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Long survival with metronomic therapy for heavily pretreated advanced gastric cancer: case report

Abstract

A 79-year-old patient with metastatic gastric cancer who failed with two previous lines of chemotherapy has for the last 9months received third-line chemotherapy with oral cyclophosphamide. This has resulted in an extraordinary long-term progression-free survival of 11months. Toxicity has been low and well tolerated. Oral cyclophosphamide seems to be potentially active agent for salvage chemotherapy in gastric carcinoma patients who failed with prior lines of chemotherapy.

Keywords: gastric, cancer, metastatic, oral cyclophosphamide

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Introduction

We present an interesting case of disease control under metronomic chemotherapy for heavily pretreated metastatic gastric cancer.

Case report

A 79Year old man with complaint of abdominal pain was diagnosed with an advanced gastric cancer in December 2009. The patient had no significant co morbidities. Upper GI endoscopy revealed a mass in gastric antrum. The biopsy was in favor of well differentiated adenocarcinoma. The total body computed tomography (CT) showed multiples liver metastasis and abdominal lymph nodes in addition to the gastric mass. The performance status was good (PS=1). The patient was, also, screened using G8 scale and the score was good (15/17). Routine Palliative chemotherapy was indicated. The patient received irinotecan (240mg/m^2 on day 1) plus capecitabine (1800mg/m^2 for 14days) this protocol was repeated every 3 weeks. The treatment was well tolerated. Only grade 1 diarrhea was occurred. The evaluation by CT scan after the third cycle showed a stable disease according the Recist criteria. Unfortunately, after the sixth cycle the disease was progressive especially in the liver.

According the new data concerning the anti-HER therapy in gastric cancer, the testing of HER was done. The HER2NEU testing was positive in immunochemistry (3+). The patient received as second line treatment consisting in association between trastuzumab (8mg/kg then 6mg/kg on day 1), oxaliplatine (130mg/m^2 on day 1) and capecitabine (2000mg/m^2 for 14days) this protocol was repeated every 3weeks. The tolerance of Oxaliplatine was very bad with grade 3 neuropathy. The evaluation after 3 and 6cycle showed a stable disease. Oxaliplatine was stopped and the patient received trastuzumab and capecitabine in maintenance. Three months later, the disease was progressive on CT-scan. Despite a long discussion with him, the patient refused intravenous third line chemotherapy.

In august 2011, according the fact that the performance status was still good, the patient received oral cyclophosphamide (50mg per day for 20days in 30days cycle). The evaluation by CT scan was done every 3months. The disease was stable for 11months. During this chemotherapy, no significant side-effects were observed. After this period, the liver metastasis and abdominal lymph nodes grown quickly and the patient died from his disease.

Discussion

Metastatic gastric cancer remains an incurable disease, with median overall survival less than 12months in general.[1] Since the publication of Toga study, the association between trastuzumab (Monoclonal antibody targeting the HER protein) and fluoropyrimidin based chemotherapy is the gold standard treatment for advanced gastric cancer with over expression of HER.[2] In second line for fit patient, irinotecan, paclitaxel or docetaxel are a treatment options.[3–7] The antiangiogenic targeted therapies are promising. Two of them the ramucirumab and afatinib showed a survival benefit in refractory metastatic gastric cancer.[8] In our context in 2013, patients with metastatic gastric after second-line chemotherapy have no treatment options other than best supportive care.

The therapeutic concept of administering agents continuously at lower doses is known as “metronomic therapy” (MT). Several studies have shown that low-dose cyclophosphamide had an immune stimulatory effect by the induction of dendritic cell maturation and the increase in tumour associated NK cells and macrophages. Some authors discussed also the anti-angiogenic of metronomic chemotherapy but this point remains controversial.[9] For our patient, oral cyclophosphamide permitted tumor control for at approximatively 11months. No serious adverse events occurred. To the best of our knowledge, no published reports have reported the efficacy of cyclophosphamide in gastric cancer.

Conclusion

This case report constitutes a potentially important window, indicating a potential role for the metronomic therapy in the treatment of heavily pretreated gastric cancer.

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None.

Conflict of interest

The author declares no conflict of interest.

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