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BREAST CANCER IN MEN ABOUT NINE CASES MANAGED AT THE MOHAMED VI CENTER FOR ONCOGYNECOLOGY

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ABSTRACT

Breast cancer in men is a rare disease. Risk factors are many and varied. The diagnosis is made at a later age than in women and at a later stage. The clinical presentation of the disease differs a little in men. All histological varieties can be seen in men with a rarity of lobular carcinoma. Hormonal receptors are often positive with a rare overexpression of her2 in men the sentinel lymph node method is technically possible. Hormone therapy plays an important role in treatment and tamoxifen remains the molecule of choice. The treatment of breast cancer in men is not as well codified as in women. For obtain the logical conclusions, investigators link multi-institutional analyzes, a prospective multicenter trial is currently underway in the US, which sets as its main objective to optimize the therapeutic strategy. The prognosis for breast cancer in men is the same as in women at the same stage. Several studies are needed to optimize the management of patients with this disease. It would be desirable that efforts of education and information of the Moroccan population with regard to this pathology, combined with an adequate psychological management of the patient and his family, be implemented in order to improve the experience and the prognosis of Moroccan patient with breast cancer. In Morocco, the incidence of breast cancer in men is estimated at 0.8 - 1%.

KEYWORDS: Breast cancer, man, carcinoma, treatment, prognosis.

INTRODUCTION

Breast cancer in men is a rare condition. Although many studies refer to this pathology, they remain infrequent and are in most cases retrospective studies with a limited number of patients. This affection still unknown to the general public makes the discovery of a breast nodule in a man does not cause the same concern as in women. Thus, the diagnosis is most often delayed making the prognosis darker. Also, breast cancer in men has several interesting psycho-social and cultural aspects that deserve to be investigated.

Indeed, in an Arab-Muslim society with a masculine spirit like ours, the dignity of man can be seriously compromised after the diagnosis of breast cancer, a real "shame" that can deprive him of his virile status. or to downgrade it to the rank of women.

MATERIALS AND METHODS

Our work is a retrospective study of 9 cases of breast cancer, treated at the Department of Surgery of the center Mohamed VI Ibn Rochd University Hospital Center of Casablanca, for a period of five years, from March 2013 to February 2018.

Through our work we plan to emphasize the epidemiological, diagnostic, therapeutic and prognostic characteristics of this rare entity.

ANALYSIS AND RESULTS

The average age of our patients was 61.88 years old. In the absence of screening, the mammary nodule was the telltale sign in all patients in the series associated with mastodynia in two patients.

- The average consultation time was 15 months.
- The lesion was located most frequently in the left breast (5 cases / 9) and bilateral in only one case.
- The predominant histological type was invasive ductal carcinoma (7 cases / 9).
- The basic salary consisted essentially of a Patey intervention.

- Ganglionic invasion was found in seven patients.

The complementary treatment was based on the combination of chemotherapy, radiotherapy and hormone therapy in five patients. An association of chemotherapy and radiotherapy was indicated in two patients. One patient had received chemotherapy alone. Only one had benefited from hormone therapy alone.

Two patients had metastases during follow-up. To date, no case of death was found in our series

Figure 1: Mass of 4 cm, retro-areolar associated with nipple retraction with exematization of the areola

Figure 2: Induration of 1,5x1,5cm with nipple retraction.

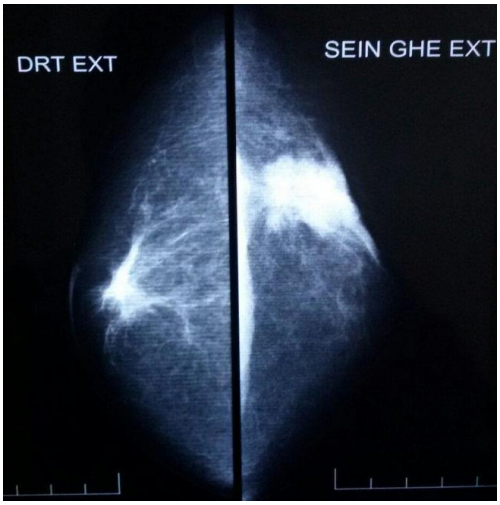

Figure 3: Mammogram showing extra retro-areolar opacity of fuzzy, irregular and spiculated contours with suspicious nipple attraction.

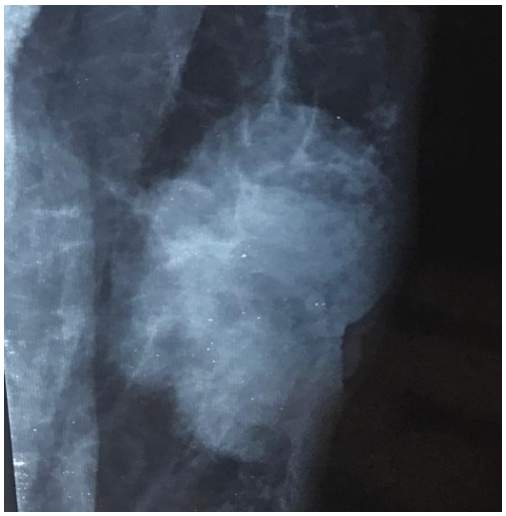

Figure 4: Retro-shaped areolar mass enclosing micro calcifications, with thickening of the skin.

Figure 5: Mammary ultrasound of the same patient showing a retro-areolar hypoechoic tissue nodule of 13mm of the left breast of irregular contours and very attenuating posterior.

DISCUSSION

Breast cancer in man is a rare disease, so little known. It accounts for only 0.6% of all breast cancers, and less than 1% of the cancerous pathology in man.[1] In Morocco, the incidence of breast cancer in men according to our two national registries (Rabat Cancer Registry and Cancer Registry of Greater Casablanca) is estimated at 0.8 - 1%.[45]

However, in Tunisia, male breast cancer represents 2.1% of all breast cancers, which is a higher frequency than ours.[9]

The highest rate was found in intertropical Africa, where its incidence is estimated at between 4 and 5% of breast cancers, or even 13%.[27]

On the contrary, the incidence is particularly low in the Japanese population, less than 5 / 1,000,000.[17]

This variation suggests the impact of the environment on incidence in populations that are similar in many ways, such as age of onset and comorbidities.[17]

According to Donegan,[41] the number of cases of breast cancer in man diagnosed annually increases gradually while in other series, the incidence remains relatively stable over time.[23,26]

The average age of onset of breast cancer in men is about 60 years old. However, some cases have been observed at the extreme ages of life ranging from 60 to 93 years.[3] This cancer is rare or even exceptional before 30 years and 2/3 of patients are between 50 and 80 years old. Indeed, its incidence increases with age. This male cancer appears 8 to 10 years later than in women. In our study, the average age of patients at the time of diagnosis was 61.87 years with extremes of 52 and 83 years. This average age is comparable to the data found in Rabat,[12] Sousse in Tunisia,[40] Lille in France,[17] Ouagadougou in Burkina Faso[27] and Istanbul in Turkey.[48] The average age found in these countries ranges from 60 to 69 years old. However, a study conducted in Algeria found an average age of 39 years.[69] This variation suggests the impact of the environment on the early occurrence of breast cancer in men in Algeria.[17] The distribution of ages appears most often, uni modal in the male sex, contrasting with that observed in the woman.[9] In addition, breast cancer appears 10 years earlier in women than in men. This shift may be due to the earlier onset of menopause in women compared with the age of decline in testosterone production in men.[9]

The pathophysiological mechanisms of breast cancer and gynecomastia are very similar (estrogen / circulating androgen imbalance). Currently, there is no evidence that gynecomastia is the precursor to cancer or if the association is accidental.

Of 123 patients studied in Tunisia, four had developed cancer on pre-existing gynecomastia.[5]

A similar result was found in a French study of 19 cases.[6]

Two cases of clinical gynecomastia without histological confirmation were reported in a study of five patients in Burkina Faso.[27]

In the meta-analysis of Sasco et al, one to 13% of patients with breast carcinoma had a history of gynecomastia, according to the authors, this association could be fortuitous due to a recruitment bias.[17]

The notion of family and genetic antecedents is found in 5 to 10% of cases.[3,7] This notion of "families of breast cancer" is related to the existence of genetic mutations on many genes and the most common of which are: BRCA1, BRCA2, p53, and c-erbB-2.

In our series, no patient had a family history of cancer and none had a genetic investigation for this reason

About physical factors, people might thought that chest trauma would have a relationship with breast cancer, any trauma (surgical, accidental...) activates pro-inflammatory cytokines, triggers neo-angiogenesis and releases growth factors without promoting the occurrence of cancer. We can not prove the causal link between the trauma and the tumor microenvironment necessary for the growth of quiescent cancer cells. Only one case of trauma was found in our series without any precision.

About Exposure to ionizing radiation, the risk is all the more important as irradiation has been carried out in young men or even children. In our study, no patient had a history of radiotherapy or a condition requiring regular radiographic monitoring.

Endocrine factors

Klinefelter syndrome: No karyotype has been performed in our patients. The most rational explanation is that this type of disease is accompanied by alteration of hormonal metabolism with a drop in testosterone, and a higher frequency of gynecomastia.

Endogenous hypereoestrogenesis: It seems that it is more of an imbalance between the estrogen level and the androgen levels that is involved. Men who have had mumps orchitis, cryptorchids, ectopias, congenital inguinal hernias or traumatic testicular lesions appear to be more exposed to breast cancer.[11,34,29] In our study no estrogen dosage was performed.

Exogenous hypereoestrogenesis: It may be more often than not estrogen-induced cancers, but mammary metastases of prostate cancer.[47]

In our series, no patients were on testosterone-based therapy

Obesity: It would be responsible for an increase in the conversion of androgens into estrogen by peripheral aromatization in adipose tissue. four of our patients were overweight. This result is similar to that found in a study of three patients[3] who found only one.

Alcohol consumption

Hepatic abnormalities in cirrhotic patients may also increase estrogen levels and predispose to breast cancer;[26,30] the risk is increased in cases of chronic alcoholism.[11]

In our study only one patient consumed alcohol

The pathological examination allows the establishment of the diagnosis of malignancy on the cytology samples, biopsies and on the operative parts. The extemporaneous examination confirms the malignancy and specifies the limits of excision. The role of the anatomopathological study is crucial to guide the complementary treatment and to establish the prognosis.[9,13]

All histological types found in women are described in man:

- Invasive ductal carcinoma largely predominates (70-90%).[9,13]
- Papillary, tubular, medullary and colloid carcinomas account for 15% of specimens.[9,14]
- Neuroendocrine carcinomas are rarely reported in the literature.[15,16]

Lobular carcinoma is extremely rare in humans due to the absence of lobular architecture in the male breast.[2,4] Rather, it is reported in patients with gynecomastia with hyperoestrogenesis or Klinefelter syndrome who associate XXY trisomy, infertility with hypogonadism, gynecomastia, and often large size.[1,14]

Paget's disease is a rare form in women, exceptional in men (0.03%).[13] The characteristic of this lesion concerns the skin of the nipple and areola, which is frequently fissured, ulcerated and oozing. His diagnosis is pathological, based on the presence of Paget's cells in the epidermis. These cells are organized in the basal layers and are isolated in the superficial layers. They are large, with clear cytoplasm that may contain mucopolysaccharides (PAS positive) or a melanin pigment. Their nucleus is bulky, strongly nucleolus;[13] non-invasive carcinomas or "carcinoma in situ" (this is ductal carcinoma in situ) account for about 5% of breast cancers in man. However, forms of lobular carcinoma in situ, now called "lobular neoplasia", have also been described.[2,16,31]

Ganglionic invasion is found in 50 to 75% of cases.[14,32] This high rate is explained by the central topography of breast cancer and the small volume of the male mammary gland,[6,33] Axillary invasion is correlated with:

1. **Tumor size:** Invasion is 35% for tumors less than 2 cm and 75% for tumors larger than 2 cm.[14,32]
2. **The histological type:** Metastases are more frequently seen in invasive ductal carcinomas and medullary carcinomas.[14,34]

The immunohistochemical study allows to note that hormone receptors with progesterone (RP) and estrogen (ER) are more frequently positive than women, with rates often very high (85% of cases), the androgen receptor is expressed in 50% of cases;[35-37] the positivity of neuroendocrine markers (synaptophysin-chromagranin A) is essential for the diagnosis of neurodocrine carcinomas.[15,16]

The other biological markers (c-erbB-2, p53, Bcl2 and vimentin) are factors with a purely prognostic value.[15,38,39,40,41]

All our patients had histological examination, seven tumors were infiltrating ductal carcinomatous in nature,

one tumor was ductal carcinomatous in situ and the ninth was galactophoric carcinomatous with mammary lympha- gitis.

This cancer is revealed in about 90% of cases by a retro-areolar tumor.[1] Nipple abnormalities are early and more frequent than in women.[5] Cutaneous ulceration is more common in men than in women.[4] Similarly, nipple discharge, almost always bloody, is found in 10 to 15% of cases.[8] Paget's disease remains rare (4 to 8%).[8] Axillary lymph nodes are palpated in almost half of the cases.[33] Clinical signs reflecting the presence of distant metastasis are present in 3 to 12% of cases. These signs are related to bone (bone pain, functional impotence, etc.) or pleuropulmonary localization.[41,42]

Imaging should not be performed routinely, but should be reserved for patients for whom the clinical diagnosis is uncertain or who has risk factors for breast cancer, as well as for biopsy guidance and extension assessment.[25]

Breast ultrasound
The lesions are similar to those found in women. Typically, they are hypoechoic with irregular contours due to invasion of surrounding tissues and the association of edema and fibrosis.[9] Eight patients in our series had breast ultrasound, which helped guide the diagnosis.

Mammography
It is of more difficult realization and of more restricted interest than in the woman. She finds her place to differentiate between a gynecomastia and a cancerous lesion. Only one incidence can be realized. It should include the same elements of study as in women (tone, dimensions, seat, contours, micro-calcifications ...) and should lead to the same classification ACR.[39] Mammography was requested in six of our patients.

MRI
Unlike conventional imaging, MRI indications for diagnostic purposes in humans are exceptional or non-existent.[17,39]

Galactography
It may find its place to locate abnormal galactophoric tissue when there is nipple discharge without an individualizable mass. In the absence of conservative treatment, its interest remains very limited in humans.

Tumor Markers
No diagnostic assays are recommended except for monitoring treatment with an initially high level of marker.[10]

Anatomo-cyto-pathological examination
The management of a breast tumor requires, first of all, the confirmation of the malignancy by histological analysis, or at least cytological analysis, with the help of a cytopunction.[10]

The treatment is based on surgery, which is primarily a modified radical mastectomy with axillary lymph node dissection according to Patey.[9] Because of the small volume of the mammary gland in man and the rapidity of tumor extension, conservative surgery is not indicated.[9]

More than 70% of breast cancers in men can be operated on, despite locally advanced forms and metastatic forms (Table VII). In some series, the operability rate reaches 100%.

In our study, it was a Patey mastectomy in seven cases and a lymph node dissection to complete the mastectomy done elsewhere in the eighth case. All mastectomies were associated with lymph node dissection.

Radiotherapy
Its postoperative application is still controversial. For some, it is systematic, for others, it is indicated only in locally advanced tumors and in case of axillary histological infiltration.[38,18,19,24,26,46]

In our series, seven patients received radiotherapy, including two at a metastatic stage

Chemotherapy
The CMF protocol (Cyclophosphamide, Methotrexate and Fluorouracil) is one of the most widely used in humans,[36,21,22,28] but it is largely an old series. The most recent ones use an anthracycline in the protocol.[28,46] As a result, the FAC / FEC or AC / EC protocols are currently the most commonly used adjuvant.

In our study, six patients received a CT. The most used protocol was AC60

Hormone
Hormone therapy can only be indicated in cases of hormone-sensitive tumors expressing at least one of the two hormonal receptors. In humans, it is offered as first-line treatment given the average age of patients, the many diseases often associated with them, and the frequent and high positivity of hormone receptors.[16]

Ablative and additive therapies have been discontinued.[9] Currently, competitive hormonal therapy with anti-estrogens (tamoxifen 20 mg / day) is proposed.[9]

Of the 9 patients in our series, 6 were on hormone therapy.

Mortality from breast cancer in man is close to that induced by salivary gland cancer.[46] The death rate from breast cancer in men is 0.1%.[20,24] Overall survival at 5 years varies between studies between 43% and 79% and 10 years between 10 and 56%.[6]

In our series, the study was spread over four years only (since the inauguration of the center to date) and all patients operated on at home are still alive. Several series

carry out a more detailed analysis of the survival according to the prognostic parameters.

The reference scheme provides for consultation every six months for five years, and then every year. This monitoring schedule must be discussed and adapted to each patient, in particular according to the criteria of severity and the risk of relapse.[16]

- Examination of the intervention scar in search of local recurrence.
- Contralateral breast examination.
- Search for contralateral lymphadenopathies on the treated side.
- Search for supraclavicular lymphadenopathy.
- Abdominal palpation to assess hepatic volume.

This clinical examination is preceded by a detailed interrogation which makes it possible to assess the general state between two successive consultations (slimming, asthenia) as well as the existence or absence of particular functional signs:

- Fixed and continuous bone pain Side point thoracic
- Hépatalgie
- Root syndrome
- Intracranial hypertension syndrome.

Unilateral annual mammography (after total mastectomy) is the gold standard for paraclinical surveillance. It can be associated with a breast ultrasound (bilateral or contralateral according to the surgery).

The first oversight mammogram should be performed one year after the initial mammogram and at least 6 months after the end of the radiotherapy. There is no indication for the systematic completion of other imaging tests (especially liver or thoracic). Other additional examinations are discussed in the presence of call signs. On the other hand, no assay of serum tumor markers is recommended in the follow-up.

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