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MALIGNANT PHYLLODES TUMOR – A RARE CHALLENGE

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Dear Editor

We read the case study by Frias *et al*. about a 54-years-old woman with a left breast phyllodes tumor (PT) with 2024 g and 30.0 x 28.0 x 19.5 cm, infiltrating the skin and the papillary areolar complex, that evolved during six years before the mastectomy[1]. Grossly, the tumoral mass presented with a grayish color, irregular edges, imprecise limits, and a nodular ulcerated surface, being classified as T4BN0M0 and 7 IIIB[1]. Histopathologic study showed an epithelial component with intraductal hyperplasia, and a mesenchymal component of numerous atypical spindle cells with irregular nuclei[1]. Immunohistochemistry revealed CD34, Ki-67, P53 protein, actin alpha-smooth muscle, CD10/CALLA Ab-2, and cytokeratin estrogen and progesterone receptors positivity[1]. The authors stressed the successful management with the zetaplasty repair for the scar closure, and the unusual follow-up without recurrence of a severe and advanced tumor[1]. In this setting, the aim of the following short comments on more recent literature is enhancing the awareness of non-specialists about this uncommon challenging tumor[2-10].

Chen *et al*. reviewed data of 1902 women with diagnoses of malignant PT of breast between 2000 and 2019 with a median follow-up of 87.5 months; and mastectomy occurred in 898 (47.2%) cases including 210 undergoing radiotherapies after surgery[2]. Age did not independently predict cause-specific survival (CSS) in tumors larger than 10 cm; mastectomy had worse CSS compared with conserving surgery in tumors smaller than 10 cm; and conserving surgery got better survival for the small tumors (T1 or T2)[2]. The authors concluded that treatment should be selected based on different tumor sizes[2]. Chen *et al*. reviewed recurrences and metastases of PT from 2008 to 2022; among 82 cases, 69 were malignant and 13 were borderline tumors, 96.3% had surgical treatment[3]. The median follow-up was 55.5 months, 20 patients had metastasis within 3 years in over than 80% of cases, and 32 had recurrence without deaths due to disease progression[3]. The survival was related to surgical method, tumor size and biological behavior; besides, the combination of antiangiogenic drugs improved the mean progression-free survival; while lactate dehydrogenase was an independent prognosis predictor for malignant PTs[3]. Hashmi *et al*. reviewed 146 biopsy-proven cases of PTs submitted to lumpectomy or mastectomy, and results were classified into benign, borderline, and malignant tumors[4]. PTs mean age was 40.65 ± 12.17 years, the mean size was 9.40 ± 6.49 cm, malignant PTs were more prevalent (43.2%), followed by borderline (34.9%) and benign (21.9%)[4]. Patients with malignant and borderline PTs were of older age groups (mean 42.82 ± 12.94 and 42.05 ± 11.31 years, respectively) than the benign PTs (mean age 34.12 ± 9.75 years); and the malignant had larger (mean 11.46 ± 6.08) sizes compared with the others types[4]. Ruan *et al*. studied a new stage- and age-stratification system and prognostic model for malignant PT, comparing 1085 patients with 382,718 invasive ductal carcinomas[6]. New T stage 1: tumor < 49 mm in greatest dimension; new T stage 2: tumor size: ≥ 49 mm, but < 100 mm in greatest dimension; new T stage 3: tumor size ≥ 100 mm in greatest dimension; and new T stage 4: tumor of any size with direct extension to the chest wall or to skin; new stablished Age Groups were: 1) age < 71 years, and 2) age ≥ 71 years[6]. They stressed the role of multi-data verification to survival-prediction of the new model. Sain *et al*. analyzed data of patients previously diagnosed or presented with PTs from 1996 to 2021, 87 patients presented with PTs, and 46 (52.87%) had actual recurrences[7]. All were females, with a mean age of 39 (15-70) years; those aged <40 years had the highest incidence of recurrence (54.35%), followed by the aged >40 years (45.65%); 55.4% of PTs were primary and 44.6% recurrent at presentation; the mean time to local recurrence from the treatment end was 13.8 months, and to systemic was 15.29 months; the authors highlighted the adjuvant radiotherapy favoring a minimal recurrence of PT[7]. Sars *et al*. performed a survey from July 2021 to February 2022 involving sixteen countries in four

continents and including 419 responses; most were according to tumor-free excision margin for benign, wider margins for borderline or malignant PTs, the multidisciplinary care in treatment and follow-up, and did not consider axillary surgery[8]. The opinions on adjuvant treatment were mixed, with more liberal regiments to locally advanced tumors, the majority preferred a five-year follow-up period for all PT types[8]. The authors concluded by a considerable variation in clinical management of PTs, and lack of consensual guidelines taking in account the wide heterogeneity of these tumors[8]. Sherin *et al*. reported a 42-year-old woman presenting with productive cough for 4 months, who underwent a modified radical mastectomy to treat a right PT 10 years ago Imaging studies showed a 10.2 cm × 9.1 cm × 4.4 cm mass in the right lung lower lobe with compression of bronchus intermedius and total obstruction of right lung lower lobe. Right middle and lower lung lobes resections were performed and the histopathological study revealed a malignant spindle cell tumor with increased cellularity, predominantly disposed in fascicles with elongated, hyperchromatic nuclei and nuclear atypia, and elevated mitotic rate, besides vimentin, smooth muscle actin, and Ki67 index of 20%[9]. These data were indicative of PT metastasis of PT with a component of leiomyosarcoma, and the images of control done after 1 year revealed scattered metastases to the brain, omentum, retroperitoneum, anterior abdominal wall, and femur; biopsy of the abdominal wall confirmed a metastatic PT with a heterologous component of leiomyosarcoma[9]. Despite of the palliative radiotherapy plus cyclophosphamide, vincristine, adriamycin, and dacarbazine schedules, the patient succumbed to metastatic disease 2 months later[9]. Tome *et al*. reported a 48-year-old female with a large ulcerated PT during the pandemic; 18 months before she was evaluated with a left breast lump (6.7 × 4.5 cm) and the biopsy diagnosis was fibroadenoma with pericanalicular myxoid stromal changes, but that occasion, she did not accept the surgical excision treatment which was indicated[10]. The tumor size (12 × 12 × 8 cm) did not allow a conservative surgery; the mastectomy confirmed the diagnosis of a borderline PT, and she did not accept adjuvant treatment[10]. The tumor presented as a biphasic proliferation with epithelial and stromal components, the leaf-like pattern and clefts, besides some benign chondroid heterologous elements, and the expansive growth had mild-to-moderate nuclear atypia and 10 mitosis/10 hpf[10]. The patient remains free of disease during the 22 months of follow-up after the surgery.

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