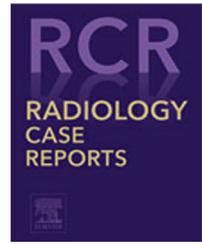
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Case Report

Classic illustrations of benign and malignant phyllodes breast tumors in two patients [☆]

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ABSTRACT

Phyllodes tumors, World Health Organization fibroepithelial tumors, are classified as benign, borderline, or malignant based on histopathology. Phyllodes must be distinguished from benign fibroadenomas, also WHO fibroepithelial tumors. The distinction of phyllodes from fibroadenomas can be challenging clinically, as these tumors may mirror one another. Here, we present 2 cases, classic clinical and imaging examples of benign and malignant phyllodes, to review the current epidemiology, classification, diagnosis, and treatment of phyllodes tumors.

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Introduction

Mammary fibroepithelial tumors represent biphasic neoplasms composed of epithelial and stromal components of the breast [1]. Among these types of World Health Organization-classified tumors are fibroadenomas and phyllodes tumors (previous name: cystosarcoma phyllodes); fibroadenomas are benign and phyllodes tumors are classified as benign, borderline, or malignant [1]. Classically, a fibroadenoma presents in younger patients (< 35 years old) as a small, well-defined mo-

bile mass that can increase in size and tenderness during periods of increased estrogen (as in pregnancy, early menstrual period) [2]. Phyllodes tumors often present in older patients (commonly postmenopausal) as a rapidly enlarging mass [1]. As opposed to fibroadenomas, phyllodes tumors may be malignant and can rarely metastasize [3]. While age may help to distinguish the 2 types of fibroepithelial tumors, fibroadenomas may be found in postmenopausal women, and phyllodes tumors have been described in younger women. The distinction of phyllodes from fibroadenomas can be challenging clinically, as these tumors may mirror one another [4].

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Table 1 – Fibroepithelial phyllodes neoplasms WHO 5th ed 2019 - Histopathologic Classification.

Benign phyllodes	Path definition: lacks stromal overgrowth, occasional mitoses up to 5 per 10 high-power fields (hpf), delimited and pushing margins, mild to moderate stromal cytologic atypia. Areas of sparse stromal cellularity may incorrectly lead to diagnosis of a fibroadenoma. Mimics giant, juvenile fibroadenoma clinically. Treatment is surgical excision.
Borderline phyllodes	Some but not all characteristics of malignant phyllodes tumor are observed. Treatment is surgical excision.
Malignant phyllodes	Path definition: stromal overgrowth, mitotic activity of > 10 per 10 hpf, permeative margins, marked stromal hypercellularity with cytologic atypia. Hallmark clinically is rapid enlargement. Treatment is surgical excision. Complications of phyllodes tumors include metastases and recurrence. Metastases are rare among all phyllodes types but are highest among malignant phyllodes and reported up to 31%.

The etiology of phyllodes tumors remains unclear [1]. Although the incidence of phyllodes tumors is rare (2.1 per million) [5], it is believed Asian and Latina women have an increased risk of phyllodes at a younger age. Birthplace may be a predictor for Latina whites as those born in Central and South America may have up to a 4-fold greater risk of malignant phyllodes tumor than Latina whites born in the United States; US born Latina whites more closely approximate the risk of other white women [6]. The typical clinical features of phyllodes tumor are palpable, painless breast masses with rapid growth and, on clinical breast exam, the tumors are circumscribed, oval or round, mobile, and firm (similar to fibroadenomas) [4,7].

While imaging studies may be the first method to detect a phyllodes tumor, it is often difficult to distinguish from a giant fibroadenoma [8]. A core needle biopsy allows for preoperative diagnosis, but given limited sampling, may be problematic in assessing the stromal and epithelial components between fibroadenoma and benign and malignant phyllodes tumor [9]. For this reason, histologic evaluation postoperatively following excisional biopsy (benign phyllodes) or lumpectomy (malignant phyllodes) is performed [4]. Histopathology demonstrates accentuated intracanicular growth pattern with leaf-like projections (Greek word: “phullon” means “leaf” hence the name) extending into the lumina and stromal hypercellularity often adjacent to the epithelium and are categorized as benign, borderline, or malignant based on histology (Table 1) [10]. Benign phyllodes tumors are characterized as lacking stromal overgrowth, with occasional mitoses up to 5 per 10 high-power fields (hpf), delimited and pushing margins, and mild to moderate stromal cytologic atypia (Fig. 1) [1]. Malignant phyllodes tumors are diagnosed by observation of stromal overgrowth, mitotic activity of > 10 per 10 hpf, permeative margins, and marked stromal hypercellularity and cytologic atypia [1] (Fig. 2). Phyllodes tumor is classified as borderline when some but not all characteristics of malignant phyllodes tumor are observed [11]. First-line treatment for phyllodes is surgical excision with negative margins, found to have low recurrence rates. Reexcision is indicated when there is a positive or narrow margin excision [7].

Here we report the cases of a 34-year-old white woman who presented to the clinic with a nonpalpable right breast mass and a 59-year-old white woman who presented to the emergency room with a very large right breast mass with accompanying skin breakdown and serous drainage.

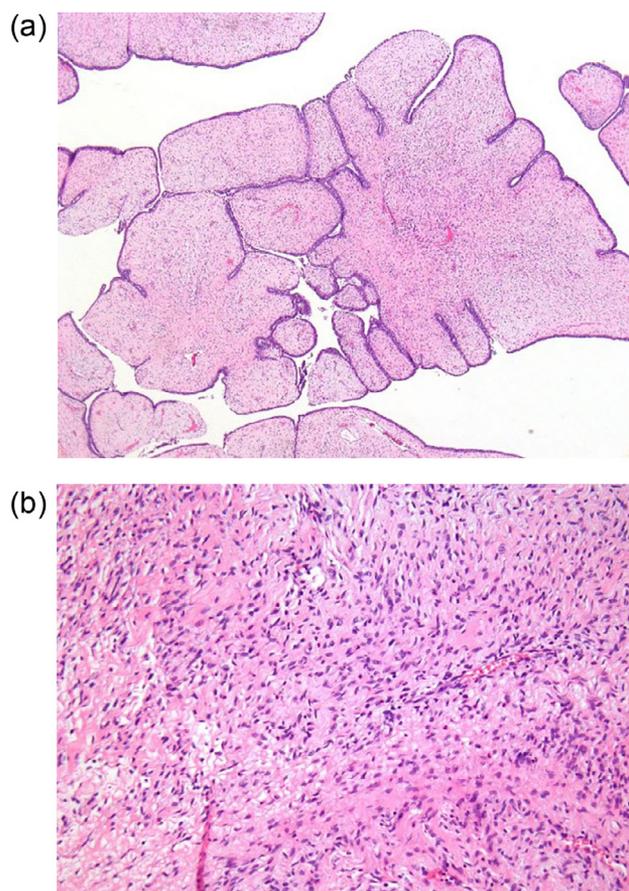


Fig. 1 – Benign phyllodes tumor. (A) Prominent leaf-like architecture and periductal stromal condensation (4x). (B) No stromal cytologic atypia and no mitotic figures (20x).

Case report benign phyllodes tumor

A 34-year-old Non-Hispanic white woman was referred for evaluation of a painless right breast mass. Two years prior, she underwent a breast core needle biopsy of the same mass yielding fibroadenoma. On imaging 2 years prior, the mass measured 2.8 × 3.4 × 1.5.

Reproductive history was significant for G1P0 with last menstrual period 1 month prior to visit. Onset of menarche oc-

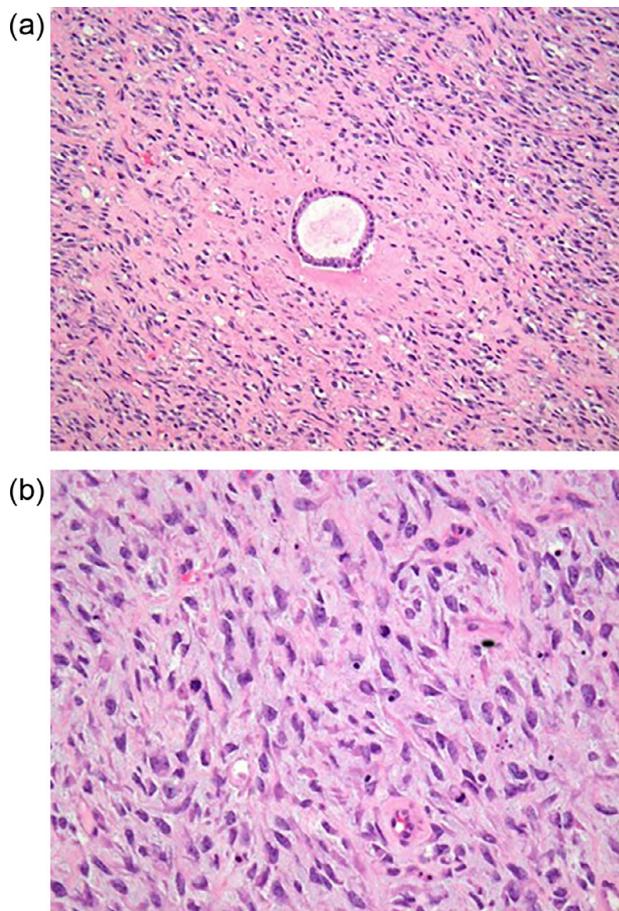


Fig. 2 – Malignant phyllodes tumor. (A) Focal benign breast epithelium, supporting the diagnosis of a phyllodes tumor (20x). (B) Marked stromal atypia and multiple mitotic figures (40x).

curred at age 11. Reported use of oral contraceptives was brief. Her maternal great grandmother was diagnosed with breast cancer in her late 80s. On physical exam of the right breast, a 3.0 cm mass in the 9 o'clock position. No evidence of skin dimpling, skin changes, or nipple discharge was noted and there was no lymphadenopathy in either axilla.

Target ultrasound of the right breast at the 9 o'clock position demonstrated a 4.8 × 4.0 × 1.8 cm oval, parallel, hypoechoic mass (Fig. 3). This study was interpreted as BI-RADS® Assessment Category 2 Benign. Surgical excisional biopsy was recommended due to interval growth. At excision, histologic examination yielded a fibroepithelial lesion with increased stromal cellularity, prominent intracanalicular growth pattern, and leaf-like projections into cystic spaces with lobulations appearing to push into surrounding fibrous tissue. Columnar epithelial cell change was observed. There was no cytologic atypia, mitotic figures, and condensation of stromal cells around ducts. Lesions had features of both fibroadenoma and phyllodes tumor but given pathologic findings, patient was diagnosed with benign phyllodes tumor 4.1 cm with margins less than 1 mm at medial, lateral, posterior, and anterior margins. Right segmental mastectomy was recommended to

lower her risk of local recurrence. On reexcision no residual phyllodes tumor was identified; the margins yielded sclerosing adenosis, fibroadenomatoid changes, duct ectasia, peripheral papilloma, and pseudoangiomatous stromal hyperplasia. At 1-week follow-up, examination of the right breast showed improved healing with no report of pain or erythema. Patient was assessed as average risk for the development of breast cancer and the tumor has not recurred in the ensuing 9 years of follow-up.

Case report malignant phyllodes tumor

A 59-year-old Non-Hispanic white woman presented to the emergency department with right breast enlargement with multiple irregular masses and an area of ulceration in the lateral aspect of the right breast draining serous fluid. She first noticed a much smaller mass 10 years earlier, had no concerns at that time, and went unmonitored.

Reproductive history was significant for G3P3 with her first pregnancy at age 19. Onset of menarche occurred at age 11, now postmenopausal. Family history was notable for breast cancer in her mother, maternal aunt, and sister, with her sister being diagnosed at the age of 59. Physical exam of the right breast was notable for 24 cm (estimated) mass replacing much of the right breast, with a 2.5 cm open wound draining serous fluid in the upper outer quadrant. The right nipple areolar complex was displaced medially (Fig. 5A). There was no sign of cellulitis or locoregional lymphadenopathy. The left breast was negative.

Bilateral diagnostic digital mammograms with tomosynthesis and targeted right breast and axillary ultrasound were performed (Fig. 4). There was a 20.9 cm oval circumscribed mass involving multiple quadrants of the right breast grossly distorting the overall breast shape. Associated features included skin and trabecular thickening. Ultrasound demonstrated an oval circumscribed heterogeneous mass, incompletely visualized due to size. There was no axillary lymphadenopathy. This study was interpreted as BI-RADS® Assessment Category 5 Highly Suspicious of Malignancy. An ultrasound guided core needle biopsy and clip placement was recommended. Core needle biopsy right breast 11:00 yielded fibrosis, granulation tissue, chronic inflammation and necrosis, a discordant result. She subsequently underwent right mastectomy. Surgical pathology of tissue specimen yielded 18.5 cm malignant phyllodes with marked stromal atypia and cellularity, stromal overgrowth, mitotic rate of 12 mitoses per 10 HPFs, and infiltrative tumor borders (Figs. 2A,B and 5B,C). No evidence of metastatic tumor was observed in lymph node excision. Negative surgical margins, pT4 and pN0 staging classification. She is scheduled to begin radiation therapy and will be followed-up in 6 months.

Discussion

Fibroepithelial lesions of the breast occur in 10%-15% of women; phyllodes tumors account for 2.5% of them [10]. Phyllodes tumors share similar histological characteristics to fi-

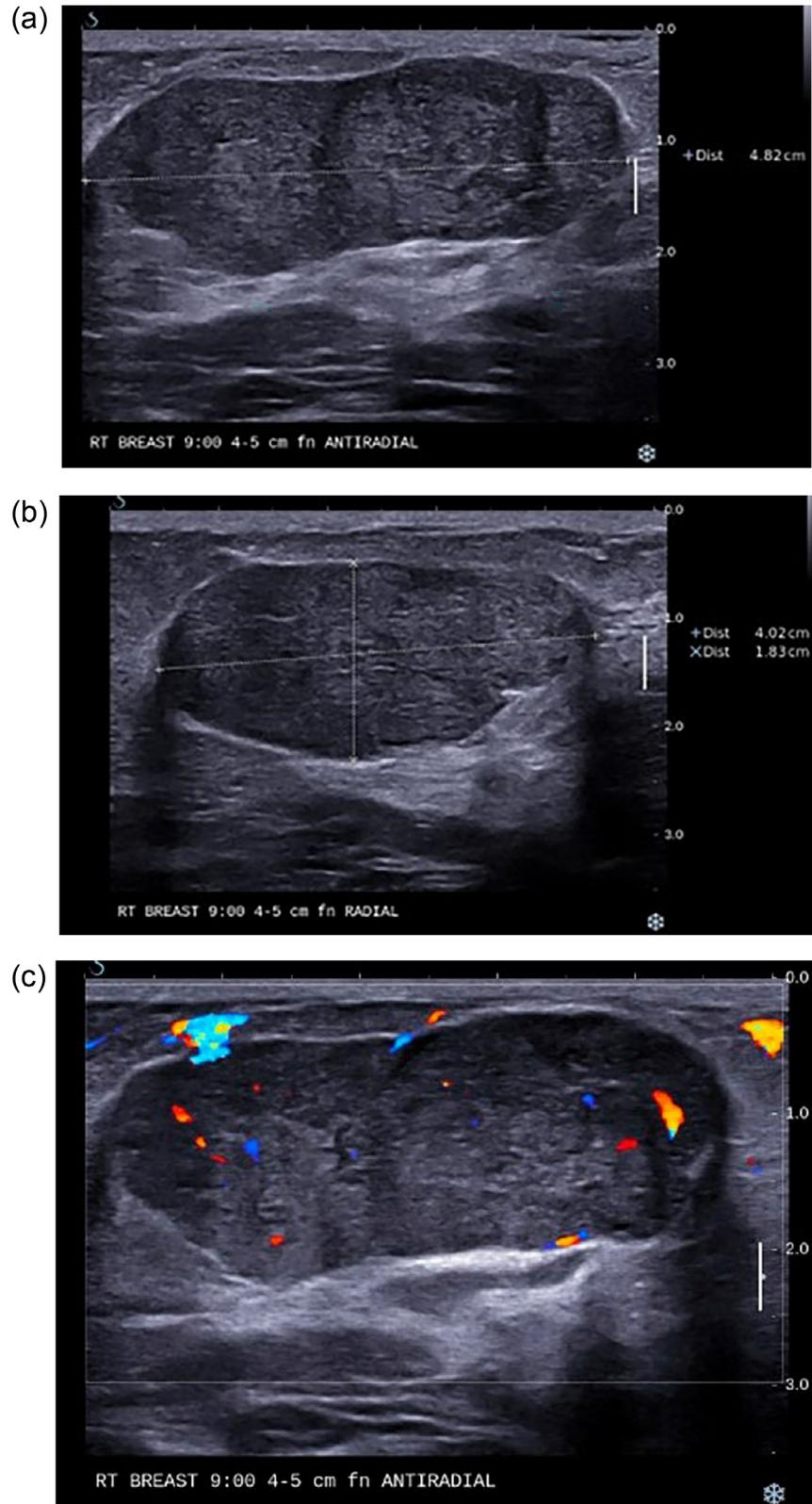


Fig. 3 – Patient case presentation 1. (A,B) Focused ultrasound of the right breast at 9 o'clock position showed a 4.8 x 4.0 x 1.8 cm oval, parallel, circumscribed hypoechoic mass in gray scale antiradial and radial planes. (C) Internal blood flow is shown by Doppler antiradial plane.

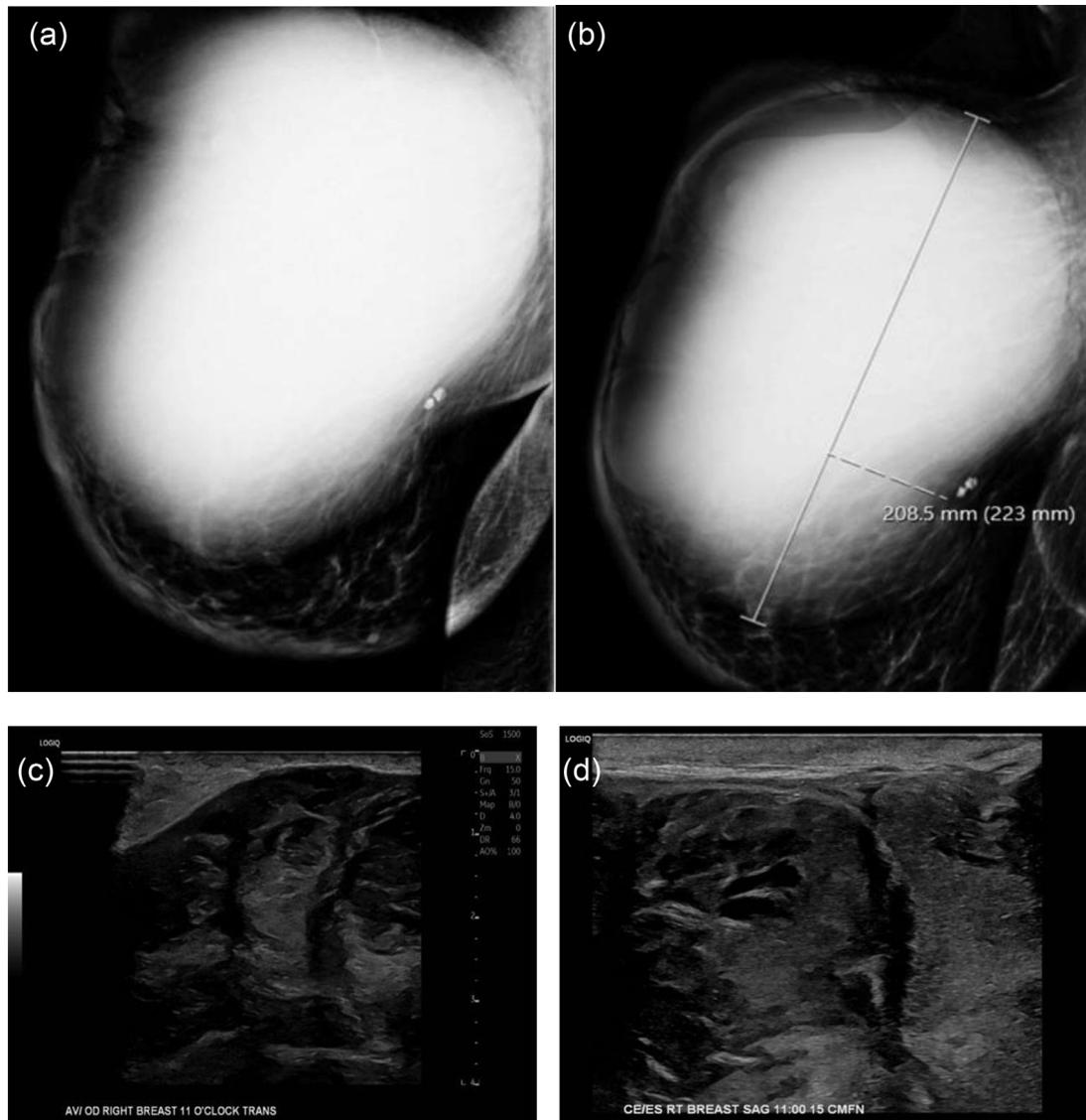


Fig. 4 – Patient case presentation 2. (A, B) Right MLO mammogram without and with calipers demonstrated a very large 20.9 cm oval high-density mass replacing the normal parenchyma and resulting in overlying skin thickening and trabecular thickening. (C, D) Accompanying ultrasound of the right breast in gray scale transverse and sagittal planes at 11 o'clock position showed a large oval, parallel heterogeneous mass (incompletely included because of its prohibitive size).

broadenomas and can be difficult to distinguish. It is believed that some fibroadenomas may transform into phyllodes tumor, which may be due to the *MED12* mutant pathway [12]. In our first case, a biopsy-proven benign fibroadenoma later developed into phyllodes tumor upon 2-year interval growth. Although rare, previous case reports have also documented the progression of fibroadenomas to borderline or malignant phyllodes tumors across various patient ages [13–15]. Currently, there is no preventative or screening method specific to the prevention or detection of phyllodes tumor.

Complications of phyllodes tumors include metastases and recurrence. Metastases are rare among all phyllodes types but are highest among malignant phyllodes and reported in up to 20%, most commonly to lung, bone, and abdominal viscera [7]. Phyllodes recurrences are reported in up to up to 12%,

with locoregional recurrence incidence significantly higher for the patients younger than 40 years of age and for those with close/positive final surgical margin [16]. Generally, the prognosis of phyllodes tumor is favorable with tumor histological features influencing this factor. In a report of 124 patients with 125 PTs (86 malignant and 39 borderline), the disease-specific survival (DSS) was 94%; in the patients without uniformly poor pathologic features, the 10-year DSS was 100% compared to 66% in the patients with uniformly poor features [16].

As illustrated in each case presented, the treatment for phyllodes tumor is surgical excision. The decision to pursue partial versus total mastectomy is most frequently based on tumor size. Management of recurrent phyllodes tumor with medical therapy remains unclear. The role of chemotherapy in malignant and metastatic phyllodes tumor is limited [17].

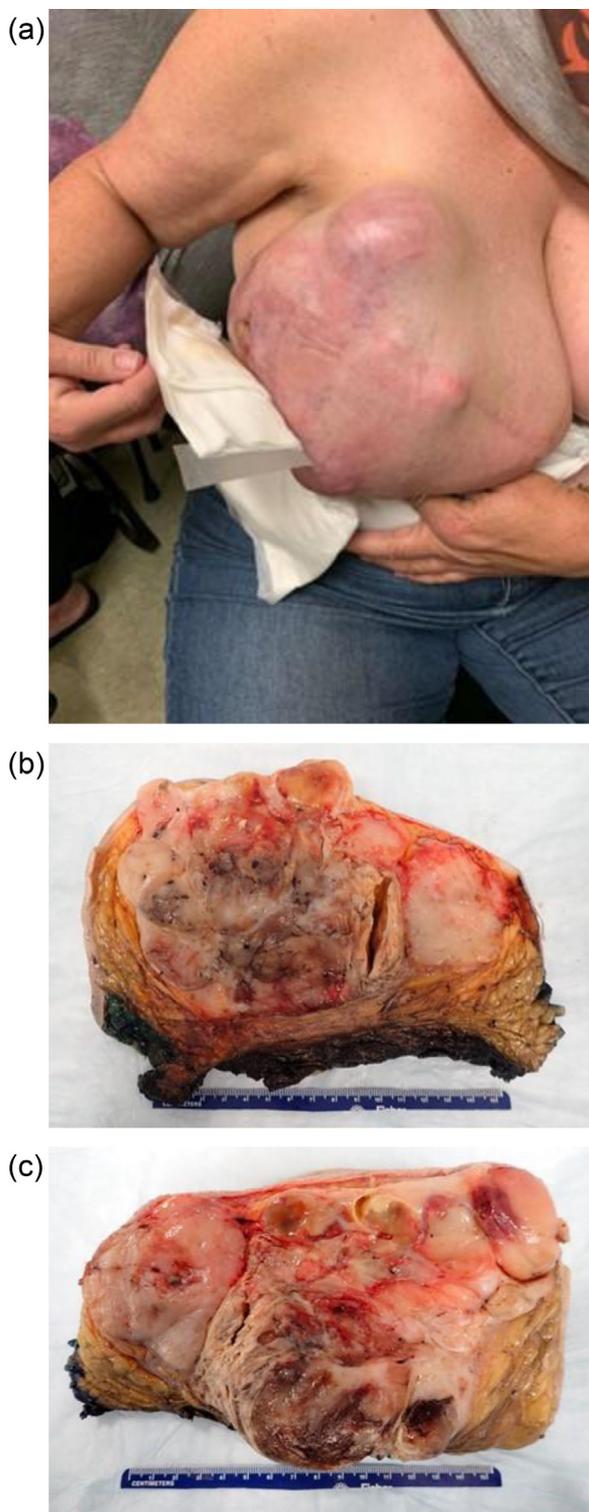


Fig. 5 – Patient case presentation 2. (A) Clinical breast exam demonstrated a very large mass replacing much of the right breast, with a 2.5 cm open wound draining serous fluid in the upper outer quadrant, as well as areolar complex displaced medially. (B, C) Gross cross-sections from 2 sites in mastectomy specimen of tumor showed heterogeneity, including some white, firm, whorled areas along with areas with hemorrhage and necrosis.

Adjuvant radiation therapy has shown no well-defined role in the treatment; radiation may reduce local recurrence rates in malignant phyllodes without improving long-term and overall survival [18].

Patient consent

Written consent for publication of this case was obtained from the patients, available upon request.

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