

Usefulness of ultrasounds in the management of breast phyllodes tumors

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SUMMARY: Usefulness of ultrasounds in the management of breast phyllodes tumors.

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Introduction. Breast phyllodes tumors (PT) are uncommon fibroepithelial lesions having potential malignant features. These tumors have characteristic features, like pleomorphism, mitoses and overgrowth of the stroma with possible infiltrative margins. The clinical behaviour could be unpredictable, since the relatively high recurrence rate despite correct surgical strategy. Conventional diagnostic examinations show high sensitivity and specificity, but cannot demonstrate the differences between benign and malignant PT. MRI is not more effective.

Patients and methods. Sixteen patients affected by PT have been surgically treated at our Institution. All patients received mammography and ultrasonography (US) as preoperative diagnostic work-up.

Results. In 13 patients, US was effective in preoperative diagnosis of PT. Mammography was ineffective in detecting breast lesions in 5 cases, while in 11 cases mammographic findings presented benign features, with a round opacity with moderate tissue density and well-defined wall.

Conclusion. US remains the most useful diagnostic test in detecting PT. However, there is no test effective in identifying malignant PT. In case of suspicion, fine needle biopsy should be performed.

RIASSUNTO: L'ecografia nei tumori filloidi della mammella.

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Introduzione. I tumori filloidi della mammella sono rare neoplasie fibroepiteliali con potenziale malignità. Questi tumori hanno caratteristiche tipiche, come pleomorfismo, mitosi e crescita anormale dello stroma, con possibile infiltrazione dei margini. Il comportamento clinico può essere imprevedibile, a causa dell'alto rischio di recidiva locale anche dopo una resezione chirurgica adeguata. Gli esami diagnostici convenzionali hanno elevata sensibilità e specificità, ma non riescono a dirimere circa la malignità della lesione. La risonanza magnetica non sembra offrire informazioni aggiuntive.

Pazienti e metodi. Sedici pazienti affetti da tumore filloide sono stati trattati chirurgicamente presso il nostro Dipartimento. Tutti i pazienti hanno eseguito mammografia ed ecografia mammaria prima dell'intervento chirurgico.

Risultati. In 13 pazienti l'ecografia è stata efficace nell'identificazione preoperatoria del tumore filloide. La mammografia non ha rilevato la lesione in 5 casi, mentre nei restanti 11 casi ha evidenziato caratteristiche di benignità della lesione, con opacità rotondeggiante e margini ben definiti.

Conclusioni. L'ecografia mammaria rimane a tutt'oggi l'esame diagnostico principale per la diagnosi dei tumori filloidi della mammella. Nessun esame diagnostico è in grado di prevedere un eventuale comportamento maligno della lesione. In caso di sospetto va realizzata una biopsia con ago sottile.

KEY WORDS: Phyllodes tumors - Breast - Ultrasounds.
Tumori filloidi - Mammella - Ecografia.

Introduction

Breast phyllodes tumors (PT) are uncommon fibroepithelial lesions, accounting for 0.3 to 1.0% of all

primary breast tumors (1) and having potential malignant features in approximately 25% of cases (2). These tumors are structurally similar to fibroadenomas, but have characteristic features, like pleomorphism, mitoses and overgrowth of the stroma with possible infiltrative margins, thus making the distinction from fibroadenomas straightforward (3).

PTs have been first described by Miller in 1838 (4), and named cystosarcoma phyllodes, and since the first description, they have been named in more than 60 synonymous (5). Currently, the term of cystosarcoma phyllodes should be reserved to tumors having histological

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sarcomatous features. It has been demonstrated that the stroma of PT is mainly monoclonal, while the epithelium is polyclonal, and the interactions between stroma and epithelium could be essential in the mechanisms of tumor development (6).

The clinical behaviour of these tumors could be unpredictable, due to relatively high recurrence rates, despite of correct surgical resection (7). Local recurrences develop in 8 to 40% of patients in various reports, while distant metastases occur in 0-21% of patients, thus depending on the number of cases and of aggressive lesions (7).

Conventional diagnostic examinations i.e. Mammography (MM) and Ultrasonography (US), show high sensibility and specificity rates (8), but cannot discriminate between benign and malignant PT. Magnetic Resonance Imaging (MRI) is not more effective (9), and, due to few data and the high costs, it is not used routinely.

Patients and methods

From 1996 to 2006, 16 female patients (age 27-54, median 43) affected by breast phyllodes tumor have been surgically treated in our Departments.

All patients received preoperative MM and US; breast MRI was performed in 3 cases. In four cases, ultrasound-guided Fine Needle Aspiration (FNA) was performed by 19-21 Gauge needle.

Site, form and size, outlining, tissue density and possible presence of microcalcifications were assessed by MM.

US scan was performed using a real-time multifrequency linear probe (7.5-10 Mhz) and a convex probe for larger tumors (2.5-3.5 Mhz) (Hitachi H19, Esaote, Genoa, Italy) evaluating possible intralesional features, such as echogenicity, posterior enhancement or acoustic attenuation of the echoes, and assessing the intralesional blood supply by means of color-Doppler device.

Results

The lesions were found in the right and in the left breasts in nine and seven patients, respectively. In 83.3% of cases the patients presented a palpable breast lump.

In all cases the lesion was reported to have rapidly increased in size, with local pain and, in three cases, local reddening of the skin.

US demonstrated in all cases the presence of a breast lesion. In 13 patients, US was effective in preoperative diagnosis of phyllodes tumor, showing the presence of a solid, round shaped mass with regular smooth margins, posterior acoustic enhancement, remarkable size (from 4 to 15 cm), and absence of microcalcifications (Fig. 1). In one case (Fig. 2), US detected the presence of a grossly malignant neoplasm, having large size, irregular shape and margins, with hypo- and hyperechoic areas. In the remaining two cases, US was unable to di-

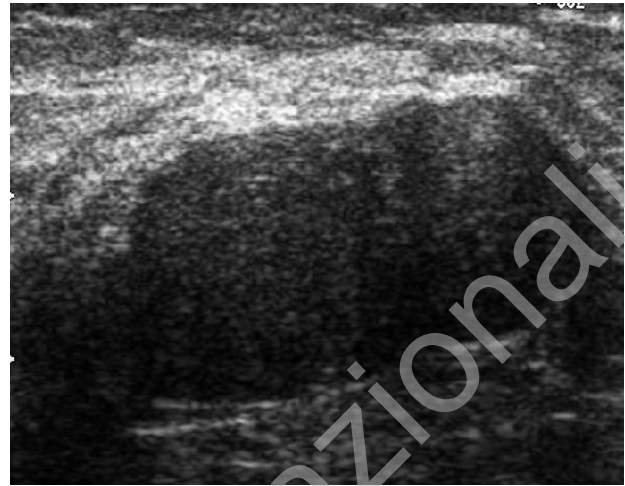


Fig. 1 - Phyllodes tumor: sonographic findings.



Fig. 2 - Malignant phyllodes tumor: sonographic findings.

stinguish PT from fibroadenomas. Color-Doppler assessment always showed intra- and peritumoral hypervascularization (Fig. 3).

MM was ineffective in detecting breast lesions in 5 cases, while in 11 cases MM findings presented a round opacity with moderate tissue density and well defined margins (Fig. 4).

Due to the uncertainty of preoperative diagnosis, MRI was performed in three cases, showing low signal intensity on T1- and T2-weighted images, and increased signal (T2-weighted images) in the tissue surrounding the tumor in two of these three cases. Preoperative cytology was performed in four patients having lesions > 4 cm, always showing the presence of a proliferative process (Not Otherwise Specified, NOS), thus recommending for excisional biopsy.

All patients underwent surgery, and in all but one case conservative surgery was performed.

Histology showed the presence of phyllodes cysto-



Fig. 3 - Phyllodes tumor. Color-Doppler evaluation of intralesional vascularization.



Fig. 4 - Phyllodes tumor. Mammographic findings.

sarcoma in three cases, low-malignancy grade phyllodes tumor in five, and benign phyllodes tumor in eight cases. Of the four patients who presented local recurrence, two had a pathological diagnosis of phyllodes tumor with low malignancy degree, and two of malignant phyllodes tumor.

During follow-up, four patients showed local recurrence, with need for further surgical excision. In three of these cases the tumor was treated and controlled by local excision, while one patient underwent four surgical excisions, being her initial histological diagnosis of phyllodes tumor with high rate of interstitial atypia. This patient finally received radical mastectomy, and definitive histologic diagnosis showed liposarcomatous degeneration.

Discussion

PT is currently defined as a peculiar variant of fibroadenoma with the potential to grow to a very large

size, to relapse after surgical excision, and to present malignant features (1, 8, 9). According to World Health Organization classification (1), there are three types of PTs, depending on the histopathological features: benign, malignant and borderline.

The etiology of PTs is still unknown, while it mainly affects Asian women in the age group of 35-55 years (6, 9). Several Authors believe that pathological features of PTs are fundamental to optimize their management (10-11), while others emphasize that there is no relationship between biologic behaviour and histologic finding (6, 7), and that all PTs should be treated as potentially malignant lesions. The only factor that could be considered predictive for local recurrence is the status of the margins of the resected specimen (6), while tumor size, advocated by some as potential predictor of malignancy and/or local recurrence, has been found not to be an important prognostic factor and, in some series, absolutely benign tumors > 12-15 cm have been reported (12, 13). Another sign which may rise the suspicion of malignancy is the rate of tumor growth. Although tumor size is not related to its recurrence, it may influence the management, and possibly suggest the choice of mastectomy, in case of a large tumor-to-breast ratio. In the other instances of PTs, conservative surgery, with adequate resection margins, remains the treatment of choice.

The diagnostic work-up includes MM and US, while the employment of MRI is still limited mainly due to its costs. Furthermore, recent studies have not shown a clear superiority of MRI over US in the diagnosis of PT (8). While MM usually cannot show the differences between fibroadenomas and PT, often revealing the presence of a well-defined mass with no specific features (14), US is more effective, as PT appears as a round shaped lump, with smooth or lobulated margins, and heterogeneous hypoechoic texture, presence of fluid-filled spaces (cystic foci), and the absence of microcalcifications and sometimes posterior acoustic enhancement (15). Some of these features can also be found in fibroadenomas (16-18), that usually appear as hypoechoic and relatively homogenous ovoid tumors with smooth and rarely lobulated margins.

Currently three characteristics can be useful in the diagnosis of malignancy for PT:

- a) size of the lesion: usually malignant PT are larger than benign ones (5-15), even if several studies report benign PT larger than 5-7 cm in diameter;
- b) vascularization: malignant lesions exhibit neoangiogenesis (19, 20), which can be evaluated by the use of color "and pulse" Doppler (15, 17), showing perilesional or intralesional hypervascularization. However, some recent studies (21-23) have shown no significant differences between

- benign and malignant PT in terms of vascularization and number of intratumoral vessels;
- c) the “retrotumor acoustic phenomenon”: posterior enhancement is considered to be an indeterminate sonographic feature, whereas posterior shadowing is considered to indicate a malignant tumor (24, 25). Several studies have shown US posterior enhancement in 50-75% of phyllodes tumors, whereas posterior shadowing was found in 0-7% (15, 26); however, other reports indicate that the retrotumor acoustic phenomenon is not characteristic of PT, so it is not helpful in distinguishing benign from malignant PT (17).

In our experience US proved very useful in the diagnostic work-up of PT, as it did identify phyllodes tumors in about 90% of cases, thus giving indications for surgery. The problems we encountered were mainly due to the uncertainty of preoperative identification of malignancy, and this issue was encountered by other Authors who have previously dealt with this condition. Currently, preoperative cytology and/or histology are effective in showing the presence of PT, but there is no test that can distinguish benign from malignant lesions. In relation to cytology, this is, probably, to be referred to

the non homogenous features of this tumor that do not allow adequate cytologic sampling (3, 11). Stromal proliferation and nuclear polymorpha with increased mitotic activity, typical of malignant phyllodes tumor, are not always demonstrable on cytologic smears. However, the current indication for FNA in case of PT is the high suspicion of malignancy detectable by US, as it has been suggested by previous researches (15, 17).

Conclusion

At present, US is the most useful imaging test to diagnose PT, with an actual effectiveness of about 95-100% (100% sensitivity and 87.5% specificity), as it has been demonstrated by the present research and, also, by previous papers. However, there is no test available yet to distinguish benign and malignant PT, and to recommend FNA in case of suspected malignancy.

Conflict of interest statement

The Authors state that this is an original study and there is no conflict of interest concerning this paper.

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