

Reverse Surgery (“Liver-First Approach”) for Hepatic Metastases from Breast Cancer: Case Report

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Abstract

Background: Hepatic resection for liver metastasis from breast cancer (LMBC) can lead to long-term survival. Since BC has been a very sensitive neoplasm to both chemotherapy and targeted therapy, surgical resection of residual LMBC after systemic therapy has presented an important role to attain long-term survival. Reverse approach (“liver-first approach”) has been performed for liver metastasis from colorectal cancer (LMCRC), especially to the multiple synchronous metastases that have presented partial response after systemic treatment.

Case Report: LMBC in young female who has undergone successful “liver-first approach” after partial response to systemic therapy. At first, she underwent open right hepatectomy with caudate lobectomy and atypical resection of three small lesions in left lobe. After two postoperative cycles of chemotherapy associated a target therapy, she has finally submitted a radical mastectomy and selective axillary lymphadenectomy. To date, thirty-two months after hepatic resection, she is alive without any recurrence.

Conclusion: Reverse approach for LMBC by means chemo-targeted therapy associated a HR may lead a long-term survival in selected cases as we have observed in this report. In fact, new studies must be performed to answer if this strategy can be validated.

Keywords: Breast Cancer; Hepatic Neoplasms/Surgery; Liver/Surgery; Hepatectomy

Introduction

Hepatic resection (HR) for liver metastasis of breast cancer (LMBC) has been a studied topic over last years. Recent series has suggested that HR for LMBC can lead long-term survival for many patients, especially those who presented good response to systemic therapy. Therefore, in this specific sample, the overall survival has been comparable to patients with colorectal metastasis on the similar conditions. Finally, HR for LMBC has been considered an approach reasonable for selected situations [1-6].

Recently, “liver-first approach” or reverse surgery has been extensively studied for treatment of synchronous liver metastasis of colorectal cancer (SLMCRC). Long-term results may be similar to those observed when is performed the classical approach [8,9]. However, for other primaries besides colorectal (CRC), this approach is poorly studied in the literature. Nonetheless, in our point of view, reverse approach can be also used in other very chemo-responsive primary tumors besides CRC such as BC.

Present authors report a case of long-term survival (32 months) in a patient with synchronous bilateral LMBC who was successfully submitted a reverse approach after initial systemic response.

Case Report

A 25-year-old female was referred to our unit with a 2-months history of lump in her right breast. Physical examination revealed a 6,0 X 5 cm tumor in the lower outer quadrant of the right breast. Biopsy specimen by core needle biopsy from right breast lump showed an invasive ductal carcinoma (moderate grade) that was both estrogen receptor (ER)- and progesterone receptor (PgR)- negative with a HER2 of +3 by immunohistochemistry assay. A PET/CT scan showed uptake of 18F-fluoroglucose in the right breast besides right axillary lymph nodes and bilateral liver lesions. These hepatic lesions were small among 0,5 to 3,5 cm. Systemic staging of this patient was considered T3N1M1 with exclusive hepatic metastases according to the UICC classification.

She received preoperative systemic chemotherapy associated with target therapy. The scheme was the following: docetaxel and carboplatin associated with both trastuzumab and pertuzumab. She received six cycles with partial response of both primary lesion and hepatic metastases (Figure 1 - PET-Scan). This way, we proposed a “liver-first approach” because we observed a good response after systemic therapy besides that she was a healthy young woman. She underwent an open right hepatectomy and caudate lobectomy with atypical resection of three small lesions into left lobe. She was carried out at fifth postoperative day without any complication. Pathological evaluation showed only both fibrosis and necrosis in hepatic lesions. It was considered complete histological response. Subsequently, she received four more cycles (four) of the same initial scheme (except carboplatin). There was maintenance of the response (in primary tumor) and she was finally underwent radical mastectomy with selective axillar lymphadenectomy. Pathological evaluation evidenced absence of microscopic residual tumor (complete pathological response). Since this time she is receiving only both trastuzumab and pertuzumab. To date, thirty-two months after hepatic resection, she is alive without any recurrence (Figure 2 - PET-Scan). Actually, she also presents a very quality of life.



Figure 1: PET-Scan after initial treatment - bilateral hepatic metastases.



Figure 2: PET-Scan - Thirty-two months after hepatic resection of bilateral hepatic metastasis.

Discussion

Breast cancer is the most frequent malignant neoplasm in Brazil, it is estimated that there have been about 57000 new cases per year of this disease in our country at 2014. Although, the liver is the third most frequent site of metastasis in BC, only 5 - 25% will have isolated liver metastasis [1]. Since BC is usually very sensitive neoplasm to both chemotherapy and target therapy, the resection of LMBC after systemic treatment seems to present an important role in the removal of clones which can be resistant to cytotoxic treatment. This aggressive approach can lead to long-term survival that can be associated with a good quality of life due to the fact that these patients can avoid the use of cytotoxic therapy for long time after surgical debulking of their liver metastases. This strategy has been designated as “adjuvant surgical debulking” when LMBC are resected by means HR after systemic therapy [1-6]. For these patients with disease exclusively confined to the liver, the HR can be a very interesting alternative because can lead to prolonged survival. Recent studies have observed between 36 and 58% of 5-year survival rates after HR for exclusive LMBC [1-4]. More recently, Ercolani, *et al.* [1] in a large Italian series have also observed 8,9% of 10-year survival rates without recurrence after HR for LMBC. These results seem similar the most recent series published by our team for the surgical treatment of liver metastasis from colorectal cancer (LMCRC) [10].

Once HR is indicated for the LMBC treatment becomes necessary to recognize and select those cases what else would benefit of surgical treatment. To answer this question is very necessary better knowledge oof the BC biology as well as their prognostic factors. In fact, some questions still need to be answered, for example: How should we select the patients who may present a true benefit with an aggressive surgical treatment? Better knowledge of the prognostic factors can help in the selection of patients who can benefit from HR. Many prognostic factors (PG) have been studied in this particular scenario in order to select LMBC candidates to the HR. The more important prognostic factors for LMBC that have been described in the literature are the following: both number and diameter of lesions, extra-hepatic disease, disease-free survival time between primary lesion treatment and development of the liver metastasis, response to systemic therapy, microscopic margins, microscopic vascular or lymphatic invasion, hormone receptors (ER and PgR) and more recently receptor of HER2 [1-6]. These prognostic factors have been shown as significant to attain a long-term survival [1-6].

Currently, new biological prognostic factors have been largely studied in relation for cancer, especially those designated as biomarkers. Both markers of immunohistochemistry and molecular biology have been useful instruments to select good candidates for liver resection [1-6]. Specifically for BC, it seems that the most important have been hormone receptors, besides the size of lesions and also response to systemic therapy (as chemotherapy as hormone/target therapy) [1-6]. More recently, Temukai, *et al.* [7] have shown a case report where patient has presented long-term survival (seven years) after aggressive HER2-directed chemotherapy and hepatic resection. Could we say that these biomarkers are more important to select patients for HR than the classic prognostic factors? This question needs to be also answered in order to further select the candidates for multimodal treatment with systemic therapy and HR.

In parallel, over the last years, a great scientific knowledge on this topic has been largely published in regarding LMCR. Nowadays, genetic signature of the CRC has been important to delineate a specific treatment. At same time HR for LMCR has presented a great evolution even for synchronous lesions. The new principle of the “liver-first approach” have presented a very good results to the patients in which present partial response to the initial chemotherapy [8,9].

Since that a massive hepatic disease generally causes death of the patient, the main principle of the “liver-first approach” is can offer an adequate patient selection in regarding the surgical resection. This way, patients that present adequate response to the initial chemotherapy may benefit from resection of hepatic metastases. Thus, the hepatic disease is initially treated by means systemic therapy (when primary CRC is uncomplicated) following HR. Once hepatic control of the metastatic disease was observed, the primary tumor can be finally treated by means of surgical resection. Long-term results of this “reverse approach” seems similar to classic approach [8,9,11]. In our view point, perhaps this principle of the reverse approach can be extended to other very responsive primary tumors besides CRC, especially for those that present an excellent response to upfront systemic therapy like we observed in the present case. Since that we have observed an excellent response after neoadjuvant systemic treatment and this patient was very fit, we have purposed “liver-first approach” for this case. Indeed, we have considered a wise choice because this patient has presented a long-term survival. To our knowledge, this present case was the first successful reported case of “reverse approach” for treatment of LMBC. Furthermore, in this case, as described by Temukai, *et al.* [7], our patient has presented a very favourable prognostic factor that was positive HER2 receptor. In addition, the complete histological response in the liver can also have contributed to long-term survival. In our viewpoint, this long-term result seems to signalize us that this new strategy may be also used in very selected cases of LMBC. Young fit patients with both good initial response to multimodal treatment and very favourable biomarkers can be selected for this approach.

Conclusion

Reverse approach for LMBC by means chemo-targeted therapy associated a HR may lead a long-term survival in selected cases as we have observed in this report. In fact, new studies must be performed to answer if this strategy can be validated.

Conflicts of Interest

None.

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