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Challenging Stereotypes: Cases of Breast Cancer in Men

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ABSTRACT

Breast cancer is the most common malignant tumor in women, internationally, and the leading cause of death from cancer. However, breast cancer in men is an uncommon pathology, corresponding to less than 1% of neoplasms in men. The lifetime risk of breast cancer in a man is approximately 1:1000, compared to 1:8 for a woman.

Currently, an increase in timely diagnosis has been demonstrated thanks to the programs that are carried out for the early detection of breast cancer worldwide. Although, unfortunately, early diagnosis is still difficult due to the lack of information that a large part of the population has regarding self-examination, not only in our country, but also around the world, and in the case of breast cancer in men, being such an uncommon condition, its diagnosis is more difficult.

The incidence of breast cancer is increasing in the developing world, due to longer life expectancy, increased urbanization and the adoption of Western lifestyles. Among the risk factors that have been seen to increase the risk of breast cancer in men, with scientifically proven evidence, are mainly hormonal disorders, family history and mutations of certain genes that predispose to the disease. The hormonal disorders mentioned above refer to an increase in circulating estrogen levels and a deficiency in the synthesis or action of testosterone. These alterations can be caused by disorders at the level of testicular testosterone synthesis, such as: orchitis, orchiectomy, undescended testicle, congenital inguinal hernia and others. Patients who voluntarily consume exogenous estrogens as part of the treatment of prostate cancer or transsexuals should also be taken into account. Another risk factor that has been found to be implicated in the presentation of this type of neoplasia are medications; many frequently used medications are testosterone antagonists. Alcohol is also implicated, since it decreases testosterone synthesis and the number of testicular receptors for gonadotropin.

A higher prevalence has also been seen in patients with obesity, in whom there is a double risk, because as they have a higher peripheral aromatization of androgens, they synthesize a greater amount of circulating estrogens.

Approximately 20% of men with breast cancer have a first-line family history, which indicates a two to three times higher risk of developing the disease at some point in their lives and that this risk doubles exponentially with the number of affected family members.

Currently there are many programs and organizations that promote the fight against breast cancer, such as the World Health Organization, where there are comprehensive national cancer control programs that are integrated with non-communicable diseases and other related problems.

Comprehensive cancer control encompasses prevention, early detection, diagnosis and treatment, rehabilitation and palliative care. Raising awareness of the general public about the problem of breast cancer and control mechanisms, as well as promoting appropriate policies and programs, are key strategies for population-based breast cancer control.

Based on what has been mentioned above, the work will be carried out in order to have a better approach to breast cancer in men, due to the little information we have about it, as well as to raise awareness among the general population about the risk factors, prognostic factors, timely diagnosis and treatment of patients with this type of pathology.

KEYWORDS: breast, cancer, tumor.

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INTRODUCCION

The normal male breast consists of the nipple and a rudimentary ductal system that ends in terminal buds without lobule formation. Among the most relevant male breast pathologies in the field are mastitis and carcinoma, the latter of which we will focus on below.

Carcinoma originating in the male breast is a rare neoplasm. Between 4% and 14% of cases in males are attributed to BRCA2 germline mutations. There is a 60 to 76% chance of a BRCA2 gene mutation in families with at least one affected male. Between 3 to 8% of cases are associated with Klinefelter syndrome.1,2

Inheritance of one or more susceptibility genes is the primary cause of approximately 12% of breast cancers. Penetrance varies between 30 to 90%, depending on the specific mutation present.1,2

Within the classification of breast carcinoma, more than 95% of breast neoplasms are adenocarcinomas, divided into

carcinoma in situ, which is when the neoplasm is limited to the ducts and lobules by the basement membrane, and invasive carcinomas, which are also called infiltrating, because they have penetrated the stroma through the basement membrane, in this particular case of neoplasia the cells can already invade the vasculature and therefore reach the regional lymph nodes and distant sites.3,4

Lobular carcinoma in situ and invasive ductal carcinoma, as we will show in the following clinical cases, are the histological types of carcinomas most commonly found in patients.3,4

In cases of lobular carcinoma in situ, they are usually incidental findings in biopsies, because they are not associated with calcifications or stromal reactions that produce mammographic densities. This type of carcinoma consists of noncohesive cells with oval nuclei and small nucleoli. The cells lack cell adhesion protein E-cadherin, but do have ER and progesterone receptor expression. 3,4

In cases of invasive ductal carcinoma, these comprise the majority of carcinomas, 70-80%, most of these tumors are firm or hard, and have an irregular border. Cutting or scraping in these typical cases produces a gritty sound, due to the existence of small central punctate foci or rows of stroma with chalky white elastosis. 5,6

Recently developed techniques that comprehensively examine the DNA, RNA and proteins of carcinomas have provided a new way for their molecular classification. Gene expression profiling, which can measure the relative amounts of mRNA of virtually every gene, has identified five major patterns of gene expression in the invasive ductal carcinoma group: luminal A, luminal B, normal, basal cell-like, and HER2-positive. These molecular classes are related to prognosis and response to treatment and thus have become of great clinical importance.5,6

Luminal A, found in 40-55% of cancers, this is the largest group and is composed of ER positive and HER2/neu negative cancers, these cancers are slow growing and respond well to hormonal treatments.5,6

Luminal B, which are found in 15-20% of cancers, cancers in this group also express ER, but in general are higher grade, have a higher proliferation rate and often express HER2/neu, have a higher risk of lymph node metastasis, as we will be able to observe below in the patient of our first case.5,6

HER2-positive cancers, which are found in 7-12% of cancers, this group comprises ER-negative carcinomas that overexpress the HER2/neu protein. In more than 90% of HER2/neu-positive cancers, overexpression is due to amplification of the DNA segment at 17q21 that includes the HER2/neu gene; these cancers are usually poorly differentiated, have a high proliferation rate and are associated with a high frequency of brain metastases.5,6

OBJECTIVE

A bibliographic review is made implementing two clinical cases of the Sinaloa Institute of Cancerology to have more focus on breast cancer in male patients as it is a pathology little prevalent and without studies on the subject.

Clinical case (1).

Resident: Ejido La Campana, Sinaloa.

Occupation: Laborer

Inherited family history of oncology: Negated Personal pathologic history: No chronic degenerative disease.

Non-pathological personal history: Smoking (+) for 8 years at a rate of 3 cigarettes per day.

This is a 57-year-old male patient in 2017, self-detected a nodule in left retroareolar breast palpable and not painful, then went to consultation to perform excisional biopsy on May 23, 2017 in private environment with report of infiltrating lobular carcinoma and in situ of 1.5 cm. Post-operated left radical mastectomy on June 12, 2017 with report of infiltrating retroareolar ductal carcinoma of 1.7 cm, histological grade II, with apparent vascular permeation and perineural infiltration, there is tumor of 3 mm from the surgical bed, free margins, 7/7 negative nodes.

Diagnosed with Left breast cancer in 2017 with stage IIA pT2 pN0 M0 with immunohistochemistry: estrogen R. +++ 90%, progesterone R. +++ 80%, Her2 (-), ki67 10%. Luminal A molecular subtype.

Inherited family history of oncology: Negated

Pathological Personal History: No chronic degenerative disease.

Non-pathological Personal History: Denies drug addictions.

This is a 38 year old Male patient in 2013, self detected a nodule in right breast of 5 months of evolution, with progressive growth, went to breast ultrasound on September 23, 2013 which reports: heterogeneous, amorphous, immense mass in the subcutaneous cellular tissue with right axillary adenopathy, later a bilateral mastography was performed which reported spiculated ovoid image in right breast measuring 19x12x28 mm, BIRADS 4b.

Physical examination: right breast with retroareolar nodule 3x2 cm, hard, fixed, with nipple retraction, orange peel skin with ipsilateral axillary lymphadenopathy, hard, removable, 1.5 cm.

Trucut biopsy was taken on October 08, 2013 with report of: infiltrating ductal carcinoma, moderately differentiated, no specific pattern, histological grade II, with lymphovascular invasion.

Diagnosed with Right breast cancer in 2013 with stage IIIB T4b N1 Mx with immunohistochemistry: estrogen R. (-), progesterone R. +++ 60%, Her2 (-), ki67 20%, p53 (-), cD34: vascular proliferation at 40x:13 vessels. Luminal B molecular subtype.

Received neoadjuvant chemotherapy with TEC scheme (docetaxel + epirubicin + cyclophosphamide) for 6 cycles from December 09, 2013 to March 24, 2014, Postoperative radical mastectomy Madden type on July 03, 2014 with report of moderately differentiated infiltrating ductal carcinoma of 1.5 cm, without lymphovascular invasion, free edges, 8 negative nodes, later started adjuvant radiotherapy for infiltration to external skin to right chest wall and lymph node areas 50 Gy in 25 sessions from October 03 to November 12, 2014 and hormone therapy for 5 years with Anastrozole.

She had bone recurrence after approximately 7 years on January 18, 2021 in left iliac wing with pain on palpation in left hemipelvis, limited hip mobility arches. Iliac bone biopsy was performed with report of trabecular bone fragments with multiple invasive carcinoma implants, so she received palliative radiotherapy to left hemipelvis and knee of 37.5 Gy in 15 fractions and started palliative systemic treatment with docetaxel on March 11, 2021 with partial response after 4 cycles. Hormone therapy was modified with letrozole in June 2021 and palliative zoledronic acid was started on October 5, 2021 every 3 months.

He had recurrence to the lung with multiple nodules of metastatic aspect of 1.0 cm with decreased interstitial infiltrate and elevated tumor marker CA-15:3: 118.8, by progression started capecitabine on February 7, 2022.

He progressed again in thoracolumbar spine receiving palliative radiotherapy on June 08, 2022 to June 21, 2022 30 Gy in 10 sessions and new treatment was added.

Currently 48 year old patient with recurrent breast cancer to lung and bone, in treatment according to NCCN guidelines with letrozole + palbociclib + denosumab in follow-up by medical oncology.

Clinical case (2).

He was referred to medical oncology to assess adjuvant treatment with hormone therapy with tamoxifen on July 12, 2017 and radiotherapy for 3 mm tumor of the surgical bed being a candidate for hypofractionated external RT to the left chest wall 42.5 Gy in 16 fractions on October 20, 2017.

Again assessed for non-adherence to treatment by his own will for 5 years, with presence of left supraclavicular nodule of 3.5 cm, hard, movable, regular, another one more towards the central region of the neck, suspicious of metastasis, ultrasound-guided FNA is taken with report on September 15, 2022 positive for neoplastic cells, with trucut biopsy on November 29, 2022 with report of infiltrating ductal carcinoma, without specific pattern, poorly differentiated, grade III and immunohistochemistry R. estrogen 0%, R. progesterone 0%, Ki67 15%, Her2 (-) and recurrence with multiple nodules in both lungs and bone in distal third of the body of the sternum T7, L1 and L3. She started palliative systemic treatment with taxane (docetaxel) on October 6, 2022 for 8 cycles every 21 days.

Currently a 62 year old patient with left breast cancer with recurrence at 5 years at supraclavicular level with triple negative molecular profile, initially diagnosed as Luminal A, in palliative treatment with taxane in cycle 7/8 and in follow-up by medical oncology.

Gathering information we searched for evidence comparing the biological characteristics and management of these tumors in men and women. Primarily the age of diagnosis is usually between 60 and 70 years, which is higher than the average age of presentation in women. Here it is noteworthy that based on the clinical cases, the age at diagnosis is very uncertain.

The most common clinical presentation in men is a palpable, non-painful retroareolar nodule and the most frequent histology coincides with that described in the literature, with invasive ductal carcinoma predominating due to the absence of terminal lobules of the male breast, as does the immunohistochemistry consistent with hormone receptor positive (estrogen and progesterone) descriptions, with the molecular subtype being luminal.

Staging was performed following the guidelines for breast cancer in women with TNM regulations. In both the treatment of choice was surgery, performing a total mastectomy, together with adjuvant therapy with chemotherapy and radiotherapy was indicated according to the criteria of the oncology committee, being the guidelines that can be extrapolated to studies performed in breast cancer in women.

of cases, the studies published so far do not allow us to establish conclusive evidence regarding the management of this cancer in men and, therefore, all behaviors are derived from the existing literature in women.

The indication of hormonal therapy was also discussed, being tamoxifen the indicated drug in the cases, due to the fact that aromatase inhibitors in men have an unclear efficacy and have a limited use. Adverse effects could be one of the factors that limit their tolerability, among which are: decreased libido, weight gain, hot flashes, deep vein thrombosis, etc. It is therefore necessary to optimize the therapeutic effect of AIs.

Multiple risk factors have been proposed, but the only one with a proven association is genetic alterations. It is of utmost importance the genetic study in our male patients, because BRCA mutations increase the tendency to the expression of proliferation genes. BRCA2 is present in 70% of cases, and BRCA1 is present in 10%.

In none of them the genetic test could be performed, due to the economic limitations that the patient himself must pay for, so we do not have a history of any genetic defect.

As for radiotherapy, men have a greater tendency to receive radiotherapy due to the greater frequency of lymph node, skin and nipple-areola complex involvement, thus achieving a local control rate. The determinants of relapse are due to the number of lymph nodes involved and the extracapsular extension.

Based on adjuvant treatment with chemotherapy, the benefits of chemotherapy in men with breast cancer are more difficult to demonstrate because most tumors are hormone receptor positive. The most commonly used schemes in the series are based on anthracyclines, taxanes and less frequently CMF (cyclophosphamide + methotrexate and 5-FU). Neoadjuvant therapy has less impact in men, due to the lesser importance of conservative surgery. However, it could be applicable to evaluate tumor response and offer the benefit of complete pathologic response.

With all the information gathered we must prioritize that although the incidence is low in male patients, breast cancer is a pathology that can also occur in men. In terms of risk factors, symptoms and clinical signs are similar to its female counterpart. Although there are no screening programs for the early detection of breast cancer in men, it is necessary to make society aware of this disease and to encourage them to performself-examination; it is believed that the prognosis is more unfavorable mainly due to late diagnosis and, as described, it is probably also associated with specific molecular characteristics of the tumor such as proliferation markers. Although the same evidence is not available for the different treatment strategies, the therapeutic approach is the same as in breast cancer presenting in women. Due to the limited number

PSYCHOLOGICAL IMPACT

Breast cancer involves a situation that physically and psychologically affects the quality of life. One of the phases in which there is a greater emotional deterioration is during treatment, due to the side effects, collateral effects and sequelae of treatment.

The impact of cancer and cancer treatments limit the social, family and personal life of patients, hence the importance of intervening in these issues in order to improve the quality of life of patients and reduce the emotional suffering they present.

Currently, the emergence of new chronic diseases has impacted many people around the world, in addition to the fact that the methods that have been used to combat them are increasingly aggressive for people. There has been a great interest in developing technologies that decrease the incidence and progression of different diseases, however, it is also important to develop and provide populations with skills that promote better health care, not only to prevent them, but also to have a better control over them.

Among the chronic diseases that exist, studying cancer has become of utmost importance. It brings with it various complications that present themselves in a new way in the life of the sufferer, which implies a change in lifestyle, and most of the time this change brings with it various psychological conflicts that affect their personal development as well as their quality of life and their position in the face of the disease.

The appearance of this disease in the male sex has impacted society in two ways. First, "they are the interpersonal or social expression of emotions and feelings, such as anger or sadness. Second, "emotions also involve psychophysiological reactions, for example fear and anxiety. From the above, it is possible to observe the impact that breast cancer causes in men, producing different emotions and the intensity with which they are presented, will be mediated by the coping styles that are available.

The most striking emotion in man is confusion (no clarity of diagnosis) experienced depressive symptoms and these are correlated with stress, as there are perceptions of cancer as a stressful event with intrusive thoughts.

At the cognitive level, cognitions, better known as beliefs, ideas and thoughts, are another psychological component to consider. These regulate emotions and therefore behaviors. Cognitions are the interpretation of reality, inferences or evaluations that people make about themselves, others and the world around them. The emotional suffering of patients is mainly due to the acceptance of their diagnosis so infrequent in their sex, which causes dysfunctional beliefs related to the loss of personal attractiveness, of their value as a person and of sexual identity. As can be seen, the cognitive aspect refers mainly to the evaluation of the self-concept of the man, which influences the magnification or adaptation of these beliefs.

Functional beliefs can lead to behaviors such as therapeutic adherence, adaptation and recognition of the disease, which improve physical and psychological well-being; or conversely, irrational beliefs can lead to maladaptive behaviors, such as inconsistency in following medical treatment, failure to keep appointments, etc., which lead to various physical and psychological complications in the long term.

Not only is the independent part of the man affected, but also the part of the couple. By detecting the phase through which they are going through as a couple, before the diagnosis of breast cancer; it is a way to open the horizon with respect to the maturity they have as a couple (which implies a greater degree of dependence and care). It will be equivalent, in a way, to the help, as well as support that the couple will receive in the performance of the new tasks that the oncological patient cannot carry out.

It is common for the couple to present a variety of feelings such as:

1. "Isolation and loneliness", you will find it difficult to converse with the patient regarding their activities, feelings and thoughts.
2. "Confusion and feeling of uselessness", the man finds himself with the obligation to take care of the home and his children and this will make it a change of role, the couple will coexist in the medical field; not knowing how to care for his patient, how to make decisions and seek solutions to problems, are aspects that make him present these feelings.
3. "Powerlessness and frustration", the partner feels this way when they do not know how to manage their emotions, communicate or help their partner feel better.
4. "Ambivalence and guilt", the life plans of the relationship are no longer clear or are interrupted; she becomes aware that her husband's health does not depend on her; it causes her not to know how to react or do anything; it leads her to feel guilty.
5. Among the most common feelings found in cancer patients are "Fantasies about death", because of the unpleasantness of the care and the disorders that the disease entails, the couple may have the desire for everything to end and return to their previous lifestyle, either by being cured or by the death of their spouse, which is why they may feel bad about these thoughts. For this reason, joint therapy is of great importance to know how to cope with the difficulties of this disease.

Although each of these components may contribute to relative changes within a health-illness context, they work together and affect each other at all times throughout life.

Receiving psychological support involves working with a mental health professional to face the challenges that arise when receiving this type of diagnosis. That is why different strategies for psychological help should be proposed; one of them is the restructuring of dysfunctional ideas, mainly those related to body image, acceptance and change of ideas related to the concept of being a man. Another important strategy is emotional self-regulation, in combination with cognitive techniques (imagery) can extinguish emotional responses conditioned to a situation, and recondition their responses to thoughts, emotions and rational behaviors to the same situation and finally the behavioral changes of each patient, as well as providing various forms of acceptance and the search for information mainly.

It is therefore of utmost importance to work on these psychological aspects in order to improve and prevent the appearance of other disorders that affect the patients' quality of life. Psycho-oncological support is important for patients to learn new emotional, cognitive and behavioral self-regulation skills that allow them to diminish the effects of these bodily changes and thus facilitate the person to feel more comfortable with him/herself and less limited. These psycho-oncological support alternatives should respond to the needs of patients in the different phases of the disease and oncological treatment.

CONCLUSIONS

Breast cancer has become a disease of great relevance worldwide. Every year one million new cases are reported, of which approximately half occur in developed countries, where most of the deaths from this cause are registered.

As previously mentioned, the incidence of breast cancer in men is much lower than in the case of women, but it is equally important to raise awareness among the general population that despite being a minority, this pathology can be detected in early stages with proper screening and knowing the warning signs that may occur in the early stages of the disease.

Therefore, this information should be made available to the general population, regardless of their sex, since the real importance of having this knowledge among the male population may be underestimated due to the low incidence of reported cases.

As is the case with most chronic degenerative diseases in our country, it is much easier to prevent the diseases and it gives patients a better prognosis for life than if they live with the disease and later with the complications it entails. Therefore, our duty as the health sector is to inform patients, get them more involved with their health, raise awareness and spread all the tools we have at our disposal to reach more people.

Making a timely diagnosis will ensure that patients receive early treatment, which can prevent, in the case of breast cancer, metastasis, as we saw in the previously mentioned cases, that by the time the patients were diagnosed, they no longer had metastases.

had a localized pathology, but had spread to different areas of the body.

As we have seen, it is of much better prognosis for patients that the diagnosis is made in the early stages of the disease, where tumor resection can be chosen in conjunction with adjuvant therapy, as opposed to cases when they are already in more advanced stages and the treatments that can be offered to patients are even more limited and with a more precarious prognosis of life for our patients.

In terms of risk factors are similar tumors to the female counterpart. It is believed that the prognosis is more unfavorable mainly because it is also associated with specific molecular characteristics of the tumor such as proliferation markers. Although the same evidence is not available for the different treatment strategies, the therapeutic approach is the same as in female breast cancer. Due to the limited number of cases, the studies published so far do not allow us to establish conclusive evidence regarding management and, therefore, the behaviors are derived from the existing literature in women.

Unadjusted overall survival rates are lower for breast cancer in men than for women. However, much of this difference can be explained by later stage diagnosis of the disease and older age at diagnosis, as well as a lower overall life expectancy for men than for women. The most important prognostic indicator is the stage at diagnosis and lymph node involvement.

RECOMMENDATIONS

1. Eliminate drug addictions.

Among the risk factors for the disease, alcohol consumption and smoking are among the main habits that can lead to breast cancer.

Alcohol consumption may have a certain immunosuppressive effect that makes it difficult for the body to identify a cell that has undergone transformation and therefore favors the development of cancer.In the case of cigarettes, an article from the Oncoguia Institute, reveals that the substances present in tobacco are involved in carcinogenesis (the process of formation of cancer), and increases the risk of developing all types of this condition by up to 30%.

2. Physical activity.

Having a sedentary lifestyle, with little or no physical activity also contributes to an increased risk of breast cancer.

Currently, the mechanisms that explain the benefits of physical activity in cancer prevention are not yet fully established. However, an analysis conducted from observational studies, published in 2019 in the US National Library of Medicine, suggests that exercise can prevent about 25% of breast cancer cases. In addition, the research also shows that breast cancer survivors who were more physically active had a 40% lower risk of death than those who were less active.

3. Healthy eating and weight control.

Excess weight causes a state of chronic inflammation in the body because the immune system is always acting to contain excess fat.

The problem, however, is that this defense system mechanism, when over-stimulated, can attack healthy cells and contribute to disordered cell growth, i.e. the development of cancer. One aspect that demonstrates this relationship is that breast cancer is very incident in the most developed countries, where the intake of ultra-processed foods, sedentary lifestyles and obesity are also more frequent.

4. Self-examination.

Breast self-examination is also an option to identify cancer. However.

Among the data sought in search of breast pathology are:

Breast skin with increased color, temperature, shrinkage or orange peel appearance.

Existence of any nodule, fixed and generally painless.

Small lumps in the armpit region or neck.

Spontaneous discharge of any type of fluid from one of the nipples.

6. Know the family history.

Most of the cases that have been reported are related to a genetic mutation. Of these, almost half are associated with a mutation in the BRCA1 or BRCA2 gene, which are also related to cases of ovarian, pancreatic, prostate and melanoma (skin) cancer.

To identify if there is any genetic propensity to breast cancer, there are DNA tests that look for mutations in these genes. They are usually performed under diagnostic suspicion due to the high cost of the studies, and are performed in cases of patients who have a direct relative (mother, father, grandparents, siblings) under 50 years of age, especially under 40 years of age, with a history of breast cancer.

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