Diagnostic difficulties in giant benign phyllodes tumor

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Abstract

Phyllodes tumors (PTs) are rare tumors of the breast, which encompass both stromal and epithelial components. The maximum incidence is in the fourth decade of life. Most of these tumors are benign, but about one third can be malignant acting as sarcomas. Due to their rarity and atypical clinical behavior (especially for the giant ones), the management of these tumors is usually difficult. We report a case of a 24-year-old woman who presented in the Department of Oncology for rapid increase in volume of the left breast. She had no personal pathological or family history. Initial clinical exam showed a large irregular mass in the left breast of approximately 30 cm and palpable lymph nodes in the ipsilateral axilla. A core needle biopsy for the tumor was performed with histopathological (HP) result that revealed an aspect suggesting fibroadenoma/PT. Contrast-enhanced computed tomography (CT) scan identified lymph node enlargement in the left axilla and a peripheral nodule in the lung about 5.5/3.4 mm with no specific features. The patient was then transferred to the Department of Surgery, where left mastectomy and axillary lymph node sampling were performed. HP result of the surgical specimens confirmed the presence of both benign PTs and fibroadenoma/PT.

Keywords: phyllodes tumor, fibroadenoma, breast cancer, benign tumor, surgical treatment.

Introduction

Phyllodes tumors (PTs) are rare breast tumors, accounting for less than 1% of breast tumors [1, 2], which develop later than fibroadenoma and earlier then invasive lobular or ductal breast cancer, the average age being reported around 40 years [3]. In most cases, phyllodes are benign tumors, but in 8–29% [4] they are malignant acting as sarcomas and generating hematogenous distant metastasis. The common places for the metastasis are usually represented by the bones and lungs but rarely also in other organs [5]. Pathophysiologically, they are characterized as being biphasic – stromal and epithelial –, with a microscopic appearance of a leaflike pattern that arises from the intensified intracanicular extension pattern, cleft-like spaces covered by epithelium, and hypercellular stroma [6]. By clinical behavior, histopathological (HP) features regarding presence or absence of stromal overgrowth, stromal cellularity and cellular atypia, mitotic activity, and the nature of tumor margins there are three subtypes of PTs: benign (60–75%), borderline (15–26%) and malignant (8–29%) [2, 3, 7]. Surgical treatment remains the main therapeutic resource for all types, but for the proper surgical planning, the pathology plays a very important role in the preoperative diagnosis. About 10–16.1% of patients have local recurrence, while 6.3–31% of patients with malignant PT may develop distant metastases [8]. A few studies have demonstrated that immunohistochemical markers like Ki67 and p53 protein correlates with HP classification, helping to distinguish between malignant and benign PTs [9]. About 20% of all PTs are larger than 10 cm in diameter and they are considered giant PTs [10].

Aim

Management of giant breast tumors rise numerous diagnostic and therapeutic challenges. Those aspects were highlighted by our clinical case, where the patient presented with a large breast tumor that was measuring about 30 cm (29/27/18 cm), with a rapid growth during the last eight months. To have a better understanding regarding giant benign PTs proper diagnostic and treatment, we selected and analyzed 16 cases including our own.
Case presentation

A 24-year-old female without significant familial or personal history, referred to the Department of Oncology, Emergency County Hospital, Craiova, Romania, in October 2020, accusing a tumoral growth in the left mammary gland that was detected eight months before presentation. According to the patient, the growth rhythm was accelerated in the last three months.

The initial physical examination revealed a large painless mass in the left breast exceeding 30 cm in diameter. The skin covering the mass was thin and had small erosions due to containment attempts. Intertrigo was present in the submammary sulcus and on the sternum and tortuous dilated veins were obvious under the distended skin (Figures 1 and 2). Palpation identified a polylobate tumor extended to the whole breast, with a hard consistency, mobile on the deep planes but adherent in certain areas of the skin. In the ipsilateral axilla, we found palpable enlarged but mobile lymph nodes with a firm consistency. Right breast and axilla were found clinically normal.

Ultrasound (US) of the left breast revealed multiple hypoechoic structures, with sizes between 5 mm to 85/61 mm. The tumors were imprecisely delineated, with complex echostructure and tortuous blood vessels disposed at the periphery of each nodule but also inside, especially in the largest ones. Mammography showed an enlarged left breast through the presence of multiple non-homogeneous opacities spread over the entire glandular area, with irregular and macro-bosselated outline. Microcalcifications were present, and BI-RADS score 5 was established (Breast Imaging-Reporting and Data System score – American College of Radiology) (Figure 3, A and B). Right breast and axilla were found normal.

US-guided core needle biopsy was performed and classical Hematoxylin–Eosin (HE) staining of six specimens described lesions compatible with fibroadenoma and benign/borderline PT but failed to overrule malignancy.

Concurrent computed tomography (CT) scan of the chest, abdomen and pelvis revealed tumoral enlargement of the left breast through the presence of multiple formations with tissue densities, which distorted the entire glandular and interstitial breast tissue, with infiltration of subcutaneous tissue over a distance of about 68/13 mm (Figure 4, A–D). Left axillary and retrosternocleidomastoid lymphadenopathy (Figure 5, A and B) were present.

Based on clinical and paraclinical elements, the Tumor Board established the diagnosis of giant PT with unknown features – possible malignant with immediate indication for surgical removal with adequate oncological margins. Breast reconstruction was considered hazardous in the same procedure, remaining to be scheduled at distance depending on the follow-up. Conservative surgery was excluded due to local extent and unclear histology on the core needle biopsy. Left mastectomy with level I axillary lymphadenectomy was performed. The left mammary gland containing the giant tumor was resected with the fascia of the pectoralis major. Following the tumor excision, the left axillary region was surgically evaluated and five enlarged lymph nodes of 1.5 cm to 2.1 cm with elastic consistency, all situated in the lower part of the axilla, were resected.
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The excised tumor together and the axillary lymph nodes were labeled, then fixed in 10% neutral buffered formalin solution and sent to the Laboratory of Pathology for HP examination. Fragments of about 2/1.5 cm were taken from the tumor, which were embedded in paraffin, using the usual HP protocol. Due to the high tumoral volume, the margins were evaluated in 36 points. After microtome sectioning, the sections were stained with HE and examined under a Nikon 55i microscope (Nikon GmbH, Wien, Austria) equipped with a 5 MP color charge-coupled device (CCD) camera and analyzed using Image-Pro® Plus Advanced Microscopy Suite (AMS) software package (Media Cybernetics, Bethesda, MA, USA).

Microscopic examination showed that the tumor was composed of canalicular structures as narrow as slits, branched like a “fern leaf”, lined by a double-layered epithelium, with rare nuclear atypia and rare mitotic cells. The stromal component was abundant, consisting of dense connective tissue with a relatively small number of fibroblast-like cells, without nuclear atypia, collagen fibers, and blood vessels (Figures 6–8). In some areas, intracanalicular stromal proliferations have been observed, compressing and deforming the epithelial ductal structures. Thus, classical HP exam using HE staining confirmed PT together with phyllodes-like fibroadenoma, with clear resection margins over 1 cm, but also failed to exclude borderline lesions and recommended immunohistochemistry (IHC). Five of six axillary lymph nodes that were analyzed had reactive changes. For the IHC study, we used a large spectrum of antibodies to reveal multiple characteristics of the tumor, both in the epithelial structures and in the stromal component: anti-MNF116 [monoclonal mouse anti-human cytokeratin (CK), clone MNF116, 1/100 dilution, Dako]; anti-CK7 (monoclonal mouse anti-human CK7, clone OV-TL 12/30, 1/50 dilution, Dako); anti-CK20 (monoclonal mouse anti-human CK20, clone KS20.8, 1/40 dilution, Dako); anti-alpha-smooth muscle actin (α-SMA) (monoclonal mouse anti-human SMA, clone 1A4, 1/100 dilution, Dako); anti-p63 (monoclonal mouse anti-human p63 protein, clone 4A4, 1/50 dilution, Dako); anti-cluster of differentiation (CD)17 [polyclonal rabbit anti-human CD17 (c-Kit), 1/400 dilution, Dako]; anti-epidermal growth factor receptor (EGFR) (monoclonal mouse anti-human EGFR, clone H11, 1/40 dilution, Dako); anti-p16 [anti-p16INK4a antibody (1D7D2), clone MA5-17054, 1/100 dilution, Invitrogen]; anti-p53 (monoclonal mouse anti-human p53 protein, clone DO-7, 1/50 dilution, Dako); anti-CD34 (monoclonal mouse anti-human CD34 Class II, clone QBEnd 10, 1/50 dilution, Dako); anti-Ki67 (monoclonal mouse anti-human Ki67, clone MIB-1, 1/50 dilution, Dako).

Ductal epithelial cells were intensely positive for anti-pan-CK MNF116 antibodies (Figure 9), anti-CK7 antibody (Figure 10) and negative for anti-CK20 antibody (Figure 11). Both ductal and stromal cells were moderately positive for α-SMA (Figure 12), p63 (Figure 13), CD117 (Figure 14), and EGFR (Figure 15), and negative for p16 and p53 (Figures 16 and 17) immunomarkers. The CD34 immunomarker marked intensely the stromal cells and the vascular endothelial cells, but not the ductal cells (Figure 18). Regarding the Ki67 cell proliferation marker, it had a weak reaction, marking 4–6 cells, stromal or epithelial, on a microscopic field with medium power objective (×20) (Figure 19). However, Ki67 labeling index in stromal cells, calculated on high-power field was less than 1%.

Figure 5 – CT coronal sections showing axillary (A) and retrosternocleidomastoide (B) lymphadenopathy, respectively.

Figure 6 – Microscopic image of the phyllodes tumor with the epithelial component represented by leaf-shaped branched duct, lined by a bilayered epithelium and surrounded by an abundant stromal component, consisting of connective cells, collagen fibers and blood vessels. Hematoxylin–Eosin (HE) staining, ×100.

Figure 7 – Tumoral area with abundant connective stroma, consisting of fibrous connective tissue dissociating adipose tissue, with a large amount of collagen fibers, but with a small number of stromal cells. HE staining, ×100.
Figure 8 – Detailed image showing the ductal double layered epithelium with vacuolization of the cells: extensive cytoplasmatic clearing in the external layer. HE staining, ×200.

Figure 9 – Ducts with intense pan-cytokeratin MNF116 immunoreaction in the internal layer. Immunolabeling with anti-MNF116 antibody, ×200.

Figure 10 – Ductal epithelial cells with intense immunoreaction to cytokeratin 7 (CK7). Immunolabeling with anti-CK7 antibody, ×200.

Figure 11 – Ductal cells with a negative reaction to cytokeratin 20 (CK20). Immunolabeling with anti-CK20 antibody, ×100.

Figure 12 – Positive, moderate reaction of ductal basal cells (myoepithelial) and stromal cells (myofibroblasts) to the alpha-smooth muscle actin (α-SMA) immunomarker. Immunolabeling with anti-α-SMA antibody, ×200.

Figure 13 – Positive, intense reaction of basal cell nuclei (myoepithelial cells) to the p63 immunomarker with just a few positive cells in the stroma. Immunolabeling with anti-p63 antibody, ×200.
Figure 14 – Ductal epithelial and stromal cells both with inconsistent reaction (positive/negative) to the cluster of differentiation 177 (CD117) immunomarker. Immunolabeling with anti-CD117 antibody, ×200.

Figure 15 – Moderately positive reaction to the epidermal growth factor receptor (EGFR) immunomarker in both ductal epithelial cells and stromal cells. Immunolabeling with anti-EGFR antibody, ×200.

Figure 16 – Negative reaction of ductal and stromal cells to the p16 immunomarker. Immunolabeling with anti-p16 antibody, ×200.

Figure 17 – Negative reaction of canalicular and stromal cells to the p53 immunomarker. Immunolabeling with anti-p53 antibody, ×100.

Figure 18 – Stromal tumor cells with an intense reaction to the cluster of differentiation 34 (CD34) immunomarker, while ductal cells remained negative to the same. Immunolabeling with anti-CD34 antibody, ×200.

Figure 19 – Reduced proliferative reaction of tumor cells (4–6 positive cells to the Ki67 immunomarker). Immunolabeling with anti-Ki67 antibody, ×200.
At one year evaluation, the patient had no signs of recurrence. In November 2021, the Tumor Board decided that reconstruction was safe, but the procedure was postponed for six months due to coronavirus disease 2019 (COVID-19) reasons.

Discussion

For a comprehensive view on giant benign PT, we performed a search of the literature using PubMed, Web of Science and Google Scholar from 2000 to 2021 using the terms “giant”, “phyllodes” and “benign” as keywords. We’ve extracted 16 cases of giant PTs, which were larger than 10 cm. These cases have been described in Tables 1 and 2 and discussed further together.

From clinical point of view, PT appears as a palpable, painless tumor, mobile on the superficial and deep planes. They are usually fast-growing with dimensions of 10 cm or larger, the average being 5 cm [10, 11]. When a PT has a diameter above 10 cm, it can be classified as a giant PT [12]. Most of the cases in our review presented local signs of inflammation, venous congestion [13, 14], bleeding [10, 15, 16], “peau d’orange” [17, 18] or even necrosis or skin ulcers [7, 10, 14–16, 19–21] while others had no other clinical manifestation than the enlargement of the affected breast [22–25]. Local complications are attributed to the increased pressure that the rapid tumoral growth exerts on the skin but can be difficult to interpret since they are encountered also in malignancy [26]. In our case, superficial small erosion of the skin was secondary to patient’s attempts to contain the tumor. We’ve also noticed skin thinning, areolar diversion, and a slight nipple retraction due to the eccentric tumoral growth. Ipsilateral axillary lymph nodes were palpable, mobile, but firm, 1–2 cm in diameter. Lymphadenopathy is reported in about 20% of PTs [10] but in most cases is probably reactive to local inflammation.

Table 1 – Principal characteristics across the literature reported cases of giant PTs between 2000 and 2021

| Study [Ref.] | Age [years] | Disease duration | Size [cm] | Clinical characteristics | Axillary lymph node surgery | Margins status | Recurrence | Reconstructive breast surgery |
|--------------|-------------|------------------|-----------|-------------------------|-----------------------------|----------------|-----------|--------------------------------|
| Likhitmaskul et al. [7] | 36 | 5–6 months | 20 | Cutaneous necrosis, intermittent local pain | Yes, level 1 | Free surgical margins | – | Immediate, musculocutaneous flap |
| Islam et al. [8] | 44 | 1 year | 50 | Ulceration, fungating, anemia, malnourished | Yes | Free surgical margins | Malignant pleural effusion after several months from surgery | – |
| Fernández-Ferreira et al. [10] | 40 | 3 years | 25 | Blisters on the nipple; erythema; venous network; foul smell; skin ulceration; bleeding; rapid growth in the last year | No | Free surgical margins | None | – |
| Câmara et al. [13] | 58 | Unknown | 13 | Local pain and inflammatory characteristics | No | Free surgical margins | Yes, after 4 years and 7 months | Immediate breast reconstruction with latissimus dorsi muscle flap (and breast expander) |
| Kolia et al. [14] | 38 | >2 years | 24 | Skin ulcer in the lower outer quadrant, dilatations of superficial veins on the breast | No | Free surgical margins | Is not specified | Reconstruction with tissue expander |
| Zhang et al. [15] | 42 | 1 year | 30 | Ulceration, bleeding, fever, infection, lung adenocarcinoma | No | Free surgical margins | None for 12 months | Refused by the patient |
| Yap et al. [16] | 43 | 13 months | 28 | Engorgement of superficial veins, ulceration with necrosis, spontaneous bleed, pale and tachycardic, hemoglobin 4.3 g/dL, serum albumin 2.2 g/dL | No | Free surgical margins | None for 6 months | – |
| Tee & Valayatham [17] | 46 | 6 months | 20 | Three ulcerated lesions and “peau d’orange” skin changes, confusion, seizure and hypokalemia and hypoglycemia | No | Free surgical margins | None at 4 months | – |
| Sarvanandan et al. [18] | 36 | 3 years | 40 | Infermedially deviated and retracted nipple with “peau d’orange” skin changes | Yes | Free surgical margins | None at 12 months | Latissimus dorsi pedicle flap reconstruction |
| Bhattacharjee et al. [19] | 13 | 8 months | 13 | Both breasts, dilated veins, nipples retraction, ulcer, mild serous discharge | Yes | Free surgical margins | None at 2 months | – |
Table 2 – Comparison between pre-op diagnosis and post-op histopathological results across reported cases of giant benign PTs between 2000 and 2021

| Study [Ref.] | Age [years] | Disease duration | Size [cm] | Clinical characteristics | Axillary lymph node surgery | Margins status | Recurrence | Reconstructive breast surgery |
|--------------|-------------|------------------|-----------|--------------------------|----------------------------|----------------|------------|-----------------------------|
| Ur Rab et al. [20] | 23 | 18 months | 22×16 | Bloody discharge from the nipple, non-tender swelling, bosselated, hard in consistency, ulceration of skin overlying the tumor | No | Does not say | Does not say | – |
| Bhasin et al. [21] | 16 | 3 years | 56 | Bilateral, mild pallor, five lumps in the right breast, multiple ulcers in right breast | Unclear | Does not say | None at 18 months for the right breast and none at 6 months for the left breast | No |
| Baldiwala & Vaidya [22] | 14 | 2 months | Unclear | Enlargement of left breast five times as compared to right breast | No | Does not say | None at 7 months | – |
| Liang et al. [23] | 70 | Unknown | 12 | | No | Yes | Free surgical margins | None for 6 years | – |
| Okamoto et al. [24] | 45 | 5 months | 14 | Post-lumpectomy status | No | Free surgical margins | None for 7 years | NSM and immediate reconstruction of the breast |
| Paryani [25] | 50 | 6 months | 61 | Weakness, anorexia, dull aching pain, pallor | No | Free surgical margins | None for 8 months | – |
| Our case | 24 | 8 months | 30 | Grating injuries on the skin covering the mass, painless, venous congestion | Yes | Free surgical margins | None at 12 months | Awaiting reconstruction |

NSM: Nipple sparing mastectomy; PT: Phyllodes tumor.

IHC: Immunohistochemistry; Pi: Proliferation index; Post-op: Postoperative; Pre-op: Preoperative; PT: Phyllodes tumor.

Time since onset of symptoms and patients’ presentation varied between two months and three years. In our case, we observed a biphasic growth pattern with a slower phase for five months then an accelerated one for three months in which the tumor doubled its volume according to the patient. Same pattern was observed and reported in other cases [10] and somehow can be misleading, because it raises the suspicion of a malignant transformation appeared in a previously benign tumor, or a fibroadenoma turning in a PT [6, 27].

A particular aspect of our case is related to patient’s age at the time of diagnosis. The patient was diagnosed at a much younger age (24 years old) compared to the average age of diagnosis for this type of tumor. Personal and familial history were negative for Li Fraumeni syndrome, breast cancer, trauma, pregnancy or other factors that were cited in relation with the development of PT [27]. Endocrinological consult and hormone tests showed a normal endocrine profile.

Preoperative imagistic methods, such as mammography, US and nuclear magnetic resonance imaging (MRI) could assist the clinician in creating the differential diagnosis between PT and fibroadenomas and other breast neoplasm. These aspects were demonstrated in a retrospective study that included 72 patients with fibroadenomas and 70 patients with PTs. The important elements found in patients with PT were size greater than 3 cm, irregular shape, irregular macrobosselated margins, and hypervascularization [28]. In our case, BI-RADS scores of 5 and 4, respectively, established by two different examinators on US and nuclear magnetic resonance imaging (MRI) could assist the clinician in creating the differential diagnosis between PT and fibroadenomas and other breast neoplasm.
distant metastases or other tumoral pathology, but not for characterization of primary lesions since it lacks specificity for breast tissue. The presence of a pulmonary nodule can mimic a metastasis as Zhang et al. reported [15]. In our case, the nodule was small, without tumoral features, but determined us to perform a follow-up CT at six months.

For a correct treatment planning, a core needle biopsy is usually indicated to exclude other pathological entities and confirm clinical suspicion, but it cannot always differentiate between fibroadenoma and phyllodes [1]. HP examination in classical HE staining performed on eight samples obtained in our case, detected areas of fibroadenoma coexisting with benign phyllodes in a myxoid stroma. HP report mentioned “probably benign lesion but cannot overrule malignancy”. Since fibroadenoma and different types of phyllodes (benign, borderline, and malignant) usually coexist in the same tumor [6] a HP result of benignity in a multifocal giant tumor can become deceptive.

PT treatment is individualized on a case-by-case basis, with the main element being complete excision of the tumor with a 1 cm margin or mastectomy, depending on the size of the tumor in relation to the breast [1]. Radiotherapy remains a controversial topic but can be applied in local recurrences. Chemotherapy is reserved for malignant phyllodes with distant metastases that should be treated as a soft tissue sarcoma [3, 30]. Mastectomy, performed in various fashions (simple, radical, radical extended, etc.) did not show superior results compared to local excision [31]. However, local excision is not feasible for giant phyllodes especially when the lesion is multifocal and extended to the whole mammary parenchyma, as in our case. Axillary lymphadenectomy is not recommended in PT since less than 1% cases reported in the whole literature had positive lymph nodes [3, 32]. Six of the patients including our own underwent axillary lymphadenectomy [7, 8, 19, 20, 23]. In a larger retrospective study in USA published in 2009, Gullett et al. reports axillary lymph node dissection, performed in various extents, in more than 25% of all cases of phyllodes, but only in nine cases positive lymph nodes were found [33]. It seems that, despite recommendation, the clinical or imagistic detection of enlarged lymph nodes in the axilla of a patient with a large breast tumor and unclear histopathology, becomes a subliminal indication for the surgeon to resect at least some nodes.

Breast reconstruction after mastectomy can be performed in the same procedure after resection or at some distance in time [23]. In three of the revised cases, breast reconstruction was immediate [7, 13, 24]. In our case, the Tumor Board decided to perform the reconstruction in a second operation since the diagnostic of benignity was doubtful.

Rare tumors like the phyllodes and fibroadenoma are both fibroepithelial tumors which include stromal and epithelial components. The differential diagnosis between these two entities is challenging due to many common features [34, 35]. One of the elements that emphasize the difficulty of differential diagnosis is related to the possibility of their common origin. This aspect is suggested by the presence of a common somatic mutation – MDM2 – identified by genomic sequencing tests [6].

Given the fact that fibroadenomas have a low risk of local recurrence while PTs have an increased risk and potential for metastasis, an accurate HP diagnosis is important in choosing the right therapeutic attitude. This fact has been reported in a study which aimed to differentiate between fibroadenomas and PTs based on HP features. The study included 61 patients on whom eight HP features (among which stromal mitosis, stromal fragmentation and overgrowth, fat entrapment) were analyzed on initial core biopsy and on the surgical specimens. The conclusions of the study highlighted two important findings: ≥3 mitoses and/or ≥3 HP features are the main criteria in specifying the existence of PT on subsequent excision [36].

It is also important to distinguish between the three HP subtypes of the PT. Even though it is known that most of them are benign, there is a need for precaution in diagnosing malignant PTs, because about 22% of them have distant metastasis. Lung and bones are the most frequent sites of distant metastasis, but there are also three cases of pancreatic metastasis described in the literature [5].

Only HP features are sometimes insufficient in distinguishing the subtype of the PT or might not be always predictive for their clinical behavior [37–39]. Thus, there is a need for further characteristics which can help in achieving an accurate diagnosis. This fact has been reported in a retrospective study which analyzed the link between the expression of three immunomarkers (Ki67, p53 and CD10) and the HP grade of the PTs. The expression of these markers was evaluated both in the stroma and in the epithelium [40]. There was a statistically significant difference of the immunomarkers’ expression in the stroma between the three types of PTs, but not in the epithelium. Stromal Ki67 labeling index were at least double in malignant phyllodes compared with benign phyllodes. The immunohistochemical evaluation might play an important role in differentiation benign form malignant PTs, thus Ki67 and p53 could be prognostic biomarkers [40, 41]. In only four of the revised cases, including our own, immunohistochemical examination was performed on the postoperative specimen and none on the core needle biopsies. In all cases, Ki67 proliferation index was found less than 4%. Of the selected cases, four of which were considered benign PTs before surgery turned out to be borderline at postoperative HP examination.

Our immunohistochemical tests sought to highlight the exact type of PT, as some clinical features raised the suspicion of a malignant tumor (appearance in a young woman, rapid development, large size). CKs were positive in ductal epithelium but negative in stroma and together with p63 immunomarker that was found weakly positive in the stroma and intense positive in the myoepithelial cells’ nuclei, excluded a sarcomatous carcinoma. p63 was previously reported as focal positive in a subset of malignant PTs but negative in fibroadenoma and benign phyllodes [42]. In the same manner, CD34 and CD117 were reported to have an inverse relation in PT types in the sense that CD34 is expressed in most benign phyllodes, lower in borderline, and lowest or absent in malignant ones, while CD117 seems to be expressed in large proportion of malignant phyllodes, lesser of borderline ones, and only in one third of benign phyllodes [43]. In our case, CD34 stromal reaction was strong, while CD117 was weak and inconstant, advocating for a benign PT. Thus, Ki67...
low stromal positivity, CD34 intense expression and CD117 weak reaction in stromal cells, concurrently with negative p53 and moderate positive at α-SMA and EGFR [41, 44], allowed us to formulate the final diagnostic of benign PT.

Conclusions

Given the rarity of the PTs, diagnosis and therapeutic decisions remain difficult. The initial HP result on the core needle biopsy does not differentiate between fibroadenomas and PTs. Considering the unfavorable prognosis of malignant PTs due to their metastatic potential, differentiation of the PT subtype remains essential, influencing the therapeutic decision and impacting patients’ prognosis. Where there are difficulties in establishing the subtype of PT based on HP characteristics, immunohistochemical markers, such as Ki67, p53, CD34 and CD117, might be useful in this direction. The standard of treatment in PTs remains the surgical approach. Based on clinical data (young age, rapid growth), imaging examinations and initial HP examinations, which did not allow us to rule out a borderline or malignant PT, we performed left mastectomy with axillary sampling lymphadenectomy, the clinical evolution of the patient being favorable, without local recurrence or metastases at 18 months after surgery.

Conflict of interests

The authors declare that they have no conflict of interests.

Authors’ contribution

Ramona-Andreea Matei and Mihai Mehedinu-Lonescu equally contributed to the research and manuscript thus sharing first authorship.

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