

Breast Cancer in Men



BBSG – Brazilian Breast Study Group

Introduction

Breast cancer in men is rare, with about 2600 cases/year in the United States, accounting for approximately 1% of all cases. About 11% of the cases involve in situ disease. The mean age at diagnosis is 67 years, and that is higher when compared to women. Few specific prospective studies are available to better characterize biology and treatment, despite the increasing numbers of survivors.

Pathophysiology

Most cases express hormone receptors, whereas the triple-negative subtypes and HER2 represent about 1 and 5% of the cases, respectively. Lobular carcinoma is very uncommon due to lack of lobular development in men. Major risk factors include Klinefelter's syndrome (XXY), environmental risk, age, radiation exposure, family history, and other genetic abnormalities. Some drugs that alter the “hormonal environment” used to be linked to the risk of breast cancer, for example, finasteride. However, this drug does not appear to increase the risk of breast cancer in men despite increasing the risk for gynecomastia.

The presence of mutation is another important risk factor. Change in BRCA2 is found in 4–14% of the non-selected cases. The lifetime risk for breast cancer in men with this mutation is approximately 5–10%. Pathogenic mutation of BRCA1 is also reported in some families, but it is less frequent and with a lower lifetime risk (1–5%). The National Comprehensive Cancer Network (NCCN) guideline includes

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breast cancer in men as a factor for investigation of hereditary breast/ovarian cancer syndrome.

Despite some similarities, it is possible that the evolutionary behavior of breast cancer in men is different from the one in women, but this is not well understood and we do not know how to deal with these differences. The rate of cases with positive hormone receptors is higher in men, and it does not increase with age; also, histological grade does not present a direct correlation with clinical outcome, as it occurs with breast cancer in women. The prognosis of breast cancer in men is similar to that in women, though, when matched by stage. The Afro-American race has worse evolution, as it happens in women.

Clinical Condition

The palpable nodule is the most common finding, usually in a retro-areolar situation, and it may occur in another position within the breast in 20% of cases. Skin ablation and retraction can also be observed, especially in more advanced lesions, such as papillary flow and pain. Lymph node involvement is more common in men, possibly related to the more advanced staging at the time of diagnosis.

Differential Diagnosis

The main differential diagnosis is gynecomastia. In fact, most of the times that a man is investigated due to breast complaint, the conclusion is benign in more than 90% of the cases, with gynecomastia accounting for about 80% of these changes.

Propedeutics

Investigation of cases is similar to the procedure for cancer in women. When malignancy is suspected, a diagnostic mammogram can be performed for planning, and a histological sample should be obtained through needle biopsy. Occasionally, ultrasonography may aid in the diagnosis and collection of tissue. There is no definite

role for the use of magnetic resonance imaging in men. Immunohistochemistry follows the same principle for female neoplasia, as well as staging exams, which should be requested when there is presence of symptoms or in a more advanced stage.

Treatment

The approach should be multidisciplinary, in order to maximize the effectiveness of therapeutic resources.

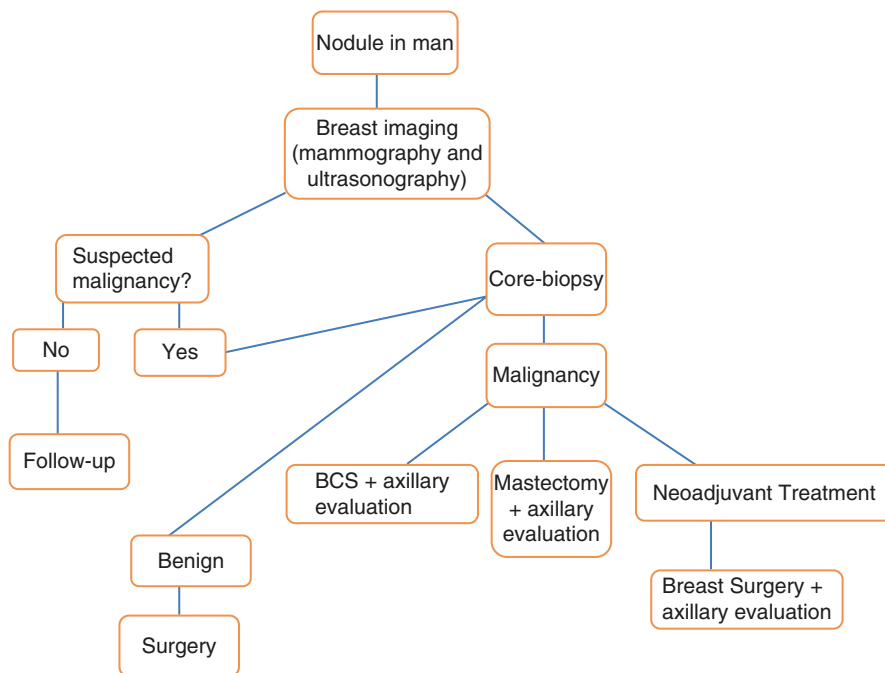
Most men undergo mastectomy because tumors often involve the central region of the breast, and breast reconstruction is rarely used, even considering lipofilling. The indications for adjuvant radiotherapy (RT) after mastectomy have been increasing over the years, and approximately one third of cases with lymph node involvement will receive treatment.

Data obtained from *Surveillance, Epidemiology, and End Results (SEER)* showed survival benefit in the addition of radiotherapy after mastectomy in male patients with positive axilla.

Conservative breast therapy is feasible, as long as the lesion is unicentric, and resection is done with free margins. Adjuvant radiotherapy is recommended. A recent study has shown comparable survival to mastectomy in early breast cancer. Sentinel lymph node (SL) can be performed if the axilla is clinically negative, following the same recommendations as invasive carcinoma in women. Some studies showed identification rates higher than 90%, with acceptable false-negative results. There are no important studies on preservation of the axilla after positive sentinel lymph node (men were not included in axillary preservation studies after metastatic SL), as well as the use of SL after neoadjuvant chemotherapy: in the latter two situations, case-by-case evaluation and common sense will determine the best approach.

In general, systemic therapy should follow the guidelines used for women. Chemotherapy, with or without biological therapy, is usually recommended for locally advanced tumors, young age, high grade, and lymph node involvement. The hormone therapy follows the same principles, tamoxifen being the usual choice. There is little data on the use of aromatase inhibitors in men, mainly because there is controversy whether it should be performed associated with gonadal suppression or not.

Flowchart



Flowchart 1 Nodule management in men

Recommended Reading

1. Dietz JR, Partridge AH, Gemignani ML, Javid SH, Kuerer HM. Breast cancer management updates: young and older, pregnant, or male. *Ann Surg Oncol*. 2015;22(10):3219–24. *Review study on breast cancer in men: mastectomy is the most used surgical approach, although conservative surgery associated with radiotherapy is acceptable in selected cases.*
2. Flynn LW, Park J, Patil SM, Cody HS, Port ER. Sentinel lymph node biopsy is successful and accurate in male breast carcinoma. *J Am Coll Surg*. 2008;206:616–21. *The sentinel lymph node in breast cancer in men had a 97% and identification rate and false-negative rate at 8%, similar to that found in women.*
3. Freedman RA, Partridge AH. Emerging data and current challenges for young, old, obese, or male patients with breast cancer. *Clin Cancer Res*. 2017;23(11):2647–54. *Review that highlights risks for breast cancer in men, as well as the differences between male and female cancer. At the moment, there is an effort of the scientific community to conduct studies that can improve the understanding of cancer in men.*
4. Shak S, Palmer G, Baehner FL, Millward C, Watson D, Sledge GW. Molecular characterization of male breast cancer by standardized quantitative RTPCR analysis: first large genomic study of 347 male breast cancers compared to 82,434 female breast cancers. *J Clin Oncol*. 2009;27:15. *The use of Oncotype Dx in men, although showing some similarities, evidenced*

a greater expression of estrogen receptor and progesterone, compared to women, as well as greater expression of Ki67.

5. Zaenger D, Rabatic BM, Dasher B, Mourad WF. Is breast conserving therapy a safe modality for early-stage male breast cancer? *Clin Breast Cancer*. 2016;16:101–4. A study that demonstrated survival after conservative breast cancer therapy in men comparable to mastectomy in cases of initial breast cancer (T1-T2, N0).