Surgical treatment and MRI in phyllodes tumors of the breast
Our experience and review of the literature


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Introduction

Phyllodes tumors (PTs) are rare fibroepithelial neoplasms which account for 0.3% to 1% of all breast cancers in females. In men, PT is an extremely rare tumor and only a few cases have been described in patients with estrogen induced gynaecomastia 1-4. The majority of PTs occur in women between the age of 30 and 55, although cases in adolescents as well as in elderly women have been reported 5.

These tumors are characterized by a combination of a hypercellular stroma and cleft-like or cystic spaces lined with epithelium into which classically the stroma projects in a leaf-like fashion 6.

The World Health Organization (WHO) classifies this breast neoplasm, according to the histological features, in benign, borderline and malignant PTs 7.

On clinical examination most patients have a smooth, round, firm, well-defined, mobile mass. Palpable axillary lymph nodes are encountered in 20% of patients with PTs, but histological evidence of malignancy is observed in less than 5% of axillary lymph node dissections for clinically positive nodes 8.

These lesions do not have pathognomonic features at mammography or ultrasonography. Mammography usually shows a round or lobulated lesion. Ultrasonography depicts a well-defined mass with single or multiple, round or cleft-like cystic spaces 9-21.

MRI may evidence characteristic features that, when present, are likely to be pathognomonic of PT. In these patients, dynamic MRI demonstrated a multi-lobulated lesion that rapidly and markedly enhanced on dynamic studies. T1-weighted and T2-weighted images showed inhomogeneous signal intensity for the presence of cystic...
areas and internal septation in the solid portion. In case of bulky masses inhomogeneous signal intensity due to bleeding within the mass, can be observed. In case of phylloides of small size, cystic areas can be absent and the lesion is more homogeneous and most similar to fibroadenomas. MRI enables complete visualization of the tumor even in the region close to the chest wall, as well as clear delineation against the healthy glandular tissue 22-26. Fine needle aspiration cytology (FNAC) frequently does not allow a clear-cut differentiation between benign or borderline PTs and fibroadenomas; under such circumstances histological confirmation is therefore required. Malignant cases are easily diagnosed by cytological examination 27,28. Wide resection with adequate margins is the treatment of choice. Total mastectomy is indicated for very large tumors and for local recurrences of borderline and malignant lesions 29-31. Subcutaneous mastectomy with immediate prosthetic reconstruction is a well-established surgical procedure and can achieve better cosmetic results 53-54. Many studies reported a significant association between local recurrence and positive microscopic margins 55-62. The purpose of this study was to reassess the relationship between MRI findings and surgical resection margins in an attempt to address the issue of an appropriate surgical management of PT. We herein report three cases of PT in which MRI was performed prior to surgical treatment.

Patients and Methods

Three female patients (aged 58, 40 and 50 years respectively) with a large palpable mass that abruptly increased in size underwent mammography, sonography and MRI. Breast MRI was performed on a 1.5-tesla scanner using coronal T1 and T2-weighted images (3D EFGRE, FA = 25°, TR<30 ms, TE<5 ms, NEX = 1, slice thickness = 2-3 mm, 0 interval, 256x224 matrix) before and six times after i.v. administration of Gd-DTPA (0.2 mmo- li/Kg at a flow of 2 ml/s). Native images were subtracted and post-processed. In all cases fat-suppression sagittal images were also acquired. Surgical management was wide excision with adequate macroscopic margin resection in two patients (one of which later underwent mastectomy) and mastectomy in the other patient.

CASE 1
A 58 year old woman on September 1999 came to our observation with a left breast tumor; she autonomously felt this tumor 4 weeks previously. There was no family history of breast disease. Menarche occurred at 12 years of age with regular menses. The physical examination revealed a large tumor, 7 x 4 cm, in the upper half of the left breast. The lump was well defined and not fixed to the underlying chest wall. An X-ray mammogram demonstrated that the left breast mass was homogeneous with well defined margins. On ultrasonography a well-defined, oval mass with fairly regular internal echoes was showed (Fig. 1a). In this case the suspicion of a phylloides tumor was based on the clinical pattern rather than on the radiological findings. In fact both on mammography and US, the images did not allow differentiation from a more common fibroadenoma; it was the rapid growth of a lump which reached 7 cm in diameter within 4 weeks in a 58-year-old woman to be compatible with phylloides tumor. Dynamic MRI demonstrated a well defined oval mass in the upper quadrant of the left breast (Fig. 1b). The lesion showed marked enhancement after contrast administration. The enhancement pattern was slightly inho-
CASE 2

On February 2000 a 40 year old woman presented with a left breast mass with a rapid increase in size over the previous 4 months. There was no family history of breast disease. Menarche occurred at 13 years of age with regular menses.

The physical examination revealed asymmetry of the left breast because of the difficulty in obtaining an adequate specimen. A wide resection of the breast tumor was performed with adequate macroscopic margins. Microscopic examination revealed a benign phylloides tumor with sclerotic areas and margins of at least 1 cm (Fig. 2a-c). Follow-up (at 6 and 12 months) consisted of mammography, sonography and clinical examination. The patient remains well with no evidence of recurrence.

mogeneous without cystic areas. There was a well evident cleavage plane with the pectoral muscle. The dynamic curve was of gradual type with 60% maximum signal intensity at minute 1, as for a benign lesion (Fig. 1c). A fine-needle aspiration was non diagnostic, primarily because of the difficulty in obtaining an adequate specimen.

A wide resection of the breast tumor was performed with adequate macroscopic margins. Microscopic examination revealed a benign phylloides tumor with sclerotic areas and margins of at least 1 cm (Fig. 2a-c). Follow-up (at 6 and 12 months) consisted of mammography, sonography and clinical examination. The patient remains well with no evidence of recurrence.

Fig. 1c: Dynamic curve: time/intensity curve shows 60% maximum signal intensity at minute 1 and gradual type morphology.

Fig. 2a: Benign phyllodes tumor with hypo- to moderately cellular leaf-like processes in cystic spaces.

Fig. 2b: Focal stromal hyalinisation.

Fig. 2c: Typical bipolar stromal cells intermingled with abundant fibrillar collagen. No mitotic figures are observed.
intensity at minute 1 (160%) and rapid wash-out as for malignant lesion (Fig. 3b-e).

A fine-needle aspiration was consistent with cellular fibro-epithelial tumor. Mastectomy was performed and microscopic examination revealed a borderline phylloides tumor (Fig. 4a-c).

Follow-up (at 6 and 12 months) consisted of mammography, sonography and clinical examination.

The patient remains well with no evidence of recurrence.

CASE 3

On April 2001 a 50 year old woman presented with a large palpable mass in her left breast. She had discovered the tumor two months previously. There was no family history of breast disease. Menarche occurred at 12 years of age with regular menses.

The physical examination revealed a large tumor in the upper half of the left breast, 8 x 6 cm. The lump was well defined and was not fixed to the underlying chest wall. An X-ray mammogram showed non-spiculated soft-tissue masses while on sonography a hypoechoic lobulated mass with cystic areas was visualized (Fig. 5a-b).

Dynamic MRI demonstrated a multi-lobulated lesion with inhomogeneous signal intensity on T1 and T2-weighted images sequences. In the solid portion there were cystic areas with internal septation. The posterior margins in some images appeared irregular with areas of linear enhancement. MIP reconstruction showed marked enhancement of the lesion, regional hypervascularization and linear enhancement in the postero-inferior region. The dynamic curve was of plateau type (Fig. 5c-n).

A fine-needle aspiration was performed with conventional and thin layer-liquid based technology. In both slides, the dominant features consisted of hypercellular myxoid tissue fragments, intermingled with isolated atypical plump stromal cells and very rare typical epithelial elements. Occasional mitotic figures were observed. The final diagnosis was of spindle cells, myxoid neoplasia consistent with malignant phylloides tumor.

A wide resection of the breast tumor was performed with adequate macroscopic margins resection. Microscopic examination revealed a malignant phylloides tumor with...
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Fig. 3c-d: MRI (coronal images of left breast before (c) and after (d) administration of paramagnetic contrast): the mass shows inhomogeneous enhancement.

Fig. 3e: Dynamic curve: the curve shows high maximum signal intensity at minute 1 (160%) and rapid wash-out as for malignant lesion.

Fig. 4a: Borderline phyllodes tumor is a neoplasm with moderately cellulated stromal component.

Fig. 4b: Epithelial elements are separated by stromal proliferation, but no overgrowth is evident.

Fig. 4c: Spindle cells are moderately irregular and hyperchromatic with scattered mitotic figures (no more than two to five per 10 HPF). In this area there are two mitoses.
Fig. 5a: Mammography: oblique projection of left breast: note a gross nodular multilobular lesion with blurred margins.

Fig. 5b: Sonography: gross area of inhomogeneous echoic structure, composed of nodular hypoechoic areas and areas of fluid contents.

Fig. 5c: MRI (coronal MIP reconstruction): in the left breast note the presence of a gross nodular enhancement area with regional hypervascularization.
Fig. 5f-g-h: MRI (axial and coronal MIP reconstruction): by cutting the enhancement area slice by slice on the coronal plane (f) the shape of the lesion is traced on the axial plane (g, h).

Fig. 5i: Volumetric image of the lesion.

Fig. 5d-e: MRI (lateral and oblique MIP reconstruction): note the linear enhancement in the inferior-posterior region of the mass.

Fig. 5: Surgical treatment and MRI in phyllodes tumors
In all cases of our series, mammography documented the presence of a nonspiculated, dense, round or lobulated mass. On sonography, hypoechoic masses with multiple septate cystic areas were visualized. Dynamic MRI demonstrated lesions that rapidly and
markedly enhanced on dynamic studies of contrast-enhanced T1-weighted imaging and inhomogeneous signal intensity in T2-weighted images. At histopathological examination, collagenous fibres and hemorrhage were seen in the hypointense areas in the solid portion in T2-weighted images. In the dynamic study, the first patient showed a gradual type, the second patient a wash-out type and the third patient a plateau type dynamic curve. In patient n. 3, an irregular posterior margin with linear enhancement adjacent to the principal mass, was documented. This was the site of a positive margin microscopically.

In our patient n. 1 a wide resection of the breast tumor was performed with adequate macroscopic resection margins. Microscopic examination revealed a benign phyllodes tumor with margins of at least 1 cm. In patient n. 2, mastectomy was performed because the lesion was too big to achieve a 1 cm margin without markedly deforming the breast. Microscopic examination revealed a borderline phyllodes tumor.

In patient n. 3 a wide resection of the breast tumor was performed with adequate macroscopic margins but microscopic examination revealed a malignant phyllodes tumor with infiltration of margins at the site where MRI had shown areas of linear enhancement. Therefore, mastectomy with immediate prosthetic reconstruction was subsequently performed. In none of our patients there was palpable axillary adenopathy; therefore axillary dissection was never performed. None of the patients herein received adjuvant chemotherapy or irradiation. All our patients currently show no evidence of local or distant recurrence.

Discussion

In 1938, Johannes Muller first described what has become known as phyllodes tumor. The name he chose, cystosarcoma phyllodes, proved to be unfortunate becau-
PTs of the breast are rare fibroepithelial tumors with an incidence of 0.3-1% of all breast neoplasms. They represent approximately 2-3% of fibroepithelial neoplasms of the breast. In men, PT is an extremely rare tumor, and only a few cases have been described in patients with estrogen induced gynaecomastia 1-4. The majority of PTs occur in women between the age of 30 and 55, although cases in adolescents, as well as in elderly women have been reported as in Haagensen’s series and in SEER analysis 5. Epidemiological data suggest that the incidence of these tumors may be higher in Caucasians in general and in Latin americans and East Asians in particular. There is no correlation between the development of PT and oral contraceptives, smoking habit, diabetes mellitus, age of menarche, allergies or family history of cancer 4,5,39.

On gross inspection, most patients have a smooth, round, firm, well-defined, mobile, painless mass; these tumors are generally indistinguishable from fibroadenoma. Microscopically, PTs are composed of epithelial elements and stromal connective tissue. The stroma contains long, branching clefts lined by one or several layers of bland epithelium. The clefts often broaden into cysts, resulting in the polypoid, frond-like appearance grossly evident on cut sections. PT differs from fibroadenoma in that the stroma is much more cellular with nuclear atypia and mitotic figures (Fig. 4-11) 29,34. The classification of PT is based on the histological features of the stromal component. The World Health Organization (WHO) classifies these tumors in benign, borderline (low-grade) and malignant (high-grade) PTs 7. High-grade malignant PTs represents a rare but aggressive breast malignancy, accounting for approximately 25% of all phyllodes tumors (range 10-54%) 5,29,36.

These lesions do not show pathognomonic characteristics on mammography or ultrasonography. Mammography shows a round or lobulated, nonspeculated lesion which only rarely contains microcalcifications. Ultrasonography shows smoothly margined masses with weak or intermediate internal echoes and internal cystic areas, without substantial acoustic attenuation. At sonography cystic areas are more common in malignant than in benign tumors, but differences are not statistically significant 15,19. Sonography cannot distinguish between malignant, borderline and benign PTs 9,21. Rich neovascularization with venous flow and low resistance arterial flow are visualized at color-Doppler US 13,14.

A substantial overlap is observed in the mammographic and sonographic characteristics of fibroadenoma and PT 9,13,14,16. The diagnosis of a phyllodes tumor should be considered in women, particularly over the age of 35 years, who show a rapidly growing “benign” breast lump (large, firm, non-tender, well-defined, mobile with gradual growth) 11,12. Usually PTs are larger than fibroadenomas. The ratio of the length to the anteroposterior diameter of PTs is smaller than the ratio of length to anteroposterior diameter of fibroadenomas. PTs are often lobulated while fibroadenomas are oval. If lobulation and heterogeneous hypoechoic internal echoes are observed and calcifications are absent, a diagnosis of PTs should be considered 9,13,14,16. MRI may show characteristic features that are likely to be pathognomonic of PT. Dynamic MRI demonstrates a multi-lobulated lesion that rapidly and markedly enhances on dynamic studies of contrast-enhanced T1-weighted imaging. T2-weighted imaging shows inhomogeneous signal intensity with a hypointense area and internal septation in the solid portion. MRI enables complete visualization of the tumor even in the region close to the chest wall, as well as clear delineation from the healthy glandular tissue 22-26. In the literature 22-26, no cases of phyllodes tumor with wash-out dynamic curves have been reported; the tumor dynamic characteristics are rather similar to those of fibroadenoma with gradual type dynamic curves. In our study the borderline phyllodes tumor showed wash-out type dynamic curves and the malignant phyllodes tumor a plateau type dynamic curve.

While our observations refer to only three patients, however it might be hypothesized that phyllodes tumors of higher malignant potential develop dynamic characteristics more similar to those of malignant breast tumors. If so, MRI would be able to provide a further parameter for the evaluation of the tumor tissue characteristics. Mammography and sonography were able to document the lesion with the detection of the site, structure and margins. MRI allowed a more panoramic evaluation in the 3 spatial planes with optimal visualization of posterior deep planes and the relationships with chest wall structures. In patient n. 3 irregular posterior margin with linear enhancement adjacent to the principal mass was present; in this case the presence of positive margins was documented.

With the recent increase in the use of fine-needle aspiration cytology to diagnose palpable and radiographically detected breast lesions, there has been growing interest in the cytological diagnosis of PT. Findings described as associated with cytological diagnosis of PT include the presence of epithelial clusters or finger-like projections (in the benign and borderline forms), hypercellular stromal fragments, single plump stromal cells (atypical in the malignant PT), naked bipolar nuclei, mitotic figures (more probable in the malignant forms). Nevertheless fine needle aspiration cytology frequently no allows differentiation between benign or borderline PTs and fibroadenomas and histological confirmation is required 10,27,28.

Surgery is the treatment of choice for PTs. Controversy exists about the extent of resection required and the need for lymph node dissection. The heterogeneity of the disease and its low incidence make a prospective study addressing these issues difficult to achieve. In the past, radical
 мастэктомия была часто проведена для PTs. В настоящее время более консервативный подход рекомендуется. Многие факторы в лечении должны быть рассмотрены, включая размер опухоли, размер молочной железы, степень распространения, хирургическое удаление маргинальных опухолей, морфологию опухоли и агрессивность, и предпочтение. Однако, основная цель — это достижение широкого, отрицательного порога. "Широкий порог" включает в себя полосу в 1 см от здоровой ткани вокруг микроскопического порога опухоли 12,39,41,44,47,55-62.

Рецензия на науку включает следующие терапевтические рекомендации: при бензине филлоидной опухоли, порог лимфатических узлов, широкое локальное исключение с 1 см без гематогенной и редких к лимфатическим узлам. В то время как пальпируемый лимфатический узел обнаружен в 20% всех пациентов с PTs, только 5% из них рентгенологически негативны. Для граничных и малигнизированных опухолей порога операции зависит от размера опухоли, который в сравнении с размером груди. Следует полностью удалить только если размер опухоли не позволяет либо достаточный порог лимфатических узлов либо хороший косметический результат. Автор не рекомендует лимфатическую диссекцию, если узлы не пальпируемые. Лимфатические лимфатические узлы обнаружены у 20% пациентов с PTs. Ретроспективные сериях пациентов с PTs, рентгенологические данные опухоли только в 5% всех пациентов с клинически пальпируемыми лимфатическими узлами. В обзоре восьми больших серьезных исследований PTs только одна публикация указывает на возможность в висцеральной лимфатической диссекции. Других (Принцесс Маргарет Хоспитал, Институт Густав Руасси, M.D. Anderson Cancer Center, Массачусетс Генерал Хоспитал, Институт Густав Руасси, M.D. Anderson Cancer Center, Massachusets General Hospital, и Italian and British multi-institution studies) не указывают на преимущество в устранении висцеральной лимфатической диссекции 5,12,29,31,39,62.

Послеоперационная радиотерапия и адъювантную химиотерапию не играют важной роли в управлении PTs. Роль радиотерапии в лечении PTs неопределенна. Рациональ для его использования на ограниченном числе случаев и в аналогии с установленной эффективностью радиотерапии, чтобы обеспечить локальную контроль и широкий порог вырезанной мягкой ткани. В некоторых исследованиях RT после локального локального исключения было показано, что уменьшение локальной рекurrencии в данных PTs; однако, не значительный эффект на выживаемость был снят 64-68.

Химиотерапия не была оценена, но полезна в бензине филлоидной опухоли, и она не показывает значительную роль. Ее роль ограничивается на лимфатическое метастазирование и возможно для паллиации неизлечимой локальной рекurrencии. Не существует демонстрируемой роли для гормональной терапии 68-73.

Адъювант систематическая терапия не рекомендуется, исключая для плохого прогноза PTs. Большинство исследований из Institute Gustave Roussy and M.D. Anderson Cancer Center утверждает, что достаточность порога определения является важным фактором в пролонгации безрецидивной и общей выживаемости 75-62.

Риск местной рекurrencии, который уменьшен в бензине форм (6-10%) и значительно выше в потенциально злокачественных формах (30-40%). Локальные повторы могут быть управляться через повторную операцию. Повторные локальные повторы часто развиваются без развития дальнейших метастазов или улучшения смертности 4,6,9,13. Большинство повторов являются рентгенологически сходными с первоначальной опухолью, которые могут быть более агрессивными 6.

В результате все пациенты с бензином и граничными PTs излечены без лечебной терапии. Для малигнизированных PTs, метастазы развиваются в 20-30% пациентов часто в легкие, плевральные, и кости 3,4,30,39,47,61,62. Размер опухоли, степень митотической активности и стromal atypia были описаны как предрасполагающие факторы для развития дальнейших метастазов 30,47,59,62. Тореталл повторы до 12% и зависит либо от прямого распространения к грудной клетке, либо от метастазов в легкие, кости или оба 3,4,30,39,47,59,61,62.

Резюме

Основной целью у всех PTs лечение должно быть полное исключение с широким порогом, и при mastectomy only when necessary to achieve clear margins. Routine axillary dissection is not indicated. MRI enables complete visualization of the tumor even in the region close to the chest wall, as well as a clear delineation from healthy glandular tissue.

Ретроспективный анализ трансформации опухоли указывает, что ошибки в диагностике могут быть устранены путем использования MRI.

Цель исследования: Этот обзор исследует характеристики филлоидных опухолей, основываясь на результатах исследования.

ОБЗОР ИССЛЕДОВАНИЙ: Наши исследователи не рекомендуют использование МРТ для оценки лимфатической диссекции, отсутствие рентгенологических и гистологических изменений в опухоли.
Sono state così ottenute immagini sottratte che hanno meglio evidenziato le aree di enhancement patologico, ricostruzioni MIP ed MPR per la visualizzazione 3D e multiplano delle lesioni e curve dinamiche relative alle regioni di interesse. Di ogni lesione sono state studiate le caratteristiche morfologiche (forma, dimensioni, margini, volume e caratteristiche di segnale) e dinamiche (morfologia dell’enhancement e caratteristiche della curva dinamica). Le pazienti sono state sottoposte ad intervento chirurgico e i risultati istologici sono stati confrontati con i segni radiologici.

L’esame mammografico ed ecografico non sono stati sempre in grado di visualizzare in maniera chiara i margini e l’estensione delle lesioni specie nella regione più profonda della ghiandola mammaria.

RISULTATI: La RM ha sempre ben documentato i rapporti delle lesioni con i piani muscolari ed ha permesso una migliore definizione dei margini e del tessuto ghiandolare sano adiacente.

Nel caso di tumore filloide benigno le caratteristiche radiologiche sono state piuttosto simili a quelle di un fibroadenoma (morfologia ovale, margini netti, struttura sostanzialmente omogenea e con curva dinamica di tipo graduale chiaramente suggestiva di lesione benigna). Negli altri due casi la RM ha mostrato masse a morfologia polilobulata, disomogenea per presenza di aree cistiche settate, aree emorragiche e porzioni solide, con enhancement marcatto e rapido. Le curve dinamiche in questi due casi hanno sempre mostrato caratteristiche di malignità (morfologia wash-out o plateau e elevata intensità massima di segnale al primo passaggio).

L’esame istologico ha rivelato un caso di tumore filloide benigno, un caso di tumore borderline ed un caso di tumore filloide maligno.

Il trattamento chirurgico di prima istanza è stato di escissione con margini di resezione indenni di almeno 1 cm nel caso di tumore filloide benigno e nel caso di tumore filloide maligno. In quest’ultimo comunque l’esame istologico definitivo ha evidenziato infiltrazione micro-metastasi di tessuto ghiandolare sano adiacente.

CONCLUSIONI: L’escissione chirurgica con ampi margini di resezione deve essere il trattamento chirurgico di scelta dei tumori filloidi della mammella. La RM può comunque definire, in fase preoperatoria, l’esatta estensione tumorale in modo da individuare il trattamento chirurgico primario più appropriato.

References


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