ORIGINAL PAPER

Cirujano General
January-March 2018
Vol. 40, No. 1 / p. 8-12

Ten-year review of malignant mammary pathology in males; Hospital General Universitario, Ciudad Real (Spain)

Casuística de 10 años de patología mamaria maligna en el varón; Hospital General Universitario de Ciudad Real (España)

Ana Alberca Páramo,* Juan Alberto Sánchez Forero,** Rafael Picón Rodríguez,*** Natalia Villsanti Rivas,**** Ricardo Pardo García,***** Aurora Gil Rendo,***** Jesús Martín Fernández******

Key words:
Cancer, breast, male.

Palabras clave:
Cáncer, mama, varón.

ABSTRACT

Introduction: Male breast cancer (MBC) is a rare condition usually diagnosed later and in more advanced stages than female breast cancer. **Methods:** A 10-year retrospective review of MBC in our hospital. **Results:** Our series included 13 cases. We analyzed the form of presentation, way of diagnosis, BRCA mutation, histology of the tumor, the type of treatment and survival. **Discussion:** The incidence of MBC is currently increasing. The average age of presentation is 62 years. They usually consult because of a nodule or painless retroareolar tumor. Lymph node involvement is often diagnosed. Diagnosis is usually late, which contributes to the infiltration of the pectoralis major muscle. There is no screening in males. Surgical treatment consists of the removal of the primary tumor. The axillary treatment is based on the selective biopsy of the sentinel ganglion (BSGC) for its staging. The use of radio, chemo and endocrine therapy is usually advised depending on the axillary and distance staging, and the type of hormonal receptors of the tumor. Overall and disease-free survival in males are below the ones in the female population. **Conclusion:** Most of the conclusions of this pathology in the male derive from studies of female breast cancer.

RESUMEN

Introducción: *El cáncer de mama en el varón (CMV) es una entidad infrecuente cuyo diagnóstico es más tardío y avanzado que en la mujer.* ***Métodos:*** *Revisión retrospectiva en nuestro hospital durante 10 años.* ***Resultados:*** *Nuestra serie incluyó 13 casos. Se analizaron la forma de presentación, modo de diagnóstico, afectación del BRCA, histología tumoral, tipo de tratamiento realizado y supervivencia.* ***Discusión:*** *Actualmente la incidencia del CMV está aumentando. La edad media de presentación es de 62 años. Consultan por nódulo o tumoración indolora retroareolar. Suelen presentar al diagnóstico afectación ganglionar. El diagnóstico suele ser tardío, lo cual contribuye a la infiltración del músculo pectoral mayor. No existe tamizaje en el varón. El tratamiento quirúrgico consiste en la extirpación por este medio del tumor primario. El tratamiento axilar se basa en la realización de la biopsia selectiva de ganglio centinela (BSGC) para su estadiaje. Se suele aconsejar el uso de radio-, quimio- y hormonoterapia en función del estadiaje axilar, a distancia y el tipo de receptores hormonales de dicho tumor. La supervivencia global y la libre de enfermedad en varones son inferiores a aquellas en la población femenina.* ***Conclusión:*** *La mayoría de las conclusiones de esta patología en el sexo masculino derivan de estudios de cáncer de mama en la mujer.*

* MIR, Fourth-year Resident in General Surgery and Gastrointestinal tract.
** Second-year Resident in General Surgery and Gastrointestinal tract.
*** First-year Resident in General Surgery and Gastrointestinal tract.
**** Fourth-year Resident in Pathological anatomy.
***** Attending in General Surgery and Gastrointestinal tract Service.
****** Chief of the Service of General Surgery and Gastrointestinal tract.

Associate Professor at the University of Medicine of Royal City, Spain.

Received: 26/03/2017
Accepted: 25/01/2018

INTRODUCTION

In 1307, surgeon John Ademe first described breast cancer in the male (BCM).[1] It is an uncommon condition, with an incidence under 1% and accounting for 0.2% of all male cancers.[2-5]

The diagnosis of this condition in men tends to be in a more advanced stage than in women.[2] It presents as a firm, painless subareolar mass.[1] The diagnosis is most frequently made by biopsy.[1]

Treatment is based on locoregional surgery followed by chemotherapy, radiotherapy or

both plus hormone therapy, according to the staging and tumor immunohistochemistry.[1]

METHODS

We conducted a retrospective review at the *Hospital General Universitario de Ciudad Real* (Spain), between January 1, 2005, and December 31, 2015. Statistical analysis was performed using SPSS software, version 18.

RESULTS

Our review included a total of 13 cases, with a mean age of 71 years (52-92). Ten patients presented with a nodule, tumor or mass (77%); one complained of breast pain (7.7%), another had an axillary mass (7.7%), and a third one had nipple retraction (7.7%).

In our 13-case series, two were brothers, two had a positive BRCA gene mutation, and four had a positive family history in first or second-degree relatives. Thus, 46.5% (six patients) in our male breast cancer population had a positive family history of breast cancer.

The most frequent histologic finding was infiltrating ductal carcinoma (85%), followed by intraductal carcinoma (7.7%) and benign phyllodes tumor (7.7%) *(Table I)*.

The tumor was located in the right breast in eight patients and in the left breast in the other five. An echogram of the nodule was obtained in 92% (12) of cases.

A CAT scan was performed in 23% (3) of patients, and fine needle aspiration (FNA) in 85% *(Table II)*.

Regarding surgical management, nine patients (69%) underwent radical modified mastectomy, and three (23%), subcutaneous mastectomy; one patient (8%) was not operated on because he died before surgery could be performed, due to his extensive baseline comorbidity. As for late complications, we only observed lymphedema in one case.

In the nine patients who underwent lymphadenectomy, the anatomopathological study corroborated lymph node involvement.

Chemotherapy and hormonal therapy were administered to 11 patients; in 8 cases, they were combined with radiotherapy.

Three patients had tumor recurrence. In two cases, it was distant (lung and bone) and in one, recurrence was locoregional (thoracic wall), over a five-year period; the patients died three to nine months after the diagnosis of recurrence. These patients were given chemotherapy that did not achieve tumor regression, so they were transferred to palliative

Table I. Objective immunohistochemistry in our patient series.

Case	ER	PR	Cerb-2	Bcl 2	P 53	Ki67	E-cadherina	CK 19	HER 2	Mutation
1	95 %	65 %	-							No
2	50 %	45 %	-	5%	-	37%				No
3	75 %	-	-							No
4	90 %	75 %								BRCA 2 +
5	90 %	90 %	-	100 %	-	20 %				No
6	-	-				7 %		-	-	No
7	100 %	100 %	-	100 %	50 %	6 %	+			No
8	95 %	70 %	+		15 %	4.5 %		+		BRCA2 +
9	90 %	50 %	-/+		10 %	17 %			-	No
10	90 %	90 %	-							No
11	95 %	95 %	-		2 %	7 %		+	-	No
12	100 %	98 %			-			+	-	No
13	95 %	10 %			-	30 %	+	+	-	No

ER: Estrogenic Receptor; PR: Progesterone Receptor; CK19: Cytokeratin19

Table II. Diagnostic tests in our patient series.

Patient	Mamography	Sonography	CT (Computed Tomography)	CNB (Core needle biopsy)
1	No	27 mm	Lymphadenopathy	CDI
2	BIRADS 5: 33 mm	32,4 mm	Affectation to distance (cerebral)	CDI
3	BIRADS 5: 23 mm	22 mm	Affectation to distance (bone)	CDI
4	Microcalcification	No	Affectation to distance (lung)	CID
5	No	14 mm	Affectation to distance (thoracic wall)	CDI
6	BIRADS IV	27 mm	Without affectation to distance	Mesenchymal proliferation
7	BIRADS IV	15 mm	Lymphadenopathy	CDI
8	BIRADS II: 30 mm	28 mm	Lymphadenopathy	CDI
9	No	16 mm	Without affectation to distance	CDI
10	No	No	Lymphadenopathy	CDI
11	BIRADS IV b	13 mm	Without affectation to distance	CDI
12	BIRADS IV b	14 mm	Affectation to distance (multiple)	CDI
13	BIRADS IV b	34 mm	Lymphadenopathy	CDI

care until their death. Four deaths occurred in patients with no breast tumor recurrence. In three cases, death was due to acute respiratory failure; in the fourth, to a non-resectable primary lung tumor. The remaining six patients have had no recurrence to date.

DISCUSSION

The incidence of BCM in our hospital is 1.3 cases per year, i.e., 0.6% of the breast cancer population; it is 0.1-0.2% in the literature.[3] This incidence is currently increasing,[6] and the disease has a similar mortality to that in females.[7] It appears in men with an average age of 62 years (10 years after the mean age in women).[8]

Risk factors are advanced age and a family history of breast cancer (BRCA2 mutation carriers have a relative risk of 0.8 to develop this condition).[4]

The reason for consultation in the patients in our series was the appearance of a painless nodule or tumor, usually retroaerolar, leading to retraction, oozing and/or bleeding from the nipple, as well as ulceration and skin retraction due to the scarce mammary tissue.[9,10]

Lymph node involvement at diagnosis is more frequent than in females.[10] The most frequent histological finding is ductal carcinoma in 90% of cases, compared to lobular carcinoma, present in 1.5% of cases.[5] In our study, 92% were ductal carcinomas and 8% were phyllodes tumors.

These tumors usually harbor positive estrogen and progesterone receptors. According to Chávez-Macgregor et al., 82% have positive hormone receptors, 15% HER2+ (in younger patients) and 4% are triple negative.[5,10]

Prognostic factors depend on tumor's size, lymph node status and lymphovascular invasion by the neoplasia.[11] The diagnosis is usually delayed because the patient underestimates the symptoms.[8] This delay contributes to the infiltration of the pectoralis major muscle.[3]

There is no study on this condition in males due to its low incidence.[11,12]

As in females, surgical treatment consists of the removal of the primary tumor by mastectomy or, in unusual cases, a broad local excision associated to axillary node dissection.[4] Although there is a tendency to perform radical modified mastectomy (which was carried out in 70% of cases in our series), given that node involvement is usually present at diagnosis, conservative surgery is also effective.[5,13]

The management of node involvement is important when determining the type of surgery to be performed. The American Society

of Clinical Oncology (ASCO) suggests that selective biopsy of the sentinel node (SBSN) for nodal staging is acceptable in men, although it may have less power due to the low incidence of this condition in the male population.[14]

Axillary surgery in males with a positive SBSN is controversial, although studies on the subject are scarce; hence, the same rules apply as in female breast cancer.[15]

Adjuvant radiotherapy on the chest wall is usually recommended, as well as axillary lymphadenectomy in case of axillary involvement, in order to decrease locoregional recurrence,[16] although some authors (Yoney et al.) have suggested that the use of radiotherapy in males with breast cancer is controversial and offers no benefits.[17] The use of chemotherapy and hormone therapy also has advantages in terms of increasing disease-free survival.[13,18]

In patients with locally advanced disease (T3N0M0 or stage III) or inflammatory breast cancer, neoadjuvant chemotherapy followed by surgery is offered, just as in females; when compared with the classic surgical protocol followed by adjuvant therapy, it is associated with both a higher rate of clinical response and a more conservative surgical procedure.[19]

The approach based on chemotherapy follows the same patterns as in female breast cancer, since there are no clinical trials that have evaluated the specific benefits of adjuvant chemotherapy in male breast cancer.[20]

Immunohistochemical studies performed in these patients allow treatment with hormones based on markers; an increase in disease-free survival was observed when compared with historic cohorts in which it was not used. Therefore, in surgically treated patients, tamoxifen should be administered for five years if hormone receptors are positive.[13]

Hormone therapy in males began in 1940, when orchiectomy was described as an approach for skeletal metastases, leading to rapid pain relief.[21]

The use of tamoxifen in breast cancer began in 1970 and has proven to achieve tumor regression in 37.5% of males,[22] although this treatment causes several adverse effects, such as impotence, hair loss, decreased libido, weight gain, hot flashes, depression, and insomnia, among others, with an incidence of 62%.[23]

The use of aromatase inhibitors in postmenopausal women with positive estrogen receptor breast cancer has led to a decrease in the risk of recurrence when compared with the use of tamoxifen.[24] However, studies conducted in males have not shown such a response to treatment.[25] If a gonadotropin-releasing hormone agonist is added to this therapy, it increases the effect of aromatase inhibition and achieves regression in tumors resistant to aromatase inhibitors.[26]

According to Yu et al., overall survival and disease-free survival in males with breast cancer are half of those in females with this condition.[27]

CONCLUSION

Most conclusions on this condition in males result from breast cancer studies in females. Therefore, it is important to publish data on this disease in men, which is infrequent and has a different prognosis than in females, particularly after a delayed diagnosis in an advanced stage.

REFERENCES

1. Borrego-Galán M, Oltra A, Espinoza S, Munárriz B, Sancho-Fornos S, Herranz C. Cáncer de mama en el varón: revisión de 27 casos. Rev Senol Patol Mamar. 1998; 11: 187-190.
2. Vilhelm MC, Wanebo HJ. Cáncer de mama en el hombre. En: Manejo multidisciplinario de las enfermedades benignas y malignas. Panamericana; 1993. Capítulo 5: 83-95.
3. Aguilar-Luque J, Sarmiento-Robles C, Merino de la Torre E, Martínez-García P. Carcinoma de mama en el varón: análisis de 5 casos y revisión bibliográfica. Rev Cubana Cir. 2001; 40: 66-72.
4. White J, Kearins O, Dodwell D, Horgan K, Hanby AM, Speirs V. Male breast carcinoma: increased awareness needed. Breast Cancer Res. 2011; 13: 219.
5. Golshan M, Rusby J, Dominguez F, Smith BL. Breast conservation for male breast carcinoma. Breast. 2007; 16: 653-656.
6. Giordano SH, Cohen DS, Buzdar AU, Perkins G, Hortobagyi GN. Breast carcinoma in men: a population-based study. Cancer. 2004; 101: 51-57.
7. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin. 2009; 59: 225-249.
8. Alonso A, Aguilar F, Santos JA. Carcinoma de mama en el varón: revisión de 32 casos. Oncología. 1983; 16: 29-35.
9. Joshi MG, Lee AK, Loda M, Camus MG, Pedersen C, Heatley GJ, et al. Male breast carcinoma: an evaluation of prognostic factors contributing to a poorer outcome. Cancer. 1996; 77: 490-498.

10. Deb S, Lakhani SR, Ottini L, Fox SB. The cancer genetics and pathology of male breast cancer. Histopathology. 2016; 68: 110-118.
11. Deb S, Jene N; Kconfab Investigators, Fox SB. Genotypic and phenotypic analysis of familial male breast cancer shows under representation of the HER2 and basal subtypes in BRCA-associated carcinomas. BMC Cancer. 2012; 12: 510.
12. Ferzoco RM, Ruddy KJ. Optimal delivery of male breast cancer follow-up care: improving outcomes. Breast Cancer (Dove Med Press). 2015; 7: 371-379.
13. Onami S, Ozaki M, Mortimer JE, Pal SK. Male breast cancer: an update in diagnosis, treatment and molecular profiling. Maturitas. 2010; 65(4): 308-314.
14. Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol. 2005; 23: 7703-7720.
15. Gentilini O, Chagas E, Zurrida S, Intra M, De Cicco C, Gatti G, et al. Sentinel lymph node biopsy in male patients with early breast cancer. Oncologist. 2007; 12: 512-515.
16. Contractor KB, Kaur K, Rodrigues GS, Kulkarni DM, Singhal H. Male breast cancer: is the scenario changing. World J Surg Oncol. 2008; 6: 58.
17. Yoney A, Kucuk A, Unsal M. Male breast cancer: a retrospective analysis. Cancer Radiother. 2009; 13: 103-107.
18. Patel HZ 2nd, Buzdar AU, Hortobagyi GN. Role of adjuvant chemotherapy in male breast cancer. Cancer. 1989; 64: 1583-1585.
19. Spence RA, MacKenzie G, Anderson JR, Lyons AR, Bell M. Long-term survival following cancer of the male breast in Northern Ireland. A report of 81 cases. Cancer. 1985; 55: 648-652.
20. Giordano SH. A review of the diagnosis and management of male breast cancer. Oncologist. 2005; 10: 471-479.
21. Farrow JH, Adair FE. Effect of orchidectomy on skeletal metastases from cancer of the male breast. Science. 1942; 95: 654.
22. Kantarjian H, Yap HY, Hortobagyi G, Buzdar A, Blumenschein G. Hormonal therapy for metastatic male breast cancer. Arch Intern Med. 1983; 143: 237-240.
23. Meguerditchian AN, Falardeau M, Martin G. Male breast carcinoma. Can J Surg. 2002; 45: 296-302.
24. Burstein HJ, Prestrud AA, Seidenfeld J, Anderson H, Buchholz TA, Davidson NE, et al. American Society of Clinical Oncology clinical practice guideline: update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. J Clin Oncol. 2010; 28: 3784-3796.
25. Giordano SH, Valero V, Buzdar AU, Hortobagyi GN. Efficacy of anastrozole in male breast cancer. Am J Clin Oncol. 2002; 25: 235-237.
26. Giordano SH, Hortobagyi GN. Leuprolide acetate plus aromatase inhibition for male breast cancer. J Clin Oncol. 2006; 24: e42-e43.
27. 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; 7: e355.

Mailing address:
Ana Alberca-Páramo
C/Santa Cruz de Mudela No. 1,
Bloque 7, 3º B, 13005, Ciudad Real, España.
Tel: 92627 8000, ext. 79183
E-mail: alpaa2500@gmail.com