

Breast Cancer in Women under 30 is Highly Aggressive with Extremely Low Frequency: A Case Report

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Abstract

Breast cancer occurrence is increasing worldwide; however, patients under 30 years of age who present with this condition are scarce. Using as a pretext, the “chance” to encounter a case of breast cancer patient less than 30 years of age in a hospital setting, in conjunction with the relatively few data in the literature on the topic, the current paper attempts to point out some of the features of breast carcinoma occurring in this category of patients. Basically, the paper highlights a very important aspect, namely that breast carcinoma in young women is more aggressive and shows a reserved prognosis, translated as a 5-year lower survival rate and a higher percentage of relapse following therapy compared to women in perimenopause or to elderly ones.

Keywords: Breast cancer; Young women; Low frequency; Reserved prognosis

Introduction

The current paper does not aim to analyze or draw conclusions on the behavior of breast cancer in young and very young (under 30 years old) women, nor is it supposed to do it based on solely one case in the context of extremely low occurrence of the disease in these age [1]. Nevertheless, due to the very occurrence of the case and the related trauma, in conjunction with relatively few papers on the topic, we attempted to point out some of the characteristics of breast carcinoma in the target population, which prove to be a slightly different in comparison to the “classical” data of the other age [2]. Last but not least, we intend this paper to be a plea in favor of accurate briefings of young women concerning the risks related to the existence of malignant lesions in the breast, in particular period of life, and to increase the awareness of the medical profession detecting the mammary tumor in this category of women.

Case Report

Patient IP, aged 27, from Craiova, is hospitalized on November 13, 2008 on account of right breast diffuse enlargement. On clinical examination: diffusely enlarged right breast, with erythema and

edema of the skin, showing a thick consistency in the central and lower quadrants, being sensitive to touch. 3 palpable lymph nodes were found in the right armpit, having a diameter between 1 cm and 2.5 cm, with a thick consistency. Ultrasonography revealed the presence of a non-homogenous glandular tissue of the right breast, with four solid nodes, non-homogeneous, with unclearly defined calcifications, vascular signal of low strength visible centrally and peripherally, highly suggestive of their equivocal character; the nodes had the following size: 2.8/2 cm, 1.7/1.3 cm, 1.5/1/0.1 cm and 1/0.7 cm, in the right armpit lymph nodes were found, having diameters of max = 20 mm, with non-differentiated sinus and periphery, and arterial vascular signal of low strength. Bone scintigraphy did not reveal the presence of bone lesions.

Laboratory tests indicated: Hb = 13.2 g%, WBC = 11720/mm³, Urea = 36 mg%, Bt = 0.26 mg % and CA 15-3 = 40.3 U. Chest X-ray revealed no damage evolution. On November 15, 2008 axillary lymph node biopsy was done. The histopathological test confirmed a poorly differentiated massive metastatic carcinoma. The immunohistochemical test revealed the following: HER2-negative, ER-negative, PGR-positive in less than 10% of the tumor cells and SR-2 (positive). The diagnosis upon discharge was: breast cancer (inflammatory carcinoma)-stage III B (T4dN2M0) [3]. In January 2009 the patient was referred to the Oncology unit where she was given chemotherapy in 5 sequences (DOCETAXEL and EPIDOXORUBICIN) [4,5]. The response to chemotherapy was partial: the erythema wore off and the skin edema was reduced (yet a slight peau d’orange was still present). Also a right axillary lymphadenopathy relic having a diameter of 1.5 cm persisted. Under the circumstances, it was decided to change the regimen by administering EPIDOXORUBICIN + 5 FLUOROURACIL + CYCLOPHOSPHAMIDE [4,5] in 4 sequences, followed by radiotherapy 50 Gy, the evolution still being favorable (disappearance of skin edema with the involution of mammary lymph nodes and axillary adenopathy). On 22 July 2009 surgery took place in the form of mastectomy with full axillary dissection.

The histopathological result of 12 August 2009 revealed the following: macroscopically-four tumors having the size of 2/1.6

cm, 1.1/1 cm, 0.9/0.8 cm and 0.5/0.3 cm, respectively, depth of resection of 1.2 cm; microscopically - post-chemotherapy and radiation tumor relic resembling lobular infiltrating carcinoma coexisting with ductal infiltrating carcinoma, fibro-hyaline stroma, extensive necrosis, moderate lymphocyte infiltration, intra lymphatic invasion. No perineural invasion was identified, and the nipple was free of tumor. Four axillary lymph nodes showed metastatic disease. Starting from August 2009, the patient complained of persistent headache, vertigo-which is why she was referred for a cranial MRI, which indicated the presence of secondary brain and left parietal tumors, therefore, during August 24, 2009 to September 18, 2009 she undertook craniocerebral radiotherapy with 27 Gy. She was administered Cisplatin and Gemcitabine in six sequences in the Oncology unit. Starting from April 2010, the patient complained of right hemithorax pain, the chest X-ray revealed a round-oval opacity of 5.6/3.7 cm, relatively well-defined, with lysis of the straight rib curves C5-C6, extending to the soft tissue at this level (secondary lesion). Treatment with Zoledronic Acid (ZOMETA) was administered, followed by Avastin (BEVACIZUMAB) in May 2010. The CT scan of the spine on 17 June 2010 highlighted the secondary tumors in the lower thoracic, lumbar and first sacral vertebra level. The patient died on 3 July 2010 with acute pulmonary edema.

Discussion

Breast cancer occurrence is increasing worldwide, with the largest number of cases being reported during perimenopause [1,2]. Conversely, both literature and current practice shows that patients with breast cancer are rare under the age of 30 [1,2,6]. Using as a pretext the "chance" to encounter such a case in the hospital and relating it to the information provided by literature, we attempted to point out some of the peculiarities and paradoxes of the disease course in young women. The majority of breast tumors occurring in adolescent and young women are benign, and out of these, fibroadenomas are the most common, their occurrence ranging between 44% and 94%, according to various reports [7,8]. The frequency of breast malignancy occurring in women under the age of 30, this is very low ranging between 0 and 9.5% [9-11]. The most common malignancies occurring in these patients are stromal tumors, such as Phyllodes malignant fibroadenomas and metastatic tumors, usually multiple ones [7,11,12].

The frequency of breast carcinoma occurring in young women varies according to different reports, however, all have a common core, namely the very low rate of this phenomenon as Simmons *et al.* [7] states that breast carcinoma occurring in young women represents 0.02% of all the excised breast tumors [8]. These findings published by the National Cancer Institute 's Surveillance, Epidemiology and End Results shows that out of the 77,368 women diagnosed with breast cancer only 1% were aged between 20 and 29 [1,3]. The statistics provided by the National Cancer Database of the American College of Surgeons indicate a 0.8 % frequency of breast carcinoma occurring in women aged under 30 [9]. Kollias *et al.* [13] revealed a frequency of 1.1‰ women with breast cancer aged between 26 and 35. Finally, in the UK, the frequency of breast carcinoma in women

aged between 20 and 24 is 1.2‰, and of 3‰ [1] in women aged between 15 and 19.

The small number of scientific reports on papers about breast cancer in young women and the small number of reported cases do not allow for the calculation of a highly accurate frequency of this disease in persons belonging to this age group. The second issue, and perhaps the most important, lies in the postulation that breast carcinoma in young women appears to be more aggressive and shows a reserved prognosis, resulting in a 5-year shorter survival rate and a higher percentage of recurrences following therapy, compared to women at perimenopause period or to the elderly [8,14]. According to many scholars, the young age itself is a negative prognostic factor for breast cancer, while other authors believe that the role of this factor is still controversial [2,15,16]. An important element that contributes to worsening the prognosis is represented by the delayed diagnosis of breast cancer [8,17].

This delay is due, more often than not, to the patient, who does not palpate the breasts regularly or ignores the existence of clinical signs and the presence of a tumor mass in the breast, a mastalgia or blood leakage from the nipple.

Likewise, the desire of these women to be pregnant may delay the diagnosis, many breast cancers becoming clinically evident during gestation or immediately after delivery [18-20]. Hence, breast palpation, ultrasonography of breasts and armpits, and biopsy of the tumor tissue (punch biopsy) are considered to be the gold standard in the evaluation of masses occurring in a woman under 30 [14]. Particular importance should be attached to the information relating to personal history (other malignancies, undergoing radiant treatments or hormone replacement therapy) or to family history, with the presence of relatives with breast cancer or with bilateral breast cancer, colon cancer or other types of cancer. The diagnosis of breast cancer in young women associated with a family history of breast, ovarian or colon cancer raises suspicion of mutations in BRCA1 or BRCA2 genes [4,21].

Some authors consider that about 10% of patients with breast cancer under the age of 40 are carriers of mutations in BRCA1 or BRCA2 [22].

The prognosis of breast cancer in young women is associated with the tumor size, metastatic disease in the lymph nodes, histological type, degree of cell differentiation and immunohistochemical markers [1,23].

There are suggestions that the average size of primary tumors is higher in women under 35 years compared to other age groups, whereas other authors do not find such differences based on statistical data [11,12,24,25].

Also, it is claimed that in young women the percentage of cases with multiple unilateral or bilateral mammary tumors is higher, with respect to the presence of the metastatic disease in axillary nodes, the majority of the statistics clearly indicate their higher frequency in young women compared to other age groups. In this climate of opinion, Bertheau reports a frequency

rate of 65% [26] and Walker goes for 69% [27] in women under 30 years, Fisher *et al.* [28] identify a frequency rate of 60% in the case of the metastatic disease in axillary nodes in women under 39 years and Kim *et al.* [15] indicate a frequency of 48% of these metastases in women under 35. It was also the case of our patient, where four lymph nodes were invaded. Regarding the histological type of carcinoma occurring in young women in most of the reported cases the ductal infiltrating type prevails, and there are rare cases of lobular infiltrating carcinoma, as considered by pathologists as always having a low degree of cell differentiation (stage III) [1,4,8,17,29].

As a peculiarity, we recorded the coexistence of the ductal infiltrating and lobular infiltrating carcinoma types in our patient, which, in our opinion, contributed to worsen the prognosis. Literature describes a particular form of secretory breast carcinoma, characteristic to childhood and adolescence and which usually has a favorable prognosis [1]. The analysis of the differentiation of tumor cells revealed the prevalence of stage III (very poor cell differentiation), followed by tumors of stage II of (moderate) cell differentiation, while emphasizing the quasi-inexistence of tumor of stage I (well differentiated cells) [1,30]. In general, in breast cancer a number of immunohistochemical markers can be identified, which can be dosed and whose expression may have a predictive value of the prognosis. High levels of markers Ki-67 and low levels of the protein p27, as well as the over expression of the marker HER2 are associated with a reserved prognosis [23]. Mammary tumors of stage II and III of differentiation are associated, to a significant degree, with positive HER2 positive and high values of the marker Ki-67; there is instead a negative association with the estrogen receptors α and β and high values of the protein p27 [31-34].

In women under 35 with breast carcinoma, low values of the estrogen and progesterone receptors, in contrast with the over expression of HER2 and high values of the marker Ki-67 and protein p 53 are frequent in immunohistochemical tests. This immunohistochemical description may explain in part the rather reserved prognosis of these patients with breast cancer [4,35,36]. The treatment of breast cancer occurring in women younger (under 30 years) is a complex one (surgery, chemotherapy, hormone therapy, radiotherapy) taking into consideration this mammary tumor aggressiveness and, of course, a range of parameters such as: stage, histological type, stage of differentiation or immunohistochemical markers. Similarly, toother age groups and young women, the type of surgery may be breast-conserving or radical, depending on local conditions and preferences of patients. Although a number of statistical studies identify a high rate of recurrence after breast-conserving surgery in young women compared to other age groups, the same authors state that the recurrence rate is the same whatever the surgery or mastectomy [37,38]. In spite of the fact that postoperative radiotherapy in the remaining breast reduces the rate of local recurrence, regardless of the age group, the rate remains higher in women aged under 40 [35,39]. Thus, Bartelink *et al.* [39] show a decrease in the rate of local recurrence in 10 years' time after surgery, from 24% to 14% in patients under the age of 40

undergoing radiotherapy in the remaining breast compared to a decrease from 7% to 4% in women older than 60 years [40].

Various empirical works reveal that hormone therapy with Tamoxifen 20 mg daily for 5 years is a standard component of adjuvant systemic therapy in young women with breast tumors bearing hormone receptors for estrogen and progesterone [32,39]. This treatment significantly reduces the risk of recurrence of breast cancer in all age groups, but it seems that this risk is, however, slightly higher in women under the age of 35 compared to those between 35 and 49 years [4,5,41]. Also the 5-year survival of patients younger than 35 years is significantly lower than that of other age groups. Specifically, Simmons *et al.* [1] indicated a 5-year survival of 50% for patients aged under 25, while Kothari *et al.* mentions a 5-year survival of 67% for patients aged under 35 [8]. Unlike the patients in perimenopause, the prognosis of breast cancer occurring in young and very young women is reserved both in terms of long-term survival and the recurrence rate, to which the quasi-inexistence of well-differentiated histological forms is added, all determining the selection of the most adequate loco regional and systemic treatment to maximize the chances of healing.

Conclusion

In conclusion, we can state that although the frequency rate of breast cancer in young women is very low, tumors occurring in these age groups, however, are more aggressive and show a more reserved prognosis than malignant breast tumors occurring during perimenopause.

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