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RESEARCH ARTICLE

PHYLLODE BREAST TUMORS (STUDY OF 14 CASES) IN CHU MOHAMED V MARRAKECH MOROCCO.

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Abstract

Phyllode Breast Tumors (PBT) are rare fibroepithelial tumors that represent less than 1% of primary breast tumors. Their diagnosis is mainly histological.

Our study was conducted in plastic, restorative and burns surgery department in CHU Mohamed V in Marrakech Morocco between 2012 and 2017, covering 14 patients with histologically certified phyllodes breast tumors.

The purpose of our study is to focus on the origin, factors, the diagnosis of PBT, to compare them to those found by other authors and the treatment that has been followed.

Phyllode breast tumors (PBT) is a rare disease that can affect women at different age. It requires early diagnosis to avoid the high potential for transformation.

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Introduction:-

Phyllode breast tumors (PBT) are rare fibroepithelial tumors that represent less than 1% of primary breast tumors (1) and 2.5% of fibroepithelial tumors (2). They mainly affect women between the age of 35 and 50 years and their diagnosis is mainly histological (3). In general, they are considered benign. However they are distinguished by a great capacity to the local recurrence and the malignant transformation. To date, there is no consensus on the criteria for distinguishing between different forms of phyllodes tumors. In addition, the correlation between these histological criteria and the clinical tumor behavior remains poor. This difficult predictability causes great confusion in therapeutic protocols.

The purpose of our work is to highlight the epidemiological, clinical, histological, therapeutic and the evolution of these tumors through a retrospective study and discuss the results against literature data.

Materials and Methods:-

This is a retrospective study conducted at the plastic surgery department in CHU Mohamed VI Marrakech in Morocco between 2012 and 2017, involving 14 patients with histologically certified phyllodes breast tumors.

Discussion:-

Phyllode breast tumors are rare fibroepithelial tumors that represent 0.3 to 0.9% of women breast tumors. (1) This pathology affects patients aged 35 to 50 years. The phyllode tumor is located in 30% of cases in the supero-external quadrant of the breast. Its size can vary from a few centimeters to several tens of centimeters of major axis.

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It is usually multi-lobed, not fixed to the skin or deep plan. We find axillary adenopathies in 20% of cases (4). They are characterized by a tendency to a local recurrence and a rarity of distant metastases.

In our study, the average onset age was 38 years. PBT are rare in adolescence. it has not been found in any teenager. They have a high prevalence for women in Latin America and Asia (5).

PBT are exceptional for men. In general they are preceded by gynecomastia (1). In our series, no case has been identified.

Studies have shown that there is no relationship between the phyllode breast tumor and the pre-menopausal or menopause periods.

They also demonstrated that the use of contraceptive pills did not increase the risk of developing a phyllode breast tumor (6). These same studies found a correlation between tumor development and parity because most women were nulliparous (6). Indeed, in our study, 14 women were nulliparous (42.8%).

All aspects can be seen, since the small tumor of a few centimeters, mobile, circumscribed, to the large one occupying the entire breast even beyond the projection of the breast. Tumor size does not seem to be related to malignancy. Bilaterality cases are rare (1). All tumors were unilateral.

In our study, most of our patients were young with an average age of 32 years.

The tumor average size was 15.22 cm and occupied the entire breast with and even surpassed the surrounding tissue for 05 patients (29.4%).

In the literature, patients had a firm mass, rarely painful, Bumpy or multilobed, mobile and well circumscribed, located in the super-external quadrant in 30% of cases (6). In our population, for 12 patients, 85% of the giant ulcero-budding irregular tumors that occupied the entire breast with destruction of the surrounding tissue were found to be able to be explained by the delay of the consultation due to the low socioeconomic level of the patients and also to the general state of preservation and the painless nature of the tumors.

In the majority of cases, the axillary lymph nodes are not palpable because the diffusion metastatic of these tumors is mainly hematogenous. 10 to 15% of patients would develop axillary lymphadenopathy, which most often results from hyperplasia reacts to infection of a necrotic tumor rather than metastasis (6).

Mammography was performed and presented rounds or oval masses with large volume, usually single, homogeneous water tone, sometimes with polylobe contours with fast growth. According to other authors, Calcifications are rare and represent less than 10% of cases (1, 3, 5,7). In our study, only two patients had calcifications (about 10%). Most mammography performed in other studies performed by Buchberger , Al., Liberman al., Or Yilmaz as well as in our study, mammography was carried out only at 11 patients because of enormous size of tumors and their ulcero-bulgeous aspects. Mammography showed rounded opacities, well circumscribed or lobulated. (8, 9, 10)

In some cases, the mammographic appearance was that of carcinomatous mastitis with an opaque breast and this would be difficult to analyze with X-rays with cutaneous thickening (1).

All our patients were referred to our department with a diagnosis of phyllode tumor on biopsies. We had to study 13 pieces of total mastectomy, and a single piece of tumerctomy. The anatomopathological examination of these pieces confirmed the diagnosis of phyllode tumor for all the patients.

The histological grading was specified for all the cases:

1. WHO grade I phyllode tumor: 6 patients, 42.8%
2. WHO grade II phyllode tumor: 5 patients, ie 35.71%
3. WHO grade III phyllode tumor: 3 patients, ie 21.42%

The number of phyllode breast tumors described on the MRI is limited. No MRI has been performed to our patients..

Morphological signs reported by most authors are: (11,12,13,14,15)

1. Oval or lobulated mass
2. Regular contours
3. With intra-tumor septas (50% of the cases).

Studies describing MRI signs performed on women with mild PBT found oval masses sometimes lobulated of regular contours, presenting a hyper-signal in T2 or hyper and iso-signal in T2 and hypo-signal in T1, raising itself quickly after injection of the contrast product (24, 26).

Yabuuchi al. studied the correlation between MRI signs and the histological grade of phyllode breast tumors of for 30 patients (19 benign, 6 intermediate, 5 malignant).

This study reported that the signs in favor of malignancy are:

1. Irregular contours, an hyper signal in T1
2. Cystic rearrangements
3. Hypo T2 signal
4. Restriction of the diffusion coefficient "ADC".

He also reported that T1-weighted hyper-signal corresponded to the cystic hemoragy and histopathological necrosis, whereas the T2 hypo-signal and the restriction of the diffusion "ADC" coefficient corresponded to the hypercellular stroma (24).

The treatment of phyllodes tumors is usually surgical, from wide excision to total mastectomy (4). Adjuvant treatments are of little interest. Indeed, all our patients have been surgically treated, one patient have performed adjuvant chemotherapy and radiotherapy, while another patient has received only radiotherapy.

During the 1970s, radical surgery was the standard surgical treatment for all types of PBT regardless of tumor size. But that did not offer more advantage on the patient survival because local recurrences did not seem to be related to Spread of systemic disease. That's why today, a surgical approach procedure has been adopted (5, 11).

Curator approach:-

Conservative treatment consists of a wide excision with a safety margin of 1-2cm. It is recommended for all types of mammary phyllodes tumors, benign, borderlines or malignant. (3, 6,17,18,19,20). In our study, only one patient (7.11%) has benefited of a large lumpectomy.

Enucleation was proscribed (5, 6,21,22) because of the recurrence risk and malignant degeneration.

If the lumpectomy fails to obtain a margin more than 1cm, it is recommended to operate again the patient to obtain a greater safety margin to avoid the risk of local recidivism.

If there is a local recurrence of benign PBT, it is recommended to make a re-examination with a margin major than 2-3 cm. This wide margin is recommended to avoid any risk of malignant transformation or sarcomatous proliferation (6). As for local recidivism of borderline and malignant PTB, some authors recommend re-excision while others opt for total mastectomy (3, 5, 11,13).

Radical approach:-

Radical treatment consists in a total mastectomy (without lymph node dissection), which is reserved for the tumors larger than 5cm or multi tumors recidivating despite of the adequate margins (3, 6, 7, 17, 19).

In our series, 7 patients (57.14%) had a total mastectomy and 6 patients (42.85%) benefited of a radical mastectomy of Patey. These six patients had Grade 3 tumors, measuring more than 15 cm in diameter with suspicious axillary lymphadenopathy.

Axillary dissection is not routinely recommended, since the proportion of Axillary metastasis of malignant PBT is less than 10% (5).

In addition, and due to the fact of palpable axillary lymphadenopathies of malignant PTB are almost always reactionary, axillary dissection will not be realized in the case of clinically suspected lymphadenopathy which its metastatic type has been histologically confirmed previously. It will therefore be a lymphadenectomy of necessity (Bergl) (3,12).

In our study after mastectomies, 7 patients were self-closing by direct sutures and 6 others coverage was by thin skin grafting.

Radiationtherapy is only relevant for malignant and borderline PTB. It aims to decrease local recurrence but has no impact on survival (24,25).

After the surgery treatment, the indication for adjuvant radiotherapy is discussed according to the tumor size, the quality of margins of excision and the anatomopathological features of the tumor (the mitotic index, the presence of necrosis tumor, cellular atypia and a Rapid stromal growth) (4,18, 26). In our population, radiotherapy was indicated for one patient after conservative treatment with negative margins, but the evolution was marked by tumor recurrence within 12 months.

Barth's study has shown that conservative surgery for PTB even with negative margins was associated with a significant risk of local recidivism and that the surgery coupled with neoadjuvant radiotherapy allowed local control of borderlines and malignant PTB (19).

When radiotherapy is decided, its practical modalities are not otherwise clearly established. Often, a breast or wall irradiation of at least 50 Gy, associated with a complement of 10-15 Gy in the tumor center is prescribed by analogy with soft tissue sarcomas of the breast (4,17).

Different chemotherapy protocols have been used. But as for radiotherapy, its role is not clearly established. However, low response rates have been observed in pulmonary metastases, unresectable local recurrences and rarely bone metastases, with ifosfamide-based chemotherapy alone or in combination with doxorubicin (dose $\geq 60\text{mg} / \text{m}^2$) (5, 18, 16). Other agents such as cisplatin associated with doxorubicin and etoposide were also used for (21). Only one patient in our study received neoadjuvant chemotherapy.

All PTB, whether benign, intermediate, or malignant, may re-induce locally and all have metastatic potential (3, 7, 16, 22, 28).

The mortality rate varies from 3 to 12% depending on the studies (6).

According the literature, local recurrences appear in 0-59% (24). The risk of recurrence is low for benign tumors (6-10%) and potentially high for borderlines and malignant tumors (30 to 40%) (23).

In our study population Local recurrence occurs after an average interval of 33 months for benign and 22 months for malignant PTB. Histologically, these recurrences look like the original tumor in 80% of cases, and in 20% of cases are in more aggressive forms.

Predictors for recidivism are primarily related to (22,30,31) :

1. Excision margins (1-2 cm). +++
2. Histological type. +++
3. Stromal proliferation. +++
4. Tumor size.
5. Number of mitoses
6. Presence of necrosis.

In most series, local recurrence was isolated without distant metastases (5). The most patients who have been metastized, had a local recurrence later (22, 32,33). 2 cases of local metastasis were noted in our population.

The average survival rate is around 75% at 5 years. The literature has shown that the rate of survival at 5 and 10 years, was 91% and 79% for non-malignant PTB , and 82% and 42% for malignant one (6). The long-term survival

of patients with PTB is determined by the presence or absence of distant metastases (32). Metastases are most often located at the pulmonary level (70%), bone (30%), and more rarely at the cerebral, abdominal and pelvic level. Metastatic phyllodes tumors represent very unfavorable prognosis and it has not been reported long-term survival (5).

Several predictive factors for metastasis have been studied, including: (16, 23):

1. High mitotic activity.
2. Hypercellularity.
3. Stromal atypia.
4. Stromal proliferation

Conclusion:-

Phyllode tumors are fibroepithelial tumors that represent less than 1% of primary tumors of the breast. They are classified by WHO in 3 grades, benign, borderline and malignant.

They mainly affect young, nulliparous women during the periods of genital activity.

It is most often a palpable mammary nodule, the size of which may vary from a few centimeters to a large tumor occupying the whole breast. So that imaging makes suspect the diagnosis of phyllode tumor, this is not confirmed only by anatomopathological study of the operative specimen.

PTB treatment is usually surgical. It consists of a wide resection with 1-2cm margins for any type of small tumor that does not exceed 5cm. The total mastectomy, is reserved for large tumors (> 5cm) or multiple recurrent tumors despite adequate margins.

Ganglion dissection is not performed routinely. The metastatic spread of these most of the tumors are hematogenous, cleaning will be performed only in case of clinically suspect lymphadenopathy with confirmed metastatic nature histologically previously.

Adjuvant treatments are of little interest. The purpose of radiotherapy is to reduce local recurrence but has no impact on survival. As for chemotherapy, it has mainly been used for palliative purposes.

All phyllodes tumors may recur and all of them could have metastatic potential.

The prognosis is based on the histological characters of the tumor and on the quality of tumor excision.

Competing Interests:-

The authors declare no competing interests.

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