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Male breast cancer

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Abstract

Male breast cancer (MaleBC) is a rare disease, accounting for <1% of all male tumors. During the last few years, there has been an increase in the incidence of this disease, along with the increase in female breast cancer (FBC). Little is known about the etiology of MaleBC: hormonal, environmental and genetic factors have been reported to be involved in its pathogenesis. Major risk factors include clinical disorders carrying hormonal imbalances, radiation exposure and, in particular, a positive family history (FH) for BC, the latter suggestive of genetic susceptibility. Rare mutations in high-penetrance genes (*BRCA1* and *BRCA2*) confer a high risk of BC development; low-penetrance gene mutations (i.e. *CHEK-2*) are more common but involve a lower risk increase.

About 90% of all male breast tumors have proved to be invasive ductal carcinomas, expressing high levels of hormone receptors with evident therapeutic returns.

The most common clinical sign of BC onset in men is a painless palpable retroareolar lump, which should be evaluated by means of mammography, ultrasonography and core biopsy or fine needle aspiration (FNA).

To date, there are no published data from prospective randomized trials supporting a specific therapeutic approach in MaleBC. Tumor size together with the number of axillary nodes involved are the main prognostic factors and should guide the treatment choice. Locoregional approaches include surgery and radiotherapy (RT), depending upon the initial clinical presentation. When systemic treatment (adjuvant, neoadjuvant and metastatic) is delivered, the choice between hormonal and or chemotherapy (CT) should depend upon the clinical and biological features, according to the FBC management guidelines. However great caution is required because of high rates of age-related comorbidities.

Keywords: Male breast cancer; Genetics; Therapy; Surgery; Radiotherapy; Chemotherapy; Hormonal treatment; Survival; Local recurrence

1. Introduction

Male breast cancer (MaleBC) is a rare disease, showing an increasing incidence trend rising along with that of female breast cancer (FBC). Even if male and female breast cancers seem to be similar, with regard to epidemiological aspects, they deeply differ because of the lower incidence and later onset of the former. Little is known about the etiology of MaleBC: hormonal, environmental and genetic factors are involved in the pathogenesis of breast cancer in men as well as in women. The major risk factor related to MaleBC is a positive family history for breast cancer, which indicates a relevant genetic component. In fact, MaleBC susceptibility can result from rare mutations in high-penetrance genes conferring a high risk, or from more common low-penetrance genes giving a lower risk increase.

From the clinical and biological point of view, male and female breast cancers differ mainly in the frequency of their histological types and in the expression of hormone receptors and of epidermal growth factor receptor 2 (HER2).

In the lack of randomized controlled trials, principles of management of MaleBC are mainly derived from randomized trials in female patients (pts). Since it is often late diagnosed, MaleBC remains a substantial cause of morbidity and mortality in men. This last consideration together with the increasing incidence made it urgent to comprehensively review the epidemiological, genetic, histopathological and clinical aspects of MaleBC, including the diagnosis, prognosis and treatment of the disease.

2. Epidemiology

In Western countries, MaleBC accounts for <1% of all cancers in men but its incidence varies greatly in different geographical areas and ethnic groups [1,2]. The worldwide variation of MaleBC resembles that of FBC, with higher rates in North America and Europe and lower rates in Asia. A substantial high proportion of MaleBC cases have been reported in Africa [3]. Although scarce, data from this continent have shown annual MaleBC incidence rates ranging from 5 to 15% [4–6]. These relatively high rates have been attributed to endemic infectious diseases, such as bilharziosis and hepatitis B/C that, by chronic liver infection, may cause liver damage leading to hyperoestrogenisms. By contrast, the annual incidence of MaleBC in Japan is significantly lower (5 per 1,000,000) than the average incidence, comparable to the lower than average incidence of FBC in this country [7]. Recent epidemiological studies indicate that MaleBC incidence is rising [8]. The incidence of MaleBC increases with age and the bimodal age distribution seen in women is absent in men, with a peak incidence in the sixth decade [3]. Overall, due to the absence of screening programs in men, MaleBCs are diagnosed at a more advanced age and with a more severe clinical presentation than in women, with greater tumor size and a more frequent lymphonodal involvement. The mean age at breast cancer diagnosis in males is 63.4 years [9]; in the SEER data, the median ages at diagnosis of breast cancer were 67 and 62 years in males and females, respectively [3]. The mortality rates for MaleBC have been shown to remain stable [1], however, survival rates differ significantly according to race/ethnicity [10] and are not significantly different from those observed in women [3]. In general, the prognosis for male and female patients with breast cancer is similar. Overall survival rates are lower for men, but this is due to an older age at diagnosis and more advanced stage at presentation [11]. Disease-specific survival rates are higher than overall survival rates due to the older average age and deaths from other comorbid diseases [12].