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Particularities of Male Breast Cancer in the Rabat Region: A Multidimensional Approach

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Abstract:

- ***Introduction:***

Male breast cancer is a rare disease, accounting for just 1% of all breast cancers. This low incidence and lack of awareness often lead to delayed diagnosis and advanced disease. In addition to its specific clinical and epidemiological features, it has a significant psychological impact, due to its feminine connotations and the stigma attached to the diagnosis.

- ***Methods:***

This retrospective descriptive study analysed the clinical, epidemiological and psychosocial data of breast cancer patients. Data were collected from medical records, and from semi-structured interviews with patients.

- ***Results:***

The mean age at diagnosis was 63, with most patients consulting for a retroareolar mass, but also for delayed presentation, sometimes more than 6 months. Locally advanced forms were noted. The ordeal of the disease was marked by significant psychological distress: anxiety, social isolation, body image problems and feelings of stigmatisation. Several patients said they were embarrassed to talk about their illnesses, fearing a lack of social and medical understanding.

- ***Conclusion,***

Male breast cancer poses multiple problems. In addition to medical treatment, a comprehensive approach including psychological support is needed. Better information for the public and healthcare professionals would enable earlier detection and more appropriate treatment, both somatic and psychological.

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I. INTRODUCTION

Male breast cancer is an uncommon disease, accounting for 1% of all breast cancers and less than 1% of all male neoplasms [1,2] It remains less recognized in men and a diagnosis is often delayed due to lack of awareness and acceptance of the symptoms. In recent decades the incidence of male BC is also increasing [1,2]. Studies demonstrate that the average age of breast cancer incidence in men is 5e10 years later than in women, with a mean age of 65 years [3]. Male BC is usually diagnosed at worse stages (and worse prognosis). Previous data has shown that risk of death is 43% greater in men than in women [4]. Due to the infrequency of male breast cancer (BC), the staging, treatment & prognosis associated with this disease are poorly documented. The evidence-based recommendations for male BC are derived from data on female breast cancer [5, 6]. Several guidelines for male BC have been published in the last several years [7, 8]. Despite, the relative infrequency of male BC there is heterogeneity in both clinical and pathological features of BC in men compared with women.

The aim of this article is to evaluate the particularities of male breast cancer, the clinicopathological characteristics, the therapeutic management, as well as the psychological experience related to the diagnosis of male breast cancer.

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II. PATIENTS AND METHODS

This retrospective study enrolled male patients from radiation therapy of national institute of oncology, in Rabat, Morocco. This study included men diagnosed with invasive breast cancer, between January 2017 and December 2023. ded. Patients were classified based on age (<45 years, 45-60 years and >60 years), histology (invasive ductal, invasive lobular and special sub- types), clinical stage (organised according to the American Joint Committee on Cancer - 8th edition of TNM) (stages 1, 2, 3 and 4) [9], treatments (surgery, chemotherapy, radiotherapy and endocrine therapy) and time period of treatments (2017 - 2023). The data included the immunohistochemistry (IHC) status of patients. The histological type intraductal carcinoma, sarcomas, and malignant phyllodes were excluded. And for psychological aspect, questionnaires were filled in by the patients. and semi-structured interviews with patients were established.

III. RESULTS

35 male patients treated for breast cancer were included.. The demographics and clinical characteristics are included in Table 1. Age at diagnosis was mainly over 60 in 56.4% of cases. The most common histological subtype is invasive non-specific carcinoma. (84.5% patients). The mean age of our patients was 63 years, with only 3 patients < 45 and 18 patients (60%) over the age of 60 at time of diagnosis. The predominant histological type was non-specific infiltrative carcinoma at 84.3%, followed by lobular carcinoma (9%). Molecular status was luminal A at 38% and luminal B at 55% and HER 2 + positif at 7%of cases . Hormone receptors were positive in all cases. 17% of patients had family history of cancer, including one patient who had breast cancer in mother and sister.

The most common symptom leading to consultation was nodule in 93% of patients. Other patients had bloody discharge. The delay to consultation was between 1 year and 8 years, average was 20 months.

Table 1 : Characteristics of Male Breast Cancer Patients in National Institute of Cancer, Rabat

Characteristics		N	%
Histology	Non specifique Invasive Carcinoma	27	84.5
	Lobular Invasive Carcinoma	3	9.3
	Other	2	6.2
Molecular statut	Luminal A		38.0
	Luminal B		55.0
	HER2 positif		7.0
Age	<45	3	9.3
	45e60	11	34.3
	>60	18	56.4
Clinical staging Tumor (T)	T0	0	0.0
	T1	5	15.6
	T2	12	37.5
	T3	5	15.6
	T4	10	31.3
	TX	0	0.0
Clinical staging lymph nodes (N)	0	8	25.0
	1	18	56.2
	2	4	12.5
	3	2	6.2
	Nx	0	0.0
Clinical staging e metastasis (M)	0	795	87.7
	1	3	9.3
Treatment modalities	No Treatment	0	0.0
	Surgery	4	12.5
	CT	3	9.3
	RT	0	0.0
	Surgery + CT	2	6.2
	Surgery + RT	1	3.1
	Surgery + ET	3	9.3
	Surgery + CT + RT	2	6.2
	Surgery + CT + ET	2	6.2
	Surgery + CT + RT + ET	19	59.3
	Surgery + RT + ET	2	6.2

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The evolution was marked by good locoregional control in 65% of cases, locoregional relapse in 20% of cases and 15% of metastatic relapses at bone level highlighted in Figure 1 .

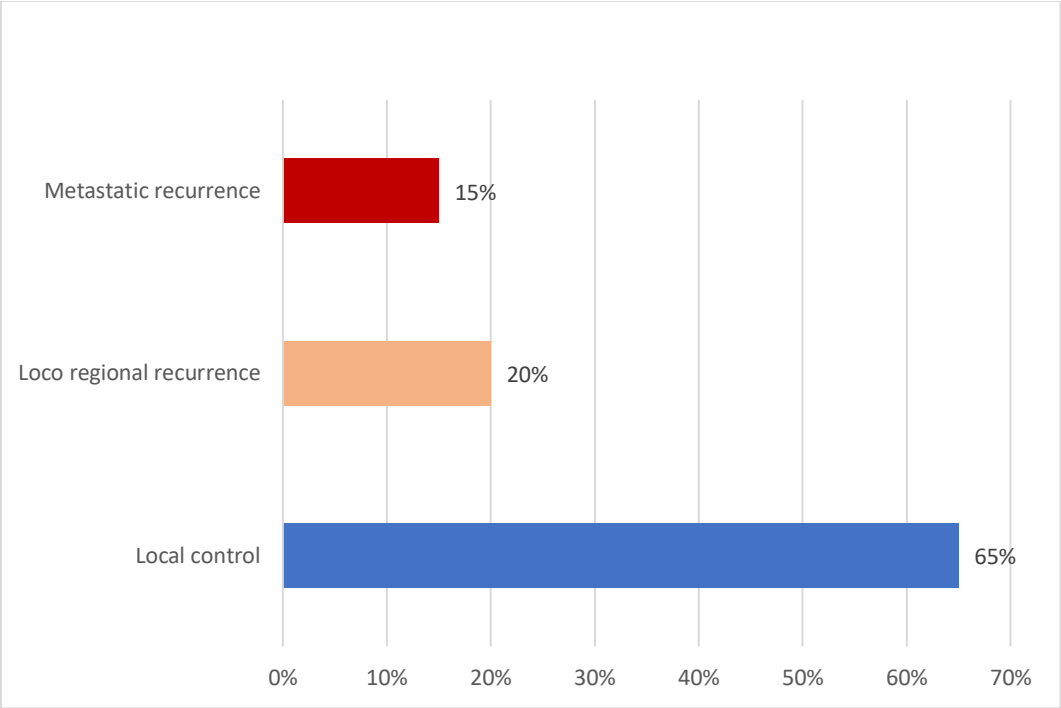

Fig 1 : Post Therapeutique Evolution of Patients with Male Brest Cancer After Treatment

In addition, the study examined the psychological aspect of breast cancer in men - in particular, its impact on body image and quality of life, as illustrated in Figure 2. Patients completed the EORTC QLQ C 30 version 3 questionnaire, the BSQ 34 body shape questionnaire and the Arabic version of the HADS anxiety and depression questionnaire. Psychologically, 25% of patients experienced anxiety during their illness, compared with 15% of patients who experienced depression. In terms of body image, 25% of patients experienced a disturbance of body image after surgical treatment and chose an avoidant attitude. Finally, quality of life deteriorated in 26% of patients after their treatment, expressed as both physical and psychological impairment.

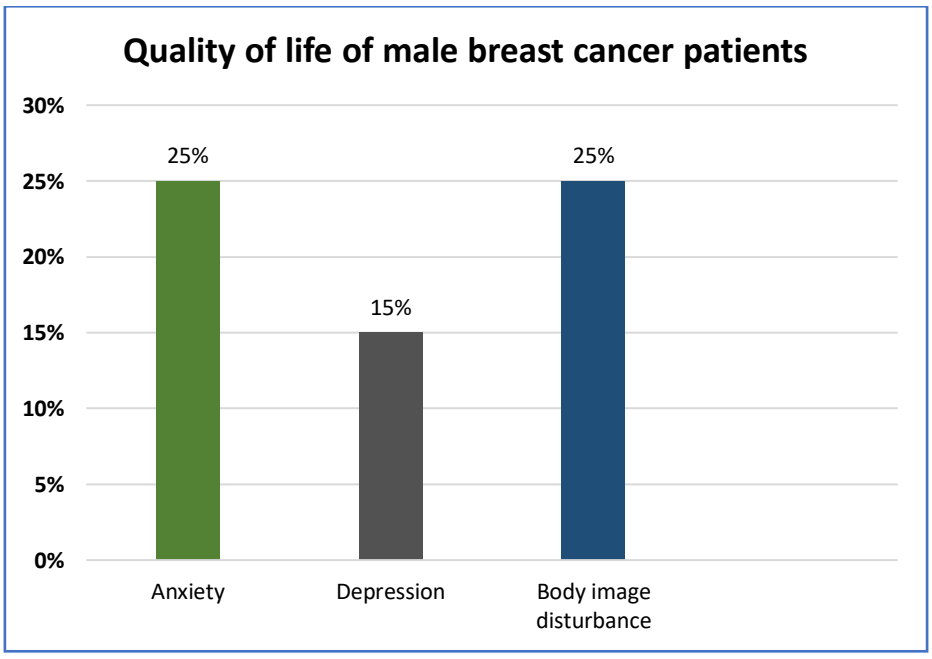

Fig 2: Quality of Life of Male Breast Cancer Patients

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IV. DISCUSSION

Male breast cancer is rare. Its incidence is estimated at 1 out of every 100,000 cases, making up less than 1% of breast cancers and less than 1% of male tumours [1,2]. The mean age at diagnosis for breast cancer in men is 67, or approximately 5-10 years older than women in the average age at diagnosis [10]. In our cohort the mean age at diagnosis was over 63, although ages ranged from 37 to 91 years. The pathophysiology of male breast cancer remains poorly understood, although a number of risk factors have been described. Obesity, through increased aromatisation of androgens, and alcoholic cirrhosis, through increased sex steroid-binding globulin, both induce a state of hyperoestrogenism favouring the appearance of tumours. [11]. Testicular anomalies (testicular ectopia, orchitis, orchidectomy), and some congenital malformations such as inguinal hernias or infertility, may also contribute to risk. A positive family history of breast cancer in women increases the risk for men by a factor of double to 2.5. Exposure to electromagnetic fields may disrupt activity of the pineal gland, leading to suppression of the secretion of melatonin, the hormone with anti-oestrogen action [11-13]. Previous radiation on the thorax (with a latent period of 20–30 years), long-term heat exposure [11] and chronic alcohol consumption have also been implicated [11,15,16]. On the other hand, gynaecomastia (either idiopathic or from drug) does not seem to increase the risk for male breast cancer [11,17].

➢ *Genetics*

As was the case in women, a family history of breast cancer is an accepted risk factor in men [11]. J.R. Weiss [11] stated that a history of breast cancer in a first-degree relative (male or female) is associated with two to three times greater risk than the general population.

BRCA1 and BRCA2 mutations lead to a substantial proportion of male breast cancer, although the absolute risk is less than women in both frequency and intensity [18]. Considering the frequency of these genetic mutations in this disease, breast cancer patients should automatically be offered genetic counselling to assess family risk and help with possible genetic and oncological treatment.

➢ *Diagnosis*

In most cases, it is characterized as a painful subareolar mass, nipple retraction or bloody nipple discharge [11, 19, 20]. Diagnosis can be particularly challenging when there is an elderly, overweight patient. Similar to women, there is a common left-sided predominance. The main differential diagnosis is gynaecomastia, which is a benign condition that affects approximately 30% of men [20]. In our series, every patient presented stating they had a nodule in the nipple. Breast imaging, and mammography specifically, provides a fundamental role in the diagnostic process. It distinguishes benign gynaecomastia - which is generally central, symmetrical and without malignancy features - from malignancy invasive cancer which will present with an eccentric, irregular nodule, with spiculated contour. This is why the sensitivity and specificity of mammography in male breast cancer is about 92% and 90% respectively [21]. Breast ultrasound is also a useful complementary examination, especially to describe the characteristics of the nodule and the axillary lymph node state. All imaging studies are routinely completed by microbiopsy, to ensure histological proof of the lesion.

➢ *Histology*

Ductal carcinoma in situ (DCIS) represents 10% of male breast cancers [10]. In the majority of cases, it is of the papillary or low-grade cribriform types [22]. Although lobular carcinoma in situ is exceptionally rare because of the lack of terminal lobules, it has been described in association with invasive lobular carcinoma in male breast cancer [23]. In our series, we did not describe lobular carcinoma in situ on any of the resection specimens; we only noted ductal carcinoma in situ in one patient. For invasive carcinomas, the histological types are comparable, however there are differences in their relative distributions [10]. Data indicated 93.7% of male breast cancers to be ductal or unclassified, 2.6% papillary, 1.8% mucinous, and only 1.5% lobular [10]. In our series, ductal carcinoma was the most prevalent, comprising 83.3% of cases. These tumours are strongly hormone-dependent; it is reported that 90% express oestrogen receptors and that 81% express progesterone receptors [10]. Hormone receptors were uniformly positive in our series. In male breast cancer, hormone receptors are expressed at a much higher rate than in female breast cancer, and with age of patient - as in females - there is an increase [10, 24]. The work-up to establish any extension included the CA15.3 tumour marker - which is primarily used for monitoring, full blood count, chest X-ray, abdominal ultrasound and bone scan. Tumour stage was established using the American Joint Committee on Cancer (AJCC) classification, for which the stage incorporates the tumour size, if lymph nodes were involved and distant metastases [25].

➢ *Prognosis*

Male breast cancer seems to have a worse prognosis than female breast cancer. Two important prognostic factors in male breast cancer are tumour size and lymph node involvement [10]. For example, men with tumours between 2 and 5 cm in diameter were 40% more likely to die from the cancer than men with tumours smaller than 2 cm in maximum diameter. Additionally, there was a 50% greater risk of death with lymph node involvement than with nodes without metastases. In univariate analysis, hormone receptor negativity and tumour grade are prognostic indicators not associated with a poor prognosis and survival [10, 26]. Male breast cancer due to a BRCA2 mutation can also be diagnosed earlier and this type of male breast cancer worsens prognosis. In general, prognosis for breast cancer in female and male patients will be similar [10]. Survival rates are lower for men but this can be

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explained by the diagnosis being made at an advanced stage of the disease [10].

➢ *Treatment*

In Early stage, local treatment is the same as in women. Most men are treated with modified radical mastectomy, sometimes associated with axillary curage or selective lymphadenectomy [27]. Generally speaking, radical surgery has been most frequently performed, but retrospective studies have shown an equivalent prognosis with less invasive surgery [28]. In our series, in 75% of cases a mastectomy with axillary curage without resection of the pectoralis major was indicated. On the other side, all the rest of the treatments - surgical (axillary lymph node or sentinel lymph node), radiotherapy, chemotherapy, hormone therapy (tamoxifen or anti-aromatases) and biotherapy (trastuzumab) can be part of the therapeutic arsenal. Axillary lymph node dissection is still mandatory [17]. Axillary lymph node dissection is associated with disabling upper limb lymphoedema in 10 to 25% of cases. Selective lymphadenectomy has only been recently studied in male breast cancer [29, 30]. Radiotherapy tends to be indicated more in men after mastectomy, as it is more likely there is either nipple or skin involvement [27]. Radiotherapy will decrease locoregional recurrence, studies have not shown any difference in overall survival [27]. In our series, we indicated radiotherapy in 63% of our patients.

In the University of Texas M.D.-Anderson Cancer Centre [31], chemotherapy has been indicated if tumour size is greater than 1 cm with lymph node involvement. When lymph nodes are free, anthracyclines are recommended as single agent, then in combination with taxanes if lymph nodes are involved. Hormone therapy is indicated if hormone receptors are positive [32]. In retrospective studies of adjuvant tamoxife, two reports showed decreased risk of recurrence and mortality. We don't know the toxicity of tamoxifen specifically in humans. There are reports of intolerance to the product, venous thrombosis, decreased libido, depression and hot flushes [33]. In the case of antiaromatases, there is one series published on five patients with metastatic disease but with no objective response [34]. There have been two cases published on patients treated with letrozole with significant reductions in tumour mass [34, 35]. While growing as a field Breast Cancer Care for Men has not actively engaged men with Stage IV Metastatic Disease. As with the Stage IV - Metastatic stage treatment for women, rationale is similar for men. The majority of patients will require hormonal treatments frequently because of receptor positive tumours. In this regard, Farrow and Adair would reasonably describe the case of a male breast cancer that had clearance of their metastatic disease after an orchiectomy. Orchiectomy, adrenalectomy and hypophysectomy have been used for many patients with metastatic disease, however hormonal therapies are now common standard of care. Tamoxifen is the preferred treatment with a response rate of 50 %, LHRH agonists are also treatment options with response rates, whether used alone or in combination with antiandrogens. In more advanced cases (hormone receptor negative or resistant) chemotherapy is appropriate. Chemotherapy can also be useful as palliative therapy and in cases where the timing of progression is rapid.While trastuzumab has not been shown to be effective in human cases of overexpression, Volm et al have suggested in stage IV Metastatic breast cancer in men metastatic disease with HER-2 overexpression be treated with trastuzumab. Primary or secondary cancers: Men who survive breast cancer have a greatly increased risk of a second primary cancer including contralateral primary breast cancer [29] at an absolute risk of 1.75%. Auvinen et al [30] estimate that men with previous breast cancer are thirty times more likely to develop contralateral breast cancer. For other sites, such as melanoma or prostate cancer, the risk is high among survivors, particularly with a genetic mutation.

On the other hand, The patient's psychological experience is profoundly altered: in addition to the typically psychiatric problems that come with any cancer announcement, from acceptance of the disease to mourning, including, depression, anxiety and fear of death [40], other problems are added: low self- and loss of self-esteem, isolation, body image and/or sexual identity problems, which can be just as repressive as the disease [41]. The patients social experience, where he is constantly running from the gaze of others, can be another brutal experience. He will reject feeling rejection or feeling as if belonging to the male race and social phobia and feelings of insecurity; or will go into a denial science regarding the disease [42]. Relationships with family will also suffer, as he may no longer view himself as the 'man of the house'. There are some suggestion that can be proposed, first to publicize the subject, educate and inform the concerned people. Men should also be encouraged to self palm during the areolar region, yes there is a family history, and seek medical guidance as a result of any abnormality; and it is imperative that the psycho-social impact be arranged on patients, suggesting appropriate quality of life self-questionnaires to discover problems and meet expectations[42]. The psychosocial aspects of care for patients and their families should form part of the treatment which must include different professionals [42].

V. CONCLUSION

Although it is rare, male breast cancer is a unique entity which has an increasing incidence. While male breast cancer tends to be diagnosed late, that often comes down to insufficient knowledge about the disease from patients and healthcare professionals, often resulting in a more guarded prognosis compared to women who are diagnosed earlier. With no specific clinical trials of male breast cancer, treatment care is based largely on extrapolating from the female protocols, which suggests the need for targeted research

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to inform the translation of treatment care to male patients. Finally, the impact of the disease can be minimised: things like stigmatisation, damage to the body image, and thoughts about isolation are factors that are important to consider in the patient's overall care. Therefore, we should approach male breast cancer with a multidisciplinary, gender-sensitive approach to optimise both clinical outcomes, and improve the quality of life for men with breast cancer.

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