up, their data showed a local recurrence rate of 22.7%, a distant metastasis rate of 6%, and a mortality rate of 4.7%. They showed that patients with tumors that were resected with at least 1 cm margins had statistically significant higher 5-year local recurrence-free survival (LRFS) and disease-free survival (DFS). They strongly advocated for re-excision to obtain at least 1 cm margins. Tumor size greater than 5 cm and age less than 45 were predictors of recurrence [23] Li et al. studied 212 patients with MPT in a retrospective study of patients diagnosed between 2006 and 2020. Recurrence was seen in 29.8% of patients with young age, presence of malignant heterologous elements, a history of prior fibroadenomatous surgery, and surgical margins less than 1 cm [24].

Axillary lymph node involvement is rare in MPT and routine lymph node sampling is not often advised. The incidence of axillary lymph node involvement in several studies ranged from 1.1%–3.8% [25-29]. Since most sarcomas metastasize hematogenously, this finding may explain why axillary metastasis is so rare. Considering the rarity of lymph node involvement, most authors have concluded that removal of axillary lymph nodes is not warranted unless they are clinically abnormal.

The role of adjuvant radiotherapy for the treatment of MPT has mixed results and no standard recommendation has been provided. However, over the past 20 years, the number of patients who received radiotherapy has grown. In a study of 3,120 patients with MPT, Gnerlich et al. showed that adjuvant radiotherapy (RT) significantly reduced local recurrence (LR), but did not impact DFS or overall survival (OS) [30]. Barth et al. prospectively treated 46 patients with MPT and showed a significantly lower rate of LR in patients treated with adjuvant RT after margin-negative resection (0 out of 46) during 56-month follow-up as opposed to reported rates of LR in margin-negative resection alone [31]. Chao et al. showed a significant decrease in LR (8% vs 12%) and metastasis (4% vs 8%) with the use of adjuvant RT with no impact on OS [32]. Despite some positive results for RT, Neron et al. found no difference in LRFS, metastasis-free survival (MFS), and OS rates with the use of adjuvant RT in a study of 212 cases of MPT [33]. In a study to evaluate the time of adjuvant RT in the treatment of borderline and MPT, Yogi et al. showed that the recurrence rate increases significantly when RT is administered after 1 month of surgery [34]. The positive impact on LR appears to be particularly relevant after BCS [35]. The benefit of RT is less clear for patients undergoing mastectomy [36]. Currently, for patients diagnosed with borderline or MPT, adjuvant radiotherapy should be considered to decrease LR in patients undergoing BCS and for those who have tumors greater than 2 cm, or for patients undergoing mastectomy with tumors greater than 10 cm [37]. Also, consideration should be given to patients who have high-grade histology, close margins, or recurrent disease. With the increased use of adjuvant RT especially in academic centers, the reconstructive plastic surgeon needs to take RT into consideration especially when deciding on treatment options for breast reconstruction after mastectomy for MPT. This may alter the decision-making of implant-based vs. autologous reconstruction and if the reconstruction should be done in an immediate vs. delayed setting.

The impact of adjuvant chemotherapy has not shown an overall benefit in LRFS or OS in the treatment of MPT [33,38]. Zhuang et al. studied 145 patients with MPT without distant metastasis with a follow-up of 54 months. The recommended chemotherapy primarily consisted of anthracyclines, including anthracycline and ifosfamide or anthracycline and cyclophosphamide/docetaxel regimens. Chemotherapy did not show better five-year LRFS or OS after propensity score matching [39]. Atram et al. studied 11 patients with MPT with heterologous sarcomatous differentiation. They utilized adjuvant chemotherapy in 8/11 (73%) of the patients using ifosfamide and epirubicin. Their data demonstrated a lower recurrence and metastatic rate in patients treated with chemotherapy [40]. Li et al. showed that patients with malignant heterologous elements who received adjuvant chemotherapy had a statistically significant reduced risk of recurrence [24]. Li et al. published a case report of a patient with MPT with predominantly osteosarcomatous and chondrosarcomatous differentiation. The patient was treated with mastectomy and adjuvant chemotherapy using anthracycline and ifosfamide. The patient was without recurrence at 8 months of follow-up [15]. There have been several case reports of concurrent presentation of invasive carcinoma and borderline and/or malignant phyllodes tumors (Table 1).

Table 1: Summary of treatment and outcomes for concurrent invasive ductal carcinoma and borderline or MPTs.

Patient	PT Type	Size of the PT (cm)	Carcinoma	ER/PR/HER2	Lymph Node Bx	Surgery	Radiotherapy	Systemic Tx	Follow-up	Reference
1	Malignant	12	IDC	Pos/Pos/Neg	No	Lumpectomy	No	No	AW 10 months	6
2	Malignant	20	IDC	Pos/Pos/Neg	Yes	Total Mastectomy	Yes	No	Death unrelated causes	6
3	Borderline	2.5	IDC	Pos/Pos/Neg	No	Lumpectomy	No	No	AW 22 months	6
4	Malignant	24	IDC	Neg/Neg/Neg	No	Total Mastectomy	Yes	No	12 months no recurrence	9
5	Borderline	10	IDC	Pos/Pos/Neg	Yes (1/2 positive)	Total Mastectomy	No	5-fluorouracil, Epirubicin, Cyclophosphamide, Tamoxifen, Goserelin	AW 15 months	14
6	Borderline	15	IDC	Neg/Neg/NA	Yes (Negative)	Total Mastectomy	No	No	AW 38 months	13
7	Borderline	3.0	IDC	Neg/Neg/Neg	Yes (1/21)	Total Mastectomy	Yes	Paclitaxel, Pirarubicin, Cyclophosphamide	AW 23 months	12
8	Borderline	7.0	IDC	Pos/Pos/NA	Yes (Negative)	Total Mastectomy	No	Tamoxifen	AW 3.6 years	45
9	Malignant	6.0	IDC	Neg/Neg/Neg	Yes (Negative)	MRM	No	Cyclophosphamide, Doxorubicin, 5 Fluorouracil, Paclitaxel	Lung metastases 32 months; Mortality 40 months	46
10	Malignant	11.0	IDC	Neg/Neg/NA	Yes (Negative)	Total Mastectomy	Yes	Yes	AW 11 years	47
11	Malignant	5.0	IDC	Pos/Pos/Neg	Yes (Negative)	MRM	Yes	Hormonal therapy	AW 39 months	47
12	Malignant	4.0	IDC	Neg/Neg/Neg	Yes (Negative)	MRM	Yes	No	Death at 56 months (contralateral breast cancer with mets)	47
13	Malignant	9.0	IDC	Pos/Pos/Pos	Yes (4/19 positive)	MRM	Yes	Adriamycin, Cyclophosphamide, Paclitaxel, Herceptin, Tamoxifen	AW 6 years	48
14	Malignant	4.0	IDC	Neg/NA/Neg	Yes (Negative)	Total mastectomy	No	No	AW 70 months	44
15	Borderline	6.5	Invasive tubular carcinoma	Pos/Pos/NA	Yes (Negative)	Lumpectomy	Yes	No	N/A	49
16	Malignant	6.0	IDC	Neg/Neg/Neg	Yes (Negative)	MRM	No	No	N/A	50
17	Malignant	3.5	Invasive carcinoma	Neg/Neg/NA	Yes (Negative)	MRM	No	Cyclophosphamide, Methotrexate, 5-Fluorouracil	Recurrence at 10 months (Excision with RT)	51
18	Malignant	21	IDC	Pos/Pos/NA	Yes (2/12 positive)	Total Mastectomy	Yes	Cyclophosphamide, Adriamycin; Tamoxifen	AW 11 months	52
19	Malignant	10	Invasive cribriform carcinoma	Pos/Pos/Neg	Yes (Negative)	Total Mastectomy	No	Cyclophosphamide, Adriamycin, 5-Fluorouracil	AW 24 months	53
20	Malignant	15.5	Invasive carcinoma	N/A	Yes (11 positive)	Total mastectomy	Yes	Yes	N/A	54

We report a concurrent invasive ductal carcinoma along with a MPT with heterologous components. Our case is unique as the carcinoma component was an incidental finding on the internal mammary lymph node biopsy. It is also unique as a case of unknown primary breast cancer with the site of origin presumed to be the ipsilateral breast. Our review presents 20 cases of concurrent invasive ductal carcinoma MPT (6 Borderline and 14 Malignant). There were 16 invasive ductal carcinomas, 1 case of invasive cribriform carcinoma, 1 case of invasive tubular carcinoma, and 2 cases of invasive carcinoma with no specified type. The average size of the MPT was 9.75 cm. The majority of the cases were treated by mastectomy (90%; 18/20) and the majority had sentinel lymph node biopsies (85%; 17/20). Of those patients who had lymph nodes sampled, 29.4% (5/17) had positive lymph nodes for carcinoma. Approximately 50% of the patients were treated with adjuvant radiotherapy and 45% (9/20) were treated with chemotherapy. The most common chemotherapy was cyclophosphamide, 5-Fluorouracil, and Adriamycin. Those patients with ER+ invasive carcinomas were treated with ant-hormonal therapy (e.g. Tamoxifen.) The majority of the patients were alive and well during the follow-up period with 1 patient deceased from lung metastasis at 40 months. Our review of the literature shows a relatively low recurrence rate in the reported follow-up times with mastectomy and adjuvant radiation and chemotherapy. It is interesting to note that none of the cases of coexistent ductal carcinoma with MPT were diagnosed in the preoperative setting with core needle biopsy or imaging.

We have previously reported the importance of routine sampling of the internal mammary lymph nodes during microvascular deep inferior epigastric artery perforator (DIEP) flap reconstruction [41]. This can be done safely and expeditiously during the internal mammary recipient vessel harvest [42,43]. It has also been reported by others that information acquired from these nodes is valuable and can often lead to upgrading the stage of the cancer and alter post-operative management. In our case, the finding of invasive ductal carcinoma was discovered through internal mammary node biopsy. The pathological evaluation of the MPT or remaining breast tissue did not reveal any invasive ductal component. The internal mammary lymph node biopsy resulted in the change in management as the internal mammary lymph node chain was included in the radiotherapy field. Our patient was ER positive, PR positive, and HER2/neu positive. She will most likely receive hormonal therapy after adjuvant chemotherapy. The benefit of Herceptin in this setting is being evaluated by a multidisciplinary team. Gemci et al. reported the coexistence of carcinoma with borderline PT of 20% (2/10) and with malignant PT of 40% (2/5) [6]. Co et al. performed a review of 557 PT cases over 20 years. Their study reported the coexistence of carcinoma in PT of 1.1%, however, they showed a statistically significant incidence of ductal carcinoma in MPT vs benign or borderline PT (4.7% vs 0.6%, $P=0.22$) [44].

Conclusion

The incidence of ductal carcinoma coexisting with PT is rising due to the higher index of suspicion and more thorough pathological evaluation, particularly in the setting of MPT. The presence of ductal carcinoma is clinically significant as it will likely change adjuvant management. Preoperative biopsy and imaging are not reliable at detecting synchronous ductal carcinoma. For patients suspected of having MPT on preoperative biopsies, size of the lesion, and clinical behavior, the breast surgeon should have a high index of suspicion for a potential concurrent carcinoma and the pathologist must thoroughly evaluate the specimen. If surgical management of borderline or MPT involves a mastectomy, consideration for a sentinel lymph node biopsy should be included. The reconstructive microsurgeon should consider evaluating the internal mammary lymph nodes at the time of DIEP reconstruction to the internal mammary recipient vessels. A strong family history of breast cancer or known genetic mutations that increase the risk of breast carcinoma (BRCA, CHEK2, PALB2, ATM, TP53, etc.) must also be kept in mind. Achieving the most accurate diagnosis with a multidisciplinary approach to treatment will increase the clinical outcomes of this unique class of patients.

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