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Review

Synchronous bilateral breast cancer patients submitted to conservative treatment and brachytherapy – The experience of a service

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ABSTRACT

Introduction: The incidence of breast carcinoma (BC) has increased in the last years. Between 2 and 12% of patients diagnosed with BC will develop bilateral breast carcinoma (BBC). The treatment of these carcinomas is more aggressive than unilateral BC.
Purpose: To perform a retrospective qualitative analysis of BBC patients whose treatment has included brachytherapy (BT) and to present a revised literature on this issue.
Material and methods: The cases of BBC whose treatment included brachytherapy were revised. The literature on this issue was refreshed.
Results: Five women, aged between 54 and 78 at the time of the diagnosis, submitted to conservative surgery followed by external radiotherapy (RT) with boost of BT or exclusive BT (APBI), in the IPO-P BT Service between 2003 and 2016.
Discussion: The patients with BBC have slightly higher rates of local recurrences, mostly in the tumor bed, where there is a higher risk of local recurrence. Patients treated with BT had lower rates of recurrences than those treated with photons and electrons.
Conclusions: BBC represents a complex challenge for doctors, because in some cases there is a tendency to use more aggressive treatments and, at the same time, it is not easy to achieve the timing for the correct treatment.

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1. Introduction

In the developed countries breast carcinoma (BC) is the most frequently detected tumor in women; its incidence has been growing over the years.[1]

The average age at diagnosis is reported to fall between 45 and 65.[2]

About 2–12% of the patients with BC will develop contralateral BC during their lifetime.[3–9]

Between 1970 and 1980, there has been a rise of about 40% in the incidence of synchronous bilateral BC (SBBC), and this figure has remained stable since then. This growth has been explained by the routine bilateral breast screening procedures at the time of the diagnosis.[1]

The annual incidence of bilateral metachronous BC (BMBC) varies between 0.1 and 1.0%[10,11] while the incidence of SBBC varies between 0.3 and 3.0%. This variation is explained by the different definitions of synchronicity.[12,13]

The main risk factors to develop bilateral BC (BBC) are: BC family history, early age at the first breast tumor diagnosis, lobular histology[14] and multicentricity.[6,7,15–22]

The prognosis also varies: the cumulative mortality rates at 10 years are lower for the Unilateral BC (UBC) (33%) and BMBC when the 2 tumors were diagnosed within at least a 10 year gap (34%). For the SBBC, the cumulative mortality rates at 10 years are average, about 45%, and they are higher for BMBC (56%) when both tumors were diagnosed within a 5 year gap.[1]

Although nowadays the therapeutic options for early breast cancer include breast mastectomy or breast conservative surgery followed by RT,[23–25] BBC treatment is usually more aggressive, with a higher number of mastectomies and axillary dissections than UBC.[14]

In our center 5 SBBC cases were treated with conservative surgery followed by RT (3DCRT) to the breast, at a dose of 50 Gy, 2 Gy per fraction, in 25 fractions with photons and *boost* with BT or exclusive BT (APBI), and were subject of a qualitative retrospective analysis.

The need to perform a literature review came from the fact that no specific guidelines for an approach to SBBC had been found.

2. Material and methods

The aim of this study is to characterize the patients with SBBC treated with BT in our institution and to review the literature concerning BBC definition and risk factors, SBCC treatment and prognosis. We included patients with SBBC who had undergone BT treatment at the Instituto Português de Oncologia do Porto (IPO-P) BT Service between 2003 and 2016, and collected demographic data and tumor features, using clinical records. The tumors considered SBBC were those in a 6 month gap or lower.

The criteria for *boost* used were those according to Fourquet.[26]

After surgery, 4 out of 5 patients underwent external beam radiation to the entire breast at a dose of 50 Gy, at 2 Gy per fraction, in 25 fractions with photons, 4 MV energy.

For the brachytherapy treatment, the patients were under anesthesia for the application of hypodermic needles, according to a template, with an interval of 14 mm between needles. The applicator reconstruction is a theoretical one, based on the Paris System modified. The total dose was 15 Gy 85% D. B. and the pulse dose: 0.8 Gy/h with Iridium 192 Pulsed Dose Rate (PDR).

A literature research was taken based on the following key words: bilateral breast carcinoma; bilateral breast carcinoma brachytherapy; bilateral breast carcinoma boost; APBI breast carcinoma brachytherapy.

3. Results

The patients' features and BBC's are displayed in Tables 1–3.

As far as the treatment with BT: patient 1 underwent APBI. 7 hypodermic needles (HN) were applied on the right breast and 9 HN on the left breast with the appropriate template. Total dose: 32 Gy 85% D.B. in 2 fractions/day during four consecutive days with Iridium 192 High Dose Rate (HDR); the remaining patients underwent a brachytherapy boost after RT. The Fig. 1 illustrates treatment planning of patient 3, that received bilateral external radiotherapy, 50 Gy, followed by BT boost, 15 Gy.

4. Discussion

4.1. *Definition of BBC*

Although it is relevant to define the differentiation of the second breast tumor as primary or metastasis,[27] this distinction is not always easy to assume.[28] Some authors suggest that BBC may derive from metastatic cells that migrated to the contralateral breast, or that it can be the result of a hormonal environment that enables the growth of several tumoral focuses.[29] Several genetic studies of BBC cases have shown that these tumors seldom metastasize to the contralateral breast.[30,31]

The molecular methods like "comparative genomic hybridization", used to distinguish a second primary from a metastasis, are very complex, expensive and have not been validated yet.[28] That is why, nowadays, the clinical criteria are most frequently used.

Chaudhary et al. suggested in 1984 four criteria for the breast second primary diagnosis: (i) the presence of carcinoma in situ in the contralateral tumor (absolute evidence); (ii) the second primary should be histologically different from the first tumor; (iii) the degree of the second primary histological differentiation should be higher than the first tumor's; (iv) if there is no histological difference, then there should not be evidence of local, regional or distant metastization of the first tumor.[7]

In our sample, we can confirm that patients 3 and 4 fulfill the 1st criterion (absolute evidence), in which the carcinoma in situ coexists with the invasive carcinoma. In patient 1 the carcinoma in situ was not detected. In patient 2 the component in situ coexisted only in the left breast. In patient 5 we did not have access to the information needed, so we can neither include nor exclude this criterion.

As for the matching of the other criteria, in patient 1 we confirmed that both tumors were histologically different and neither showed evidence of locoregional or distant metastization, fulfilling the 2nd and the 4th criteria. In patient 2,