RESEARCH ARTICLE

Very Young Breast Cancer in a Referral Center in Tehran, Iran; Review of 55 Cases Aged 25 or Less throughout 33 Years

Sadaf Alipour[1]*, Ramesh Omranipour[2], Issa Jahanzad[3], Khojasteh Bagheri[4]

Abstract

Background: Breast cancer is mostly the disease of postmenopausal women but very young affected women are seen more than occasionally in developing countries. We reviewed our cases of very young breast cancer in order to help in better understanding of such cases. Materials and Methods: The records of patients 25 years of age or less who had been admitted for breast cancer surgery in the Cancer Institute of Tehran from 1979 to 2012 were reviewed and relevant data were extracted. Results: From 5,265 cases of breast cancer, 62 patients had 25 years of age or less. There were 55 cases of breast adenocarcinoma, all female. More than 78% of the patients had presented with a palpable mass, the family history was positive in 2% of cases, and about 94% of the histologies were invasive ductal carcinoma. Gestational breast cancer constituted 10% of the cancers; another 10%were bilateral. The median size of the tumors was 5.72 centimeters, 63.2% of them had axillary lymphatic involvement, and more than half were negative for hormone receptors. Conclusions: Our study shows an incidence of 1.17% for very young breast cancer and a 10% rate of bilaterality which probably warrants special guidelines for contralateral screening. Cancer stage and features were poor in comparison with breast cancer in all ages.

Keywords: Breast cancer - very young females - incidence - Iran

Asian Pac J Cancer Prev, **14 (11)**, 6529-6532

Introduction

Breast cancer is the most common cancer in women in the world and is the most common cause of cancer death among them (Hunt et al., 2010). It is mostly the disease of postmenopausal women and ages above 40 years (Keinan-Boker et al., 2008; Gabriel and Domchek, 2010). However, its presentation in the premenopausal age is not infrequent, and although the disease incidence is several folds higher in developed regions of the world, the age is younger in under-developed areas (Harirchi et al., 2004; Shulman et al., 2010; Robles-Castillo et al., 2011). Unfortunately, very young (VY) patients are seen more than occasionally in developing countries. Since identifying the features of the disease in the VY would lead to better understanding of young breast cancer, we reviewed the cases of VY breast cancer from the beginning of our inpatient record archive in 1979.

Materials and Methods

The records of patients who had been admitted for breast cancer surgery in the Cancer Institute of Tehran, a referral center in the capital of Iran, were reviewed from 1979-2012. The cases which were younger than 26 years (≤25 years) were selected. Data including the demographic data, presenting signs, gestational and lactation status of the patients, radiologic and histopathologic features as well as hormone receptor status of the tumors were extracted. The results were classified and presented.

Results

From 5,265 cases of breast cancer, 62 patients (1.17%) had 25 years of age or less. Fifty had adenocarcinoma, 5 were bilateral; so there were 55 cases, all female. The other histologies were 8 malignant phyllodes tumor, two lymphomas, one dermatofibrosarcoma protuberans and one botryoid sarcoma. The latter was the only male of the series. These tumors were excluded from the study and only the adenocarcinomas were included. Some of the clinicopatologic features of the cancers had not been recorded in several files and the review is based on the documented details.

The youngest age of the patients was 15 years and 10 of them were 20 years or older. The median size of the tumors was 5.72 centimeters (cm) in the 24 cases who had the precise size recorded, with a range between 1.4-14 cm. The tumor was multicentric in 3 patients. The past history was positive in one case that had her contralateral breast cancer treated a few years sooner. One of the patients gave the history of infertility treated by in vitro fertilization (IVF).The clinicopathologic characteristics of the tumors are shown in Table 1.

*[1]Surgery Department - Cancer Institute and Arash Women's Hospital, [2]Surgery Department, [3]Pathology Department, [4]Breast Clinic, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran *For correspondence: sadafalipour@yahoo.com*

Table 1. Clinicopathologic Features of the Patients and Tumors

Feature		No.	%	Feature		No.	%	Feature		No.	%
Side	Right	21	44.7	Neural invasion	Positive	3	11.1	N stage[6,7]	N0	14	36.8
	Left	26	55.3		Negative	24	88.9		N1	18	47.4
	not specified	8	-	Cellular grade	1	0	0		N2	6	15.8
Family history[1]	Positive	1	2		2	13	92.9		N3	0	0
	Negative	49	98		3	1	7.1	M stage[6,8]	M0	48	96
Presenting sign/symptom	mass[2]	18	78.3	ER[9,10]	Positive	8	42.1		M1	2	4
	BND[3]	2	8.7		Negative	11	57.9	Stage[6]	0	2	4.8
	burning pain	1	4.3	PR[9,10]	Positive	6	40		I	0	0
	bone fracture	1	4.3		Negative	9	60		IIA	10	23.8
	breast abscess[4]	1	4.3	T stage[6]	T0	2	5.1		IIB	10	23.8
Histologic Subtype[5]	IDC	48	94.1		T1	0	0		IIIA	15	35.7
	ILC	2	3.9		T2	18	46.2		IIIB	3	7.1
	DCIS	1	1.9		T3	17	43.6		IV	2	4.7
Vascular invasion	Positive	11	42.3		T4	2	5.1	p5[39,10]	pos	6	66.7
	Negative	15	57.7						neg	3	33.3
								HER[29,10]	pos	1	12.5
									neg	7	87.5

*BND=bloody nipple discharge, IDC=invasive ductal carcinoma, ILC=invasive lobular carcinoma; DCIS= ductal carcinoma in situ, ER=estrogen receptor, PR= progesterone receptor, HER2= human epidermal growth factor receptor 2; [1]Positive in the sister (premenopausal), while the patient had the previous history of contralateral breast cancer; [2]Two 17 years old patients had a breast mass since childhood with enlargement during the last months; [3]Unilateral spontaneous bloody nipple discharge from one duct as the sole finding; [4]Malignant pathology in the incisional biopsy of a breast abscess in a lactating patient; [5]Cancer cells in the dermal lymphatics of one of the IDCs, confirming inflammatory carcinoma; [6]According to the 6th edition of the TNM staging classification of the American Joint Committee on Cancer; [7]Axillary lymph node involvement in 63.15%; median number of involved nodes 4.21(range 0-17); [8]One with spinal metastatic lesions, the other with suspicious liver and lung lesions responding to chemotherapy; [9]Immunohistochemistry assessment began in 1997 in Iran and was performed in limited cases in the first years; [10]Two triple negative cancers out of 15 known cases

Table 2. Comparison of the Incidence of Breast Cancer Stages I, II and II in Women≤25 Years with the Overall Incidence in Iran

Stage	Harirchi et al. All ages	Mousavi et al. All ages	Alipour et al. Age ≤25 years
I	3.4%	18%	0%
II	58.3%	57%	47.6%
III	38.3%	25%	18%

Four patients had had their cancer diagnosed in the lactating period and two others during pregnancy. Defining gestational or pregnancy-associated breast cancer as those diagnosed during pregnancy, in the first postpartum year, or any time during lactation (Keinan-Boker et al., 2008), there were overall 6 cases of gestational breast cancer. Their age range was 22-25 year with a median of 24 year. The stage of the cancers was 0 in one (DCIS), IIB in 4 and IIIA in the last one. The median diameter of the tumors was 6.5 cm, and lymph node involvement was present in half. The ER status was known in 4 cases, negative in 3.

Discussion

The incidence of breast cancer in young women is not clear because of disparities in worldwide age-specific incidence and different classifications of youth in breast cancer from under 30 to less than 45 years. Approximately 7% of female breast cancer cases between 2000 and 2005 were below 40 years of age (Gabriel and Domchek, 2010; Keegan et al., 2012; Merlo et al., 2012). There was an increase in the european incidence of the disease by about 3% and 1% each year in group ages 20-29 and 30-39 years, respectively (Merlo et al., 2012). Breast cancer is the most frequently diagnosed cancer among female patients aged 15-39 years (Keegan et al., 2012) and of all female cancers, 2% is breast cancer by the age of 20, 20% by the age of 30, and 40% by 40 years of age. Only 1% of breast cancers are diagnosed before age 30, 2.5% before 35, and 6.5% before 40 years (Anders et al., 2009).

It has been shown that breast cancer affects Iranian women at least one decade younger than the female population in developed countries (Harirchi et al., 2004; Bidgoli et al., 2010; Kolahdoozan et al., 2010), with an incidence of 20-25% for cases under 40 and about 5% for age under 30 (Mousavi et al., 2008; Harirchi et al., 2010; 2011).

Our study showed an incidence of 1.17% for breast cancer less than 26 years of age in the 5265 cases hospitalized for the disease. To our knowledge, there are no known figures about the frequency of the disease in this VY age group.

Young women attended by breast cancer usually present with breast symptoms because of the lack of standard screening breast imaging in this age group (Gabriel and Domchek, 2010). In a study in Mexico, 50% of breast cancer patients under 40 years of age presented with self-detection of a breast mass (Robles-Castillo et al., 2011) while this comprised more than 78% of cases in our study. The second presenting sign was bloody nipple discharge, which may call for additional awareness towards this symptom in the VY because it is known that bloody nipple discharge has a benign etiology in most of the cases, especially in women under 40 years of age (cancer rate 3% in younger than 40 versus 32% in older than 60 years) (Dixon, 2010).

Positive family history is seen more frequently in young patients (Anders et al., 2009). In our study, the rate of positive family history was unpredictably low (2%); this can be due to different pathophysiologic features in VY cancers in comparison with young cases, or different genetic patterns in our country, which is more probable.

The widespread hormonal manipulations used in infertility have not been associated with increased breast cancer risks in studies. In 1082 women undergoing IVF, there was an increased rate of cancer in the first year after

treatment but no increased risk afterwards (Lerner-Geva et al., 2003), and a large cohort of 5026 women undergoing in vitro fertilization (IVF), showed no excess risk for cancer (Dor et al., 2002). There was one case of infertility among our patients; this surely cannot disclose any special association between the two diseases.

About 10% of our cases were bilateral while previous studies comprising all ages had shown a frequency of 1.2% (Harirchi et al., 2004). We have not found any relevant figure for the frequency of bilaterality of breast cancer in young or VY cases in our literature search. The frequency seen in our study is really high and alarming, suggesting the necessity of a more sensitive test as MRI besides mammography for screening the other side in VY breast cancers; of course this has to be confirmed by other studies.

The most common histology of breast cancers is nvasive ductal carcinoma (Hunt et al., 2010). This histologic type included 77-89% of breast cancers in all ages in Iranian studies (Mousavi et al., 2007; Harirchi et al., 2011; Pourzand et al., 2011). Our detected higher frequency (94.11%) may be due to a higher occurrence for this pathology in the very young, or simply to the small sample size.

Breast cancer in the young population has a tendency to be more aggressive and usually presents at higher stages (Anders et al., 2009; Gabriel et Domchek, 2010). In women under the age of 35, tumors are more frequently ER and PR negative and HER2 positive, while the rate of triple-negative tumors, vascular and lymphatic invasion and high grade tumors are higher, and young age is overall a risk factor for recurrence (Anders et al., 2009; Bidgoli et al., 2010; Andre et al., 2011; Pourzand et al., 2011; Keegan et al., 2012). In the 905 patients of Yang et al., the 3-year disease-free and overall survival rate was lower in women under 35 years and tumors with positive hormone receptors had a worse prognosis in them compared with the above 35 years group (Yang et al., 2009).

Studies in Iran have showed variable but parallel results, demonstrating higher grade tumors harboring positive vascular, neural, and lymphatic invasion more frequently in premenopausal patients (Bidgoli et al., 2010), and higher stage cancers including larger size masses with more positive lymph nodes and more frequent unfavorable histopathologic features in younger patients (Harirchi et al., 2004; Pourzand et al., 2011). In none of these studies, the stage of the tumors has been defined according to the age of the patients. Nonetheless, the stage of the disease in the Iranian female population in all ages in two large studies is compared with that of our study group in table 2, demonstrating higher stages in the VY group.

Tumor size larger than 5 cm has been seen in only 7.5% of patients in all ages while the median size of the mass in our VY group was 5.72 cm, showing a large difference in tumor size. Nevertheless, the rate of lymphatic invasion (63.15%) in our cases shows a similar propensity for lymphatic metastases in VY women and other patients [45.5% (Mousavi et al., 2008) and 70% (Harirchi et al., 2010) in two different studies in all ages]. Our study shows a high level of hormone receptor negative tumors as expected, and a 20% (3 out of 15) for triple negative cancers.

Male breast cancer is very rare, and it constitutes less than 1% of all breast cancers. Most of these are seen in the sixth decade of life, the occurrence of the disease in young men is thus an exception (Hunt et al., 2010; Saleh and Ansari, 2012). In our study of VY patients, all were female.

It has been estimated that the rate of gestational breast cancer among patients under 30 years of age is 10-20% (Anders et al., 2009). In a systematic review of the subject by Keinan-Boker et al., it has been shown that it may account for up to 6.25% of breast cancers of fertile women under age 45. Their review demonstrated that the size of the tumors, the number of involved lymph nodes and the stage of the disease were higher than non-pregnant cases. The higher rate of ER and PR negative tumors that is seen in premenopausal cancers is even more pronounced in these patients (Keinan-Boker et al., 2008) and axillary lymph node metastases may be seen in up to 75% of them (Hunt et al., 2010). Around 10% of our patients had presented with the disease during pregnancy or lactation. The stage incidence of their disease was not significantly different from the non-pregnant cases, while the median diameter of their tumors was larger and lymph node metastasis was more frequent in them.

This study shows an exceptionally high incidence of bilateral disease in VY breast cancer; probably warranting special guidelines for contralateral screening in this age. Moreover, Familial inheritance, known to be frequent in young ages, is not confirmed.

References

Anders CK, Johnson R, Litton J, Phillips M, Bleyer A (2009). Breast cancer before age 40 years. *Semin Oncol*, **36**, 237-49.

Andre C, Collignon J, Rorive A, et al (2011). Breast cancer in young women. *Rev Med Liege*, **66**, 397-9.

Bidgoli SA, Ahmadi R, Zavarhei MD (2010). Role of hormonal and environmental factors on early incidence of breast cancer in Iran. *Sci Total Environ*, **408**, 4056-61.

Dixon JM BN (2010). Management of disorders of the ductal system and infections. in 'diseases of the breast', Eds Harris JR LM, Morrow M,Osborne CK. 4th ed. Wolters Kluwer, Lippincott Williams&Wilkins,USA pp 42-5.

Dor J, Lerner-Geva L, Rabinovici J, et al (2002). Cancer incidence in a cohort of infertile women who underwent in vitro fertilization. *Fertility and Sterility*, **77**, 324-7.

Gabriel CA, Domchek SM (2010). Breast cancer in young women. *Breast Cancer Res*, **12**, 212.

Harirchi I, Karbakhsh M, Kashefi A, Momtahen AJ (2004). Breast cancer in Iran: results of a multi-center study. *Asian Pac J Cancer Prev*, **5**, 24-7.

Harirchi I, Karbakhsh M, Montazeri A, et al (2010). Decreasing trend of tumor size and downstaging in breast cancer in Iran: results of a 15-year study. *Eur J Cancer Prev*, **19**, 126-30.

Harirchi I, Kolahdoozan S, Karbakhsh M, et al (2011). Twenty years of breast cancer in Iran: downstaging without a formal screening program. *Ann Oncol*, **22**, 93-7.

Hunt KK NL, Copeland III EM, Bland KL (2010). The Breast. In 'Schwartz's Principles of Surgery', Eds Brunicardi FC AD, Billiar TR, Dunn DL, et al. 9th ed. McGraw-Hill, USA pp 424-6.

Keegan TH, Derouen MC, Press DJ, Kurian AW, Clarke CA (2012). Occurrence of breast cancer subtypes in adolescent and young adult women. *Breast Cancer Res*, **14**, 55.

Keinan-Boker L, Lerner-Geva L, Kaufman B, Meirow D (2008). Pregnancy-associated breast cancer. *Isr Med Assoc J*, **10**, 722-7.

Kolahdoozan S, Sadjadi A, Radmard AR, Khademi H (2010). Five common cancers in Iran. *Arch Iran Med*, **13**, 143-6.

Lerner-Geva L, Geva E, Lessing JB et al (2003). The possible association between in vitro fertilization treatments and cancer development. *Int J Gynecol Cancer*, **13**, 23-7.

Merlo DF, Ceppi M, Filiberti R, et al (2012). Breast cancer incidence trends in European women aged 20-39 years at diagnosis. *Breast Cancer Res and Treatment*, **134**, 363-70.

Mousavi SM, Mohagheghi MA, Mousavi-Jerrahi A, Nahvijou A, Seddighi Z (2008). Outcome of breast cancer in Iran: a study of Tehran Cancer Registry data. *Asian Pac J Cancer Prev*, **9**, 275-8.

Mousavi SM, Montazeri A, Mohagheghi MA, et al (2007). Breast cancer in Iran: an epidemiological review. *Breast J*, **13**, 383-91.

Pourzand A, Fakhree MB, Hashemzadeh S, Halimi M, Daryani A (2011). Hormone receptor status in breast cancer and its relation to age and other prognostic factors. *Breast Cancer (Auckl)*, **5**, 87-92.

Robles-Castillo J, Ruvalcaba-Limon E, Maffuz A, Rodriguez-Cuevas S (2011). Breast cancer in Mexican women under 40. *Ginecol Obstet Mex*, **79**, 482-8.

Saleh FM, Ansari NP (2012). Invasive ductal carcinoma in a young male breast. *Mymensingh Med J*, **21**, 162-4.

Shulman LN, Willett W, Sievers A, Knaul FM (2010). Breast cancer in developing countries: opportunities for improved survival. *J Oncol*, **2010**, 595167.

Yang H, Wang SY, Ou W, Sun HB, Fang Q (2009). Clinical characteristics and prognosis of very young patients with breast cancer in the southern of China. *Ai Zheng*, **28**, 1310-6.