Feasibility of capecitabine monotherapy in a taxane refractory metastatic breast cancer patient: A rural cancer hospital experience

Vivek Tiwari, Piyush Shukla, Gourav Gupta

Department of Radiation Oncology, MIMS, village Mirpur, Rewari (HR) INDIA
Department of Radiation Oncology, AIIMS, Delhi
Department of Radiation Oncology, RGCI & RC, Delhi

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ABSTRACT

To manage a metastatic cancer patient in a rural setting is a daunting task owing to the lack of resources and infrastructure. Intravenous chemotherapy (CT), with its debilitating side effects often causes a decrease in the quality of life (QOL) of the patient. When the treatment is of palliative intent, efforts should be made to provide maximum symptom relief to the patient striking a balance between the patient’s wishes and a sound scientific rationale. We describe our experience with a patient with extensively metastatic breast cancer treated in our rural center with single agent oral capecitabine, without development of any severe toxicity and with a significant improvement in disease process and patient’s performance status (PS).

Keywords: Capecitabine, metastatic breast cancer, rural.

Key Messages: Even in face of lack of desired infrastructure, efforts should be made to maximize the available resources. Malignant cancers where the intent of treatment is palliative should be dealt with by striking a fine balance between the patient factors and a sound scientific rationale.

INTRODUCTION

The widening economic, regional and gender disparities in India are posing challenges for the health sector. About 75% of health infrastructure, medical man power and other health resources are concentrated in urban areas where 27% of the population.[1] Breast cancer is the most common malignancy worldwide among women attributed to various genetic and environmental factors. In India it constitutes 22.2% of all cancers with approximately 115,000 incident cases reported in 2008. The several fold difference in incidence rates between different geographical regions suggest that environmental factors influence breast cancer risk significantly.[2] The situation in rural settings is worse in the face of this increasing trend, owing to lack of proper medical facilities.

Liver metastasis occurs in over 50% of patients suffering from breast cancer, and such patients show poor survival.[3] The purpose of treatment for metastatic breast cancer is to maintain a favourable QOL, as well as to improve survival.[3] In palliative care, CT is as useful as watchful waiting.[4] However, when prescribing CT for palliative treatment, an important consideration is whether chemotherapeutic agents should be administered on a daily basis.[4] That the patient's age and wishes and the expected survival gain from treatment are factors that influence
Generally, because PS is associated with poor prognosis, oncologists are reluctant to administer CT to patients with poor PS. We report a case of a 63 year old female who presented to our rural cancer hospital, with a proven case of carcinoma breast metastatic to brain, bones, left axilla, left supraclavicular region and liver, showing progression after taxane based CT. The patient was treated in our institute with single agent capecitabine. As per patient’s insistence of avoiding any sort of in-patient procedure and injectable CT, single agent oral capecitabine was administered to the patient for three cycles and showed a significant response to the treatment.

**CASE HISTORY**

**Patient characteristics and chief complaints**

The patient was a 63 year old female with metastatic breast cancer who visited our hospital after undergoing a prolonged course of treatment for the same. The patient presented with the chief complaints of pain abdomen, pain left chest wall, anorexia, occasional headaches and generalized weakness. The patient had a poor general condition (GC) with a Eastern Cooperative Oncology Group (ECOG) PS four at presentation.

**History of presenting illness**

The patient was diagnosed with invasive ductal carcinoma of the left breast in March 2008. At presentation the clinical staging was T3N1M0. The patient underwent three cycles of neoadjuvant CT with cyclophosphamide, Adriamycin and 5-Flourouracil (CAF) based regimen. Subsequently, the patient underwent left modified radical mastectomy (MRM) in June 2008 followed by three cycles of adjuvant CAF CT till September 2008. Unfortunately, the surgical pathology was not presented to us, and no comment can be made on the same. No radiotherapy (RT) was administered, reasons being unknown. The patient was on hormonal therapy with tablet Tamoxifen 20 milligrams (mg) per day from September 2008 to September 2011. The patient developed recurrence in September 2011 with bone metastasis. She underwent six cycles of Docetaxel and Epirubicin based CT till November 2011. The patient had an episode of Generalised Tonic Clonic (GTC) seizure in March 2012, Magnetic Resonance Imaging (MRI) of brain being suggestive of left frontal lobe space occupying lesion (SOL) with multiple calvarial metastasis. The patient received palliative RT to whole brain to a dose of 30 Gray in ten fractions till April 2012. A whole body (WB) 18-F deoxyglucose (18 FDG) positron emission tomography-computerised tomography (PET-CT) scan performed in June for response assessment showed a new finding of a hyper metabolic hypo dense lesion appearing in the segment six of liver suggesting overall disease progression. (Figure 1) [June 2012 PET image showing 18FDG avid lesions in the liver (see arrow)].

**Course**

The patient presented to our rural cancer hospital in June 2012. At presentation, the patient was in a poor GC with a ECOG PS of 4. The patient had complaints of pain abdomen, pain left chest wall, occasional headaches, anorexia and generalized weakness. Given the presenting condition, history, and the fact that the patient had progressed despite a full course of Taxane based CT, we predicted a poor prognosis and conveyed the same to the patient’s relatives while opining as to the possible next line palliative chemotherapy. However, the patient, and the relatives were not in favour of any injectable chemotherapy or any treatment which would require an admission to the hospital. They were then given the option of single agent capecitabine to which they agreed. Thereafter we prescribed single agent capecitabine (1250 mg/m2per oral twice daily). The cycle of the treatment was two weeks daily administration followed by a one week rest period. Significant improvements were seen after the first course with respect to the reduction in pain abdomen, and
general well-being. The patient's appetite improved and she improved to a better GC. After 3 courses, a WB PET-CT was performed which showed complete resolution of the liver lesion, (Figure 2) [Post 3 cycles capecitabine PET image showing complete resolution of the liver lesions] decrease in the size and 18FDG avidity of left axillary and supraclavicular lymphadenopathy. The brain lesion and the skeletal metastasis were essentially unchanged. Patient did not complain of any serious adverse effect to the treatment. The PS of the patient improved from 4 to 1. Patient is being continued with the same treatment and is tolerating well.

**DISCUSSION**

5-fluorouracil (5-FU) is widely used in the treatment of cancer. Over the past 20 years, increased understanding of the mechanism of action of 5-FU has led to the development of strategies that increase its anticancer activity. Despite these advances, drug resistance remains a significant limitation to the clinical use of 5-FU. Emerging technologies, such as DNA microarray profiling, have the potential to identify novel genes that are involved in mediating resistance to 5-FU. Such target genes might prove to be therapeutically valuable as new targets for chemotherapy, or as predictive biomarkers of response to 5-FU-based chemotherapy.[5] Capecitabine is an oral prodrug that is converted to its only active metabolite, FU, by thymidine phosphorylase. Higher levels of this enzyme are found in several tumours and the liver, compared with normal healthy tissue. Capecitabine is currently approved by the FDA for use as first-line therapy in patients with metastatic colorectal cancer when single-agent fluoropyrimidine therapy is preferred. The drug is also approved for use as (1) a single agent in metastatic breast cancer patients who are resistant to both anthracycline- and paclitaxel-based regimens or in whom further anthracycline treatment is contra indicated and (2) in combination with docetaxel after failure of prior anthracycline-based chemotherapy. Single-agent and combination regimens have also shown benefits in patients with prostate, pancreatic, renal cell, and ovarian cancers.[6]

Capecitabine is active, well tolerated and improves the QOL of patients with anthracycline- and taxane-pretreated metastatic breast cancer. Based on the consistently high activity demonstrated in clinical trials, capecitabine has become the reference treatment in this setting.[8]

Single-agent capecitabine has been shown to be an effective, safe, cost-effective agent that provides superior QOL for previously treated patients with metastatic breast cancer. Capecitabine continues to develop as an important chemotherapeutic agent for the treatment of breast cancer.[9]

**CONCLUSIONS**

This case shows that monotherapy with single agent capecitabine proved significantly effective in resolving the patient's metastatic liver lesions, and caused decrease in the size and FDG avidity of left axillary and supraclavicular lymphadenopathy, whereas the metastatic lesions in the brain, skeleton and breast showed no progression at all. It is suggested that single agent capecitabine may be used to attain desirable and acceptable effects and should be used as a feasible option in palliative management of elderly metastatic breast patients, especially in the rural settings that are devoid of definitive infrastructure and facilities.

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Mirpur Institute of Medical Sciences, village Mirpur, Rewari.

REFERENCES