

Reverse surgery (“first-liver approach”) for hepatic metastases from breast cancer

Abstract

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

Case report: We report a case of LMBC in young female who has undergone successful “first liver approach” after partial response to systemic therapy. At first, it was performed 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 months after hepatic resection, she is alive without any recurrence.

Keywords: breast cancer, hepatic neoplasms/surgery, liver/surgery, hepatectomy

Volume 9 Issue 3 - 2018

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Received: Mar 26, 2018 | **Published:** June 05, 2018

Introduction

Hepatic resection (HR) for liver metastasis of breast cancer (LMBC) has been a very studied topic over last years. Recent series has shown that HR for LMBC can lead long-term survival for many patients, especially those who are considered responders 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 very selected situations.¹⁻⁸

Recently, “first-liver approach” or reverse surgery has been extensively studied for treatment of synchronous liver metastasis of colorectal cancer (LMCRC). Long-term results may be similar to those observed when is performed the classical approach.⁹⁻¹¹ However for other primaries beside CRC, this approach is little studied in the literature. Nonetheless, in our point of view, reverse approach can be also used in other very chemo-responsive primaries besides LMCRC as LMBC. Present authors report a case of synchronous bilateral LMBC that was successfully submitted a reverse approach after systemic response and she has presented long survival (30 months) without recurrence.

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 6,0X5cm 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-fluorogluco in the right breast besides right axillary lymph nodes and bilateral liver lesions. These hepatic lesions were small among 0,5 to 2,5cm. 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 “first-liver approach” because it was 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 of the same initial scheme (except carboplatin). There was maintenance of the response in primary tumor and she was finally submitted to radical mastectomy with selective axillary lymphadenectomy. Pathological evaluation evidenced absence of microscopic residual tumor (complete pathological response). Since that time she is receiving only both trastuzumab and pertuzumab. To date, thirty months after hepatic resection, she is alive without any recurrence (Figure 2–PET-Scan). She presents a very good quality of her life.

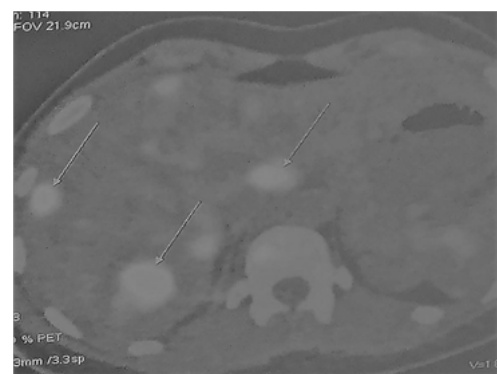


Figure 1 PET-Scan after initial treatment –bilateral hepatic metastases.

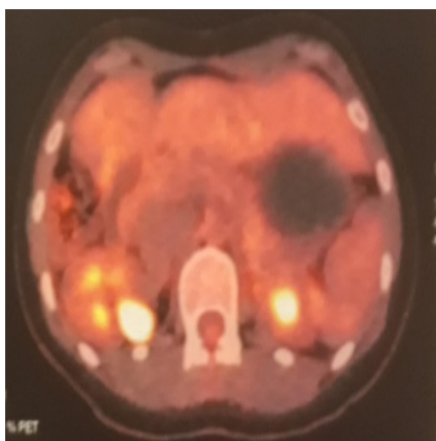


Figure 2 PET-scan—thirty months after hepatic resection of bilateral hepatic metastasis.

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. For these patients with disease exclusively confined to the liver, the HR can be an alternative very interesting because can lead to prolonged survival. Recent studies have observed between 36 and 58% of 5-year survival rates.¹⁻⁴ These results seem similar the most recent series published by our team for the surgical treatment of LMCR.¹²

Since for LMBC that were treated by means HR, long term survival or even cure can be attained. Ercolani et al.,¹ in a large Italian series have observed 8,9% of 10-year survival rates without recurrence. As BC is usually very sensitive neoplasm to both chemotherapy and target therapy, the resection of LMBC after systemic treatment seems to play an important role in the removal of clones which can be resistant to cytotoxic treatment. This aggressive approach can lead to long-term survival 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 liver metastases. This strategy has been designated as "adjuvant surgical debulking" when LMBC are resected by means hepatectomy after systemic therapy.¹⁻⁶ Nowadays this approach has been widespread in oncological scenario around the world. However, many questions still need to be answered, for example: How should we choose or even select the patients who can present a true benefit with an aggressive surgical treatment of LMBC? Better knowledge of the prognostic factors can help in the adequate selection of those cases that can benefit from surgical resection. Many prognostic factors (PG) have been studied in this particular scenario in order to select LMBC candidates to HR. The more important PG for LMBC that have been described in the literature are: both number and diameter of lesions, extra-hepatic disease, disease-free survival time between primary lesion treatment and development of liver metastasis, preoperative chemotherapy, response to chemotherapy, microscopic margins, microscopic vascular or lymphatic invasion, hormone receptors (ER and PgR) and more recently receptor of HER2.¹⁻⁸ These PG have been shown as significant to attain a long-term survival.¹⁻⁸

Currently, new biological prognostic factors have been largely

studied in relation to BC, especially those designated as biomarkers. Both markers of immunohistochemistry and molecular biology have been useful instruments to choose good candidates for liver resection.¹⁻⁸ Thus, it seems that the most important have been hormone receptors, besides the size of lesions and the response to systemic therapy (as chemotherapy as hormone/target therapy).¹⁻⁷

More recently, Temukai et al.⁸ 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 biomarkers are more important to select patients for HR than the classic prognostic factors? This question needs to be answered in order to further select the candidates for multimodal treatment with systemic therapy and HR.

In the last decade, a great knowledge on this topic has been produced mainly for treatment of LMCR. Nowadays, genetic signature of the CRC has been important to delineate your specific treatment. At same time HR for LMCR has presented a great evolution even for synchronous lesions. The new principle of "first-liver approach" have presented a good results to the patients that have presented partial response to initial chemotherapy.^{4,5} Since massive hepatic disease generally causes death of patient, main principle of "First-Liver Approach" can offer adequate selection to surgical resection of LMCR for patients who present partial response to initial systemic therapy. Thus, the hepatic disease is initially treated by means systemic therapy (when primary CRC is uncomplicated) following HR of LMCR. Once hepatic control of the metastatic disease was observed, the primary tumor can finally be treated by means surgical resection. Long-term results of this "reverse approach" seem similar to classic approach.^{4,5} Although laparoscopic approach has been our preferential via to treat liver metastasis, we have disagreed in treating bilateral hepatic lesions by means this specific approach.¹² To our knowledge, this patient was the first reported case of "reverse approach" for treatment of LMBC. Perhaps this principle can also be used in other primary tumors besides CRC, especially for those that present a good response to upfront systemic therapy as BC. Furthermore, in this case, as described by Temukai et al.,⁸ our patient has presented a very favorable prognostic factor as positive HER2 receptor. In our viewpoint, this long-term result seems to signalize us that this new strategy can be also used in very selected cases of LMBC. Young fit patients with both good initial response to multimodal treatment and very favorable biomarkers can be selected for this approach. In fact, new studies must be performed to answer if this strategy can be validated.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

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