



MALE BREAST CANCER AND PROSTATE CANCER : A case report

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Introduction

Breast and prostate cancers occur in about 1 in 8 women and 1 in 8 men, respectively. Male breast cancer is a rare disease, accounting for about 1% of breast cancers and less than 1% of all male neoplasia [1].

It is a pathology that is most often diagnosed at an advanced stage, making its prognosis poor [2]. The expected 5-year survival rate for patients with either cancer is approximately 90%. Endocrine therapy is the mainstay of management of these hormone-sensitive cancers; breast cancer, the leading malignancy in women, remains a rare disease in men.

Through a case description, we plan to emphasize the epidemiological, diagnostic, therapeutic and prognostic characteristics of this rare entity.

Patient and Observation:

This is an 84-year-old Patient, followed for adenocarcinoma of the prostate, presenting with a right breast nodule, progressively increasing in volume since 1 year. The clinical examination found a right retro nipple tumor measuring 3cm in diameter, firm consistency, poorly limited, mobile in relation to the deep plane associated with a painless right axillary adenopathy and fixed in relation to the superficial plane with inflammatory signs generalized to the whole breast, classified T4dN1Mx. Mammography found a 35 mm right retro nipple opacity, roughly rounded, with irregular contours, containing suspicious looking micro calcifications. The complementary ultrasound confirmed the presence of a right retromamma lesion of irregular contours associated with suspicious axillary adenopathies. This lesion is classified as ACR V. Biopsy of the nodule was in favor of an infiltrating ductal carcinoma of SBR grade III, 5MSBR. The immunohistochemistry study shows that 15% of the tumor cells express estrogen receptors and 10% express progesterone receptors, ki67 at 40%, HER2 negative. The extension workup was unremarkable. Given the locally advanced nature of the disease, the patient received 6 courses of AC 60-based chemotherapy, followed by a right mastectomy and right axillary dissection. The histological result is in favor of infiltrating ductal carcinoma grade III of SBR (5MSBR) of 06 cm. Histological analysis of the pectoralis major muscle did not reveal any invasion. The lymph node dissection returned 18 nodes, 11 of which were metastatic. The patient underwent radiotherapy and was subsequently put on tamoxifen-based hormone therapy.

Discussion

Male breast cancer is an extremely rare disease, accounting for 0.5 to 1% of breast cancers in Western countries and 0.4 to 1.2% of all male cancers [3]. The first description dates back to 1307 and was made by an English surgeon, John of Arderne [4]. Its incidence has increased

significantly in the last 25 years [5]. In Morocco, the incidence of breast cancer in men according to our two national registries (Rabat Cancer Registry and Greater Casablanca Cancer Registry) is estimated at 0.8-1%. In Western countries, the age of onset is approximately between 60 and 65 years [6], i.e. about 8 to 10 years later than in women [6, 7]. In our case, the age is 84 years, which corresponds to an age difference with respect to the literature series. The etiopathogenesis remains unknown, given the rarity of this disease and its association with prostate cancer [8]. For small subgroups of patients, some risk factors could be identified [8, 9]. Klinefelter's syndrome, which combines XXY trisomy, hypogonadism with infertility and gynecomastia, carries a 3-6% risk of developing breast carcinoma [8, 9]. The average age of development of breast cancer in a man with Klinefelter syndrome is 58 years [9]. Three to four percent of male breast cancers are associated with Klinefelter syndrome [9]. Thoracic irradiation in childhood: in a review by Kinne, 11 cases were reported; these were infants treated for compressive thymoma and adolescents with gynecomastia or who had repeated fluoroscopies for tuberculosis. A few cases following radiation for Hodgkin's disease have also been reported [8-10]. Cryptorchidism and testicular atrophy, whatever their origin (traumatic, iatrogenic, infectious), may increase the risk [8-11]. Family history increases the risk of breast cancer as it does in women. In general, according to J.R. Weiss [12], A family history of breast cancer in a first-degree male or female increases the risk by a factor of two to three. BRCA2 mutations in men are estimated to be between 4 and 16% [13]. Hence, genetic counseling should be offered in each case. The cumulative risk of breast cancer in men is 6.3% at age 70 [13]. The etiopathogenic hypothesis is that of an imbalance between androgens and estrogens, as in some gynecomastia [14].

Men with a family history of female breast cancer have a 2.5 times greater risk of developing breast cancer. In contrast, idiopathic or drug-induced gynecomastia is not incriminated in the occurrence of

this pathology [4, 5, 11]. Genetics Breast cancer in men is increased if there is a family history as in women [5]. In general, according to J.R. Weiss [5], a family history of breast cancer in a first-degree male or female is associated with a two- to threefold increased risk. Mutations in the BRCA1 and BRCA2 genes are implicated in a proportion of male breast cancer but with a lower absolute risk than in women and with a lower frequency [12, 13]. BRCA1 mutations are present in only 10-16% of patients with no family history [12, 14, 15]. BRCA2 mutations are more common in male breast cancer and are estimated to be 4-16% [16]. It is because of the prevalence of these mutations in male breast cancer that genetic counseling should be offered. The cumulative risk of male breast cancer is 6.3% at 70 years of age [7]. The percentage of BRCA2 mutation expression in male breast cancer varies from population to population (3.6 to 40%) reflecting genetic differences between populations [17,18]. Cowden syndrome is an autosomal dominant disease characterized by the development of multiple hamartomas associated with the germline mutation of the tumor suppressor PTEN gene located at 10q23. It is responsible for breast cancer in men and women [5, 19]. The mutation of CHEK2, a kinase involved in DNA repair, CHEK2*1100delC, has been implicated in the development of male breast cancer [5]. In our case, the patient had no family history of cancer and therefore a genetic investigation.

Diagnosis

Male breast cancer presents in most cases as painful subareolar swelling, nipple retraction or bloody discharge [15]. The delay between the first symptoms and the diagnosis is later than in women [15]. In our case, the patient consulted for a retro nipple nodule. The sensitivity and specificity of mammography in the diagnosis of male breast cancer are 90 and 92% respectively [16]. The retroareolar topography and the thin glandular tissue explain the high frequency of advanced T4 forms (with pectoral fixation and/or skin ulceration), especially in older studies [15, 16]. In our case, the tumor was

diagnosed at an advanced stage, which is consistent with the results of the literature. Bilaterality (synchronous and/or metachronous) seems less frequent than in women. Crichlow reports an overall rate of 1.4% [15]. Staging is always based on the TNM classification. As in women, the extension work-up includes the same examinations (chest x-ray, liver ultrasound, bone scan and CA 15-3 assay) [15-17]. Men do not have lobular elements, the most frequent histological type is ductal invasive carcinoma (IDC) (85-95%) [1- 10]. Inflammatory breast cancer and lobular histological type are exceptionally described in men [11-16]. Compared to female breast cancer, male breast cancer most often expresses hormone receptors [8, 16]. A recent study on a series of 75 patients showed that 5% of male breast cancers have her2-neu overexpression [15-17]. In our case the her2 gene was negative.

Prognosis

Breast cancer in men seems to have a worse prognosis than in women [14-16]. Tumor size and lymph node involvement are two important prognostic factors in male breast cancer [3]. Men with a tumor of 2 to 5 cm in diameter have a 40% increased risk of death compared to men with a tumor of less than 2 cm in maximum diameter [3-8]. We did not find any information in the literature about the stage of discovery of breast cancer in men compared to the stage of diagnosis in women. In case of lymph node involvement, In this case, there is a 50% higher risk of death than in the case of nodes without metastases [4-8]. In univariate analysis, hormone receptor negativity and tumor grade are associated with a poor survival prognosis [3, 14]. Male breast cancer due to a BRCA2 mutation occurs earlier and with a poorer prognosis [13, 14].

In general, the prognosis for female and male breast cancer patients is similar [2-4, 13-15]. The treatment strategy for the management of cancers in men is similar to that of women [9, 10].

Treatment

In the early stage, most men are treated with modified radical mastectomy combined with axillary curage or selective

lymphadenectomy [1-5;17-18]. In a series of 31 cases of ductal carcinoma in situ, Cutuli et al show three relapses after six lumpectomies (50%) while they find only one case of relapse for 25 mastectomies. The small size of the mammary gland makes it difficult to move to healthy margins [18]. Therefore, lumpectomy is not recommended [12-15]. Therefore, conservative surgical treatment has no indication in the treatment of male breast cancer because of the small breast volume and the easy acceptance of mastectomy by men. Postoperative radiotherapy improves local control and progressionfree survival but has no impact on overall survival [17-20]. In our case, the indication of radiotherapy was retained. Tamoxifen-type hormone therapy is considered the standard adjuvant therapy for patients expressing hormone receptors, but the efficacy and safety of this drug have been poorly studied in humans [12-16]. The main side effects remain the risk of thromboembolic complications, hot flushes and decreased libido [18].

In our case, the patient received adjuvant hormone therapy such as tamoxifen. By analogy with women, sequential adjuvant chemotherapy is indicated in young patients with lymph node involvement or possibly with SBR III lesions [15]. There is little information regarding the efficacy of adjuvant chemotherapy in male breast cancer. Only one prospective study has been published for this purpose in 24 men who received CMF (cyclophosphamide, methotrexate, fluorouracil) chemotherapy with a survival rate of more than 80% at five years, and significantly greater than in a similar cohort [19]. Retrospective series have shown the decreased risk of recurrence in patients [11-16]. Often the same chemotherapy protocols are used for women. In the University of Texas M.D. Anderson Cancer Center [17-20], chemotherapy is indicated if the tumor size is greater than 1cm and if there is lymph node involvement.

Anthracyclines are proposed alone if the lymph nodes are free and in combination with taxanes in case of lymph node involvement [16-20].

In the metastatic stage, the therapeutic attitude is the same as in

women. Hormone therapy is often indicated because of frequent receptor positivity. Farrow and Adair [16] described a case of male breast cancer that regressed after orchiectomy. Historically, orchiectomy, adrenalectomy and hypophysectomy have been performed to control metastatic breast cancer but are currently being replaced by hormone therapy. Tamoxifen is the drug of choice with a response rate of 50% [15-18]. LHRH agonists have also been used with or without anti-androgens and have proven to be effective in metastatic breast cancer in men [17]. Chemotherapy is appropriate for patients with negative hormone receptors or in cases of resistance to first-line hormone therapy [17-18]. The efficacy of trastuzumab in the case of overexpression in men has not been proven, but Volm et al [17] suggest that it should be tried in metastatic men with HER-2 overexpression. Palliative chemotherapy in case of rapid disease progression may be indicated [17-18]. The overall survival at 5 and 10 years for male breast cancer is around 60 and 40%.

Conclusion.

Male breast cancer is a rare disease, the delay in diagnosis and treatment of this condition in men unlike that of women is a prognostic factor. The number of invaded lymph nodes and tumor size are also powerful prognostic factors, the other pejorative prognostic factor remains the advanced age at diagnosis especially in case of presence of comorbidities which could limit the choices and the therapeutic possibilities hence the interest to carry out prospective randomized studies on a larger scale in order to improve the management and the prognosis of this affection whose psychosocial impact is considerable. Endocrine therapy is the cornerstone of treatment for breast and prostate cancer. Although endocrine therapies are associated with prolonged survival and reduced risk of cancer recurrence, they are also associated with distressing psychological and physical side effects.

Consent : Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

I declare on my honour that this work has been exempted from ethical approval by my institution, as the dissemination of research results does not allow specific individuals to be identified.

Guarantor of Submission

The corresponding author is the guarantor of submission.

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None.

Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

REFERENCES:

1. Kamilia Laabadi1,&, Sofia Jayi1 , Fatimazohra Fdili Alaoui1 , Hakima Bouguern1 , Hikmat Chaara1 , My Abdelilah Melhouf1 , Karim Ibn Majdoub Hassani2 , Said Ait Laalim2 , Hicham Anoun2 , Imane Toughrai2 , Khalid Mazaz2 . **Google Scholar**
2. Sellal N, Haddad H, Bouchbika Z, Benchakroun N, Jouhadi H, Tawfiq N, Sahraoui S, Benider A. Cancer du sein: l'homme est aussi concerné: étude de 21 cas. *Andrologie*. 2011; 21(1): 45-51. **Google Scholar**
3. Bourhafour M, Belbaraka R, Souadka A, M'rabti H, Tijami F, Errihani H. Male breast cancer: a report of 127 cases at a Moroccan institution. *BMC Research Notes*. 2011 jun29; 4: 219. PubMed | **Google Scholar**
4. Korde LA, Zujewski JA, Kamin L, Giordano S, Domchek S, Anderson WF et al.

Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol. 2010 apr; 28(12): 2114-2122. **PubMed** |

Google Scholar

5. Brinton LA, Key TJ, Kolonel LN et al. Prediagnostic sex steroid hormones in relation to male breast cancer risk. J Clin Oncol. 2015 jun; 33(18): 2041-50.

PubMed | Google Scholar

6. Brinton LA, Key TJ, Kolonel LN et al. Prediagnostic sex steroid hormones in relation to male breast cancer risk. J Clin Oncol. 2015 jun; 33(18): 2041-50.

PubMed | Google Scholar

7. PDQ Adult Treatment Editorial Board. Male Breast Cancer Treatment (PDQ). Health professional Version. 2016 Feb 12. **PubMed | Google Scholar**

8. Cutuli B, Cohen-Solal Le-Nir C, Serin D, Kirova Y, Gaci Z, Lemanski C, Male breast cancer et al. Evolution of treatment and prognostic factors: Analysis of 489 cases. Crit Rev Oncol Hematol. 2010 mar; 73(3): 246-254. **PubMed** |

Google Scholar

9. Renehan AG, Tyson M, Egger M et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008 Feb; 371(9612): 569-578. **PubMed | Google Scholar**

10. Sonnenblick EB, Salvatore M, Szabo J, Lee KA, Margolies LR. Incremental role of mammography in the evaluation of gynecomastia in men who have undergone chest CT. AJR Am J Roentgenol. 2016 Aug; 207(2): 234-40. **PubMed**

| Google Scholar

11. NCCN (National Comprehensive Cancer Network) Breast Cancer Guidelines.

12. Weiss JR, Moysich KB, Swede H. Epidemiology of male breast cancer. Cancer Epidemiol Biomarkers Prev. 2005 Jan; 14(1): 20-26. **PubMed | Google Scholar**

13. Yu E, Stitt L, Vujovic O, Joseph K, Assouline A, Younus J et al. Male breast cancer prognostic factors versus female counterparts with propensity scores and matched-pair analysis. Cureus. 2015 Oct; 7(10): e355. **PubMed | Google Scholar**

14. Evans DG, Bulman M, Young K, Howard E, Bayliss S, Wallace A et al. BRCA1/2 mutation analysis in male breast cancer families from North West

England. Fam Cancer. 2008; 7(2): 113- 117. **PubMed | Google Scholar.**

15. Zhu J, Davis CT, Silberman S, Spector N, Zhang T. A role for the androgen receptor in the treatment of male breast cancer. Crit Rev Oncol Hematol. 2016 Feb; 98: 358- 363. **PubMed | Google Scholar.**

16. Farrow J, Adair F. Effect of orchiectomy on skeletal metastases from cancer of the male breast. Science. 1942 Jun; 95(2478): 654. **PubMed | Google Scholar**

17. Volm Matthew D. Male breast cancer. Curr Treat Optios Oncol. 2003 Apr; 4(2): 159-164. **PubMed |Google Scholar.**

18. Laabadi K et al. Cancer du sein de l'homme: à propos de 6 cas. Pan Afr Med J. 2013 Oct; 16: 70.**PubMed | Google Scholar.**

19. Abreu MH et al. Male breast cancer: Looking for better prognostic subgroups. The Breast. 2015; 26: 18- 24. **PubMed | Google Scholar.**

20. Sanchez AG, Villanueva AG and Redondo C. Lobular carcinoma of the breast in a patient with Klinefelter's syndrome: A case with bilateral, synchronous, histologically different breast tumors. Cancer. 1986; 57(6):1181-1183. **PubMed | Google Schola.**

21. Tunon de Lara C, Goudy G, MacGrogan G, Durand M, Dilhuydy JM, Avril A, Stoeckle E, Bussi res JE, Debled M, De Mascarel I and Mauriac L. Cancers du sein chez l'homme:   propos de 52 cas pris en charge   l'institut Bergoni  de Bordeaux entre 1980 et 2004. Gyn cologie Obst trique & Fertilit . April 2008;36(4): 386-394.**PubMed | Google Scholar.**

22. Frank TS, Deffenbaugh AM, Reid JE, Hulick M, Ward BE and Lingenfelter B et al. Clinical characteristics of individuals with germline mutations in BRCA1 and BRCA2: analysis of 10,000 individuals. J Clin Oncol. 2002; 20(6): 1480-1490. **PubMed | Google Scholar.**

23. Basham VM, Lipscombe JM, Ward JM, Gayther SA, Ponder BA and Easton DF et al. BRCA1 and BRCA2 mutations in a population-based study of male breast cancer. Breast Cancer Res. 2002; 4(1):R2. **PubMed | Google Scholar.**