EVOLUTION OF SYNCHRONOUS BILATERAL BREAST CARCINOMA IN A YOUNG PATIENT

Elena Manea¹, Anca Munteanu¹,²
1. Radiotherapy Department, Regional Institute of Oncology Iasi, Romania
2. University of Medicine and Pharmacy “Grigore T. Popa”, Iasi, Faculty of Medicine, Romania
*Corresponding author. Email: dr.elenamanea@yahoo.com

EVOLUTION OF SYNCHRONOUS BILATERAL BREAST CARCINOMA IN A YOUNG PATIENT (Abstract) Bilateral breast cancer incidence is appreciated to be between 0.3 to 12% and is determined either by a hereditary load associated with chromosomal instability under the effect of environmental factors, or by the evolution in a particular hormonal context which gives biological aggressiveness. We present the case of a patient, aged 38 years, clinically, imagistic and bioptic diagnosed with left axillary lymph node metastases of breast carcinoma NST invasive G3, IHC - RE = 60%, RP = 30%, HER2neu = 2 +, Ki67 = 20% , in August 2013. Patient followed neoadjuvant chemotherapy treatment during September-October 2013. In December 2013 she was clinically and imaging diagnosed with bilateral breast cancer, for which surgical intervention was done which consisted of bilateral radical Madden mastectomy with bilateral axillary lymphadenectomy. BAP invasive carcinoma NST: left breast - pT2mN3a G2, right breast - pT3mN3a G2, IHC - RE = 90%, RP = 70% HER2neu = 2 +, Ki67 = 50%. During the period of January-March 2014, the patient followed adjuvant chemotherapy and Herceptin. Bilateral breast ultrasound assessment in April 2014 revealed: left axilla - liquid blade 29 / 6mm; right axilla - oval ganglion 9 / 5mm. Abdominal and pelvic ultrasound: empty uterine cavity, bosselated contour; at left ovary level multiple cystic formations. During the period of May-June 2014, adjuvant radiation therapy and ovarian irradiation was administered to the patient. Subsequently hormone therapy was initiated. Following CHT / ovarian irradiation patient continues to experience intermittent uterine bleeding, which is why a total hysterectomy with bilateral ovariectomy was done, and BAP: cervical, endometrial and left ovary with tumor multifocal infiltration with histopathological aspect of invasive breast carcinoma NST. Periodic imaging evaluations do not reveal local or distant recurrence. The particularity of this case is synchronous bilateral breast cancer diagnosis in a young patient complicated in its evolution by ovarian metastases. This form of metastasis is rare in young women and occurs in advanced stages of the disease. **Keywords:** SYNCHRONOUS BILATERAL BREAST CARCINOMA, MULTIMODAL TREATMENT, OVARIAN METASTASES.

Breast cancer is the most common type of cancer among women with increased incidence due to screening, resulting in improved prognosis and survival [1, 2]. In breast neoplasm, clinical forms and biological characteristics are very diverse. Of all breast cancers, BBC (bilateral breast cancer) is 2-6% [1]. Bilateral breast cancer incidence is appreciated to be between 0.3 to 12%. In breast cancer the most common
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Secondary dissemination are of the bone, liver, lung and brain, but may be metastatic sites other organs such as the peritoneum, ovaries and teguments.

**MATERIAL AND METHOD:**

In this paper we present the case of a patient, aged 38 years, clinically, imagistic and bioptic diagnosed with left axillary lymph node metastases of mammary gland carcinoma NST invasive G3, IHC (immunohistochemistry) ER (estrogen receptor) = 60%, PR (progesterone receptor) = 30%, Her2 neu = 2+, Ki67 = 20%, in August 2013. Neoadjuvant chemotherapy followed during September-October 2013, 3 CAF protocol cycles (cyclophosphamide 800mg, doxorubicin 80mg, 5-FU 800mg).

In December 2013, a bilateral breast ultrasound detected in the right breast a nodular formation of about 1.5 - 2cm, while on the left breast endured placard and bilateral axillary infracentimetric lymphadenopathy.

A pelvic ultrasound from December 2013 detects a heterogeneous consistence uterus, 45/36 / 72mm with two fibroid nodules 19 / 15.5mm and 12 / 15mm with 5.7mm endometrium, left ovary 40 / 24mm positioned retrouterin, normal consistency, right ovary 32 / 17mm normal echostucture and empty Douglas space.

A bilateral radical mastectomy type Madden with axillary bilateral lymphadenectomy with BAP (ID pathological) - NST invasive carcinoma: left breast - pT2mN3a G2, 11 excised lymph node metastasis; right breast - pT3mN3a G2, 15 lymph node metastasis in 19 excised IHC- RE = 90%, RP = 70%, Her 2 neu = 2+, Ki67 = 50%, FISH: HER2neu amplified. During the time period January-March 2014, the patient followed adjuvant chemotherapy: 1 CAF protocol cycle, 4 series of chemotherapy with Paclitaxel 300mg and initiated therapy with 300mg of Herceptin.

In April 2014, imaging evaluation through bilateral breast ultrasound revealed: left axillary - liquid blade 29 / 6mm; right axillary - oval ganglion 9 / 5mm. Abdominal and pelvic ultrasound: empty uterine cavity, bosselated contour; at left ovary level multiple cystic formations.

During May-June 2014 was administered to the patient adjuvant radiotherapy at ACC ClinaciX10, photons E = 10MV, DT = 42.56Gy/16fr/2.66Gy/fr/ chest wall bilaterally and axillary lymph nodes areas, bilateral supraclavicular region and right lateral-cervical (Fig.1, Fig.2) and ovarian irradiation at Clinac accelerator 2100sc, with photons E = 10MV, DT = 12Gy/4fr/3Gy/fr. Subsequently adjuvant hormone therapy was initiated with Tamoxifen.

**Fig. 1.** Treatment plan: a- target volumes delineation; a, b – patient in simulation position
In the context of abdominal and pelvic ultrasound appearance and persistent uterine bleeding even after ovarian suppression by chemotherapy and radiation therapy, total hysterectomy with bilateral ovariectomy was performed. BAP: cervical, endometrial and left ovary with tumor multifocal infiltration with histopathological aspect of invasive breast carcinoma NST.

Thorax CT (computer tomography) in September 2015 - without signs of local or distant recurrence, persistence of microadenopathies of ~ 9 / 10mm right hilar. In upper abdominal sections a simple hepatic cyst was identified in the segment IVb of ~ 4.5mm.

Pelvis MRI (magnetic resonance imaging) in November 2015 – total hysterectomy with bilateral ovariectomy without pathological contrast intake – stationery aspect, absence pelvic adenopathies.

**DISCUSSION:**

The risk of developing BBC is two to six times higher in women with history of unilateral breast cancer [2, 3].

BBC can be classified into subcategories, synchronous and metachronous. This classification is based on the time interval between diagnosis of primary tumor in the first breast and the second breast. Some previous studies have defined the synchronous bilateral breast cancer (SBBC) as the development of breast cancer in the time interval of 0-12 months [4].

According to the WHO guidelines in 2012, BBC is defined as SBBC when contralateral breast carcinoma is diagnosed within three months [1].

SBBC is defined in some studies, from an epidemiological point of view, as the development of breast cancer within 12 months [5,6]. The SBBC incidence is relatively low, between 1 and 3% of all breast cancers. SBBC and MBBC have different biological characteristics, reflected in the histopathological characteristics, stage and prognosis [7].

The appearance of the second contralateral breast tumors can be synchronous (in less than 6 months after the first primary tumor in the first breast) or metachronous (after 6 months of diagnosis of the primary tumor in the first breast) [8].

In the presented patient case, the contralateral breast cancer was diagnosed 5 months after the left breast cancer diagnosis and was considered synchronous, ac-
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cording to the interval of less than 6 months.

Some studies have indicated a worse prognosis and low survival rate for BBC. Conversely, other studies have claimed that there is no significant difference in the survival rate between UBC and BBC. Despite previous and ongoing studies, the prognosis and survival of patients with BBC remain uncertain [1].

Synchronicity and metachronicity are usually associated with local recurrence, hematologic and lymphatic spread to the lungs, bones and liver.

Early detection of contralateral breast cancer is of the most importance, emphasizing the importance of breast self-examination [9]. The standard for breast cancer screening is the mammography, some authors recommend breast MRI scan, which is more sensitive in comparison to mammography, but the high cost and lack of availability is limiting as a screening indication. There are no clear treatment guidelines for bilateral breast cancer. Patients are often treated with bilateral mastectomy, conservative surgery has an unclear importance [9].

In our case, multimodal treatment was administered according to the stage, histological and prognostic factors individually for each of the tumors.

Studies suggest that there is no significant difference in survival rate for patients with MBBC compared with those with SBBC. Synchronous tumors were associated with decreased survival in comparison to metachronous tumors [10].

Most often, patients with BBC are receiving radical surgery based on the idea that these tumors are biologically aggressive. However, scientific evidence to support this are split. Conservative treatment for BBC may be feasible also in the case of unilateral breast cancer [11].

BBC is more common in young aged women and most of these tumors are estrogen dependent. There is a concordance between the primary tumor and contralateral breast cancer from a histological point of view, of the receptors ER, PR and HER2. Some studies argue that there is no clear relationship between positive ER and PR and tumor bilateral localization. It seems that the BBC incidence is higher in cases with the overexpression HER-2 [2].

BC can metastasize to the bone, liver, lung and brain, but can affect other organs such as the peritoneum, ovaries and tegument.

Metastatic ovarian tumors, that are called Krukenberg tumors, occur frequently after the age of 40 years [12]. The appearance of these tumors at a young age is very rare and represents approximately 2% of all cases. The occurrence of ovarian metastases in breast cancer represents an advanced stage of the disease [13].

It seems that patients with Krukenberg tumors with BC as a starting point, unlike other tumor locations, have a good prognosis [13]. Surgery is the optimal treatment for these tumors, as it has been practiced in this case.

CONCLUSIONS:

The particularity of this case is synchronous bilateral breast cancer diagnosis in a young patient complicated in its evolution with ovarian metastases. This form of metastasize is rare in young women and occurs in the advanced stages of the disease. The prognosis for this patient is reserved considering the age under 40 years, synchronous neoplasia, nodal status (pN3a bilateral), the advanced stage (IIIC), Her
2neu positive status. In the case of synchronous bilateral breast carcinoma there should be applied adequate multidisciplinary management and rigorous supervision of patient to improve survival and quality of life.

REFERENCES