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Case Report Open Access

Complete Response in Patient with Metastatic Breast Cancer Treated with Metronomic Chemotherapy

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Abstract

Background: Here we report a case of complete response in patient with Metastatic Breast Cancer treated by metronomic Chemotherapy.

Case presentation: A 51 years old woman underwent righy mastectomy in may 2008. She performed first-line chemotherapy with doxorubicin every 21 days. The CT revaluation after ten cycle showed a partial response to treatment. It was decided to stop the treatment with doxorubicin and to start a metronomic therapy with cyclophosphamide 50 mg daily orally and Methotrexate 2.5 mg twice daily. After two months of this maintenance treatment, the CT scan showed a complete response.

The metronomic treatment is still ongoing, and after 45 months the patient maintains a complete response.

Conclusion: This clinical case also highlights how suitable metronomic chemotherapy can be as maintenance therapy, allowing long-term treatment with no relevant toxicity.

Keywords: Long term complete response; Metronomic chemotherapy; Breast cancer

Background

Low doses of methotrexate (M) have been shown to inhibit endothelial cell proliferation in vitro, as well as neovascularization induced by vascular endothelial growth factor in the rabbit cornea assay *in vivo* [1].

A metronomic administration of cyclophosphamide (C) in mouse models has been shown to inhibit the growth of tumors whose cells had developed resistance against the same drug administered with the conventional schedule. In this experimental model, the apoptosis of vascular endothelial cells preceded that of tumor cells, thus implying an action primarily on tumor vasculature [2].

Two clinical studies have shown that the metronomic administration of low doses of C and M can induce tumor regression in about 20% of patients with advanced breast cancer, with an overall clinical benefit (objective responses or stable disease lasting at least 24 weeks) of 30-40% [3,4]. The percentage of complete responses is about 3%. In both studies, the therapy was well tolerated.

Case Presentation

A 51 years old woman underwent right mastectomy in may 2008. Histological examination showed a ductal carcinoma Stage IIIA, pT3 pN2a Mx.

After mastectomy the ultrasound of the abdomen showed a hypoechoic round lesion of the sixth hepatic segment. The presence of liver metastases was confirmed by a CT scan (Figure 1A) and a PET (Figure 1B). The lesion measured 20 mm. She performed first-line chemotherapy with doxorubicin, for a total of 10 cycles. The CT revaluation after the sixth cycle showed a partial response to treatment. The lesion measured 6 mm (Figure 1C).

In view of the response obtained and the number of cycles performed, it was decided to stop the treatment with doxorubicin and to start a metronomic therapy with cyclophosphamide 50 mg daily orally and Methotrexate 2.5 mg twice daily, two days a week (Monday and Tuesday).

After 2 months of this maintenance treatment, the CT scan showed a complete response (Figure 1D).

The metronomic treatment is still ongoing, and after 45 months the patient maintains a complete response (Figure 1E), with no side effects.

Conclusions

Currently, treatment of metastatic breast cancer is essentially palliative, and is chosen depending on the hormonal receptor status and the presence or absence of amplification of HER2. For triple negative tumors, the therapeutic choices are currently limited to chemotherapy and bevacizumab.

The value of maintenance therapy, administered to patients who did not experience disease progression after a line of systemic treatment, is still debated, although a meta-analysis showed that longer first-line chemotherapy duration is associated with marginally longer overall survival and a substantially longer progression-free survival [3].

Metronomic chemotherapy has the potential to fulfill these requirements in a number of clinical conditions, and is suitable also for patients with triple negative breast cancers, who lack specific targeted therapies. The concept of metronomic delivery of chemotherapy has become relevant for the treatment of different types of cancer, among which breast cancer, prostate cancer [4], sarcomas [5] and melanoma [6]. Its effective use would be fostered by surrogate markers of antiangiogenic activity and predictors of response.

Among the first, measurement of circulating endothelial progenitor cells in peripheral blood is the more promising [7]. Another potential

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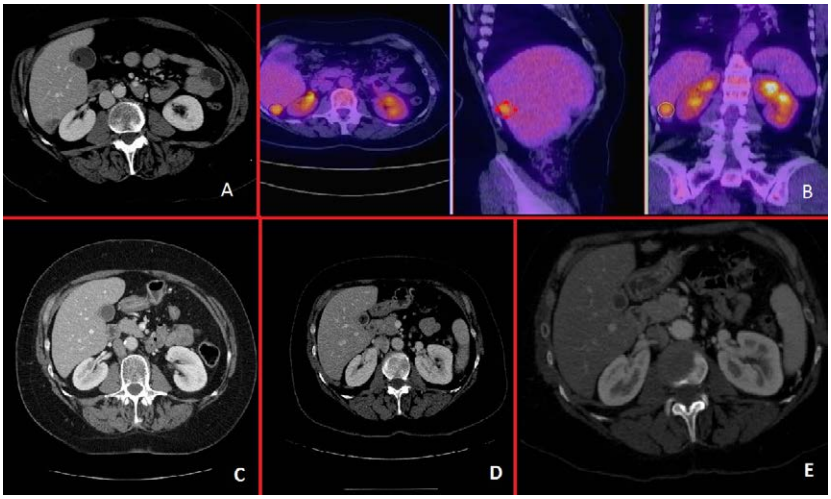

Figure 1: A) CT and
1B) PET scans confirm presence of liver metastasis (20 mm).
1C) CT re-evaluation after the sixth cycle showed a partial response to treatment, with the lesion measuring 6 mm.
1D) CT scan performed after 6 months of maintenance therapy showed a complete response.
1E) CT scan after 60 months of maintenance treatment confirmed the continued complete response.

marker is thrombospondin-1 (TSP-1), which is up-regulated by low dose metronomic cyclophosphamide [8], inhibiting endothelial cell proliferation and survival. Clinical studies of metronomic chemotherapy have shown reduction of serum VEGF levels, more evident in responders but present also in non-responder , although its clinical relevance and the contribution of platelet-derived VEGF remains unknown. The durable complete response to metronomic chemotherapy in our patient highlights the importance to assess potential predictors of benefit from this treatment, and suggests further study of VEGF at this regard.

This clinical case also highlights how suitable metronomic chemotherapy can be as maintenance therapy, allowing long-term treatment with no relevant toxicity.

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