Oral Treatments in the Patients with Metastatic Breast Cancer - A Case Series

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Abstract   Breast cancer is one of the most common malignant diagnostic tumors among women and is considered as the second leading cause of mortality in them. Numerous approaches could be recruited for breast cancer management such as surgery, radiation therapy, endocrine, and chemotherapy. In past years, oncologists have prescribed intravenous anticancer drugs for many patients, but nowadays the issue of treatment has changed with the increasing use of oral anticancer drugs. Previous studies have shown that most patients prefer to take oral anticancer drugs and their main reason for this choice is the accessibility of home-based treatment. The objective of this issue was to evaluate the effects of oral therapy regimens such as palbociclib (Ibrance) in combination with aromatase inhibitors in patients with metastatic breast cancer. Our new remedies in the oral therapy field in 2 patients lead to control the progress of malignancy.

Keywords: breast cancer, oral therapy, palbociclib, ibrance

1. Introduction

Breast cancer is one of the most common malignant diagnostic tumors among women and is considered as the second leading cause of mortality in them [1]. It is a heterogeneous disease with clinical manifestations and various staging [2]. Therefore, determining the pattern of gene expression and accurately classifying of breast tumors is required to choose the appropriated therapeutic strategies [3]. Several approaches could be recruited for breast cancer management such as surgery, radiation therapy, endocrine and chemotherapy [4]. Endocrine therapy is considered as a major treatment for the expression of estrogen receptor (ER)-α, which accounts for around 70 % of all malignant neoplasms of the breast [5]. Roughly, 10-15% of patients have an aggressive malignant form of the breast cancer and tumor mass may involve distant sites such as bone and soft tissues including lung, liver, etc. It sounds that the stage IV of a breast cancer is an incurable and metastatic subtype, so all of the therapeutic approaches should be used to increase the survival rates [1,6]. Practically, the variable characteristics of breast cancer metastasis makes it difficult to determine assorted cure [7]. Nonetheless, the percentage of metastatic and mortality is declined due to the implementation of systemic adjuvant therapy [3]. In previous years, oncologists prescribed intravenous (IV) anticancer drugs to many patients but, in recent years, the issue of treatment has changed with increasing use of oral anticancer drugs [8]. Indeed, implementation of IV regimes for conventional anticancer chemotherapy and other kinds of therapy could have numerous disadvantages for the patients such as fear of needle-stick injuries and increased costs [9]. Most patients prefer oral anticancer drugs and the first reason for this choice is the accessibility of home-based treatment [10]. We report three patients with developed breast cancer and treatments that have been effective for them.

2. Case Presentation 1

A 37-year-old woman with a suspicious mammography referred to the Kermanshah Hematology and Oncology Clinic in February 2014. After a physical examination of the patient and investigating the results of mammography, the physician asked for biopsy from the right breast and the axillary lymph nodes. The pathological report indicated an increase in cellularity along with evidence from atypical cells in the breast tissue and axillary region. Also, the results of supplementary tests such as Immunohistochemistry and FISH were as follows: Estrogen Receptor (ER), Progesterone Receptor (PR), P53 and Ki67 were positive but HER2 (c-erbB2) was negative. According to these results, the final diagnosis of her disease was infiltrated/invasive ductal carcinoma (IDC) with stage IIB. Also, the results of internal ultrasound and left breast mammograms and blood tests were normal. Therefore, treatments such as mastectomy, lymphadenectomy and radiotherapy (25 sessions) were performed for her. During this time, the patient was under combination

chemotherapy including paclitaxel with epirubicin for 6 courses. After completing this course, the patient was treated with oral Tamoxifen for one year. In December 2015, her bone scan results revealed a metastasis to the left side of the skull and vertebral column. Following this, cytotoxic combination therapies including Ibarnce orally (125 mg) along with Letrozole (2.5 mg) orally were performed and still continues. During this period, the patient's condition is satisfactory and disease progression has stopped.

3. Case Presentation 2

The patient, who was a 45-year-old woman, was admitted to the clinic with a feeling a palpable mass in her right breast in December 2010. Initial clinical examinations and mammography results confirmed the presence of the mass, therefore, the request for supplementary tests such as biopsy of right breast tissue and lymph nodes of the axillary region and immunohistochemistry were given. The results of biopsy showed that there was a mass with the diameter of more than 5 cm in right breast with the involvement of one of the axillary lymph nodes. Immunohistochemistry results indicated that HER2 was negative and that other markers were positive. According to the results, the diagnosis was IDC of the breast with lymph node involvement in stage IIIA. With the advice of the physician, the patient decided to have a right breast mastectomy followed by 25 radiotherapy sessions. Subsequently, an adjuvant chemotherapy with TAC (docetaxel/doxorubicin/cyclophosphamide), was administered for 8 courses. After the completion of this course, the patient's treatment continued with Gemcitabine and Tamoxifen, which at this time, the bone scan, abdominal and pelvic ultrasound, and left mammograms were normal. In present, because of metastases to the bones, since November 2013 the patient is undergoing combination therapy including Ibrance plus Exemestane and Capecitabine and the therapeutic response is promising.

4. Case Presentation 3

Our third patient was a 38-year-old woman referred to the clinic in March 2011. After doing a series of experiments the physician requested a biopsy of the breast tissue and the axillary region. The pathological report of the biopsy revealed a fibrotic mass in her left breast with the involvement of several lymph nodes in the axillary region. Based on the immunohistochemistry (IHC) findings below, the definitive diagnosis was IDC with stage IIIB. ER, PR and Ki67: positive, but HER2: negative. Hence the patient was subjected to mastectomy and lymphadenectomy and 16 sessions of radiotherapy. The ultrasound results of the internal organs and bone scan were normal and the patient was under TAC chemotherapy which is known as an adjuvant treatment. Then the patient's treatment continued with of hormonal therapy plus Bevacizumab. In December 2013, the liver ultrasound revealed a liver metastasis with nodules with a diameter of 9 mm. Accordingly, treatment with Letrozole

and Ibrance were used for the patient, and at the moment her condition is relatively stable.

5. Discussion

Breast cancer is a neoplastic malignant disease that is widespread among women worldwide and its annual incidence is over 1.3 million, in other words, it accounts for more than 23% of all cancers [11]. About half of women with breast cancer are diagnosed with metastases, and the average survival time for these patients varies from 18 to 30 months depending on the involved organ [12]. Despite many advances in breast cancer, unfortunately, breast cancer is still widespread in many communities and has limited therapeutic options, so that some patients will eventually become resistant to these treatments. Hence, the development of new therapies such as new targeted therapies, which is considered very important [13]. Recent studies in the field of mechanisms that affect the resistance to treatment for breast cancer patients have shown that some of the important signalling pathways, such as phosphatidylinositol 3-kinase/mammalian target of rapamycin (PI3K/mTOR) and Cyclin D–CDKs–retinoblastoma (Rb) are involved in this issue [14]. These pathways play a role in regulating processes such as cell division and proliferation, so any gene alteration or phosphorylation of the ER that causes excessive proliferation of cells, results in metastasis and resistance to treatment [14,15]. Metastatic Breast Cancer (MBC), commonly known as stage IV breast cancer, is the most common cause of death (90%) due to cancer, which is also due to its untreatable nature [13]. About two-thirds of patients with metastatic breast cancer have increased their hormonal receptors (HR+) [16]. The average overall survival rate for MBC patients is usually between 2 and 3 years from the time of diagnosis [17]. Conventional chemotherapy is a combination of Complex regimes that are consumed intravenously, and greatly affects the lives of patients by creating severe complications and a large amount of time spent on treatment and concerns about the risk of transmitted diseases in intravenous therapy [18,19]. Also according to previous studies, Oral chemotherapy treatments have most important in the treatment of metastatic breast cancer. Hence, oral chemotherapy has expanded in recent years. Oral treatments can improve the quality of life of patients, especially in metastatic diseases. Factors that can promote the use of oral treatments include high performance, adequate tolerance, acceptable availability with internal and interpersonal changes, and the use of a limited number of pills/capsules per day [18]. In these patients, average age of cancer detection was 40 years and average age of metastasis was 42 years (mean time between the diagnosis of the disease and the presentation of metastasis was 31 months). The characteristics of all three patients are listed in Table 1. We used oral treatments like Ibrance, Letrozole, Everolimus, Capecitabine and Exemestane along with other treatments. Regarding the patient's condition after taking oral medications and stopping the progression of their breast cancer, it can be concluded that oral treatments can be useful along with other therapies.

Table 1. Patients' characteristics

Characteristics	Patient 1	Patient 2	Patient 3
Age at diagnosis	37	45	38
Type of tumor	Ductal invasive	Ductal invasive	Ductal invasive
Staging	IIB	IIIA	IIIB
Local treatment	Mastectomy lymphadenectomy	Mastectomy	Mastectomy lymphadenectomy
Radiotherapy	+	+	+
First line treatment	Paclitaxel+Epirubicin	Docetaxel+Doxorubicin+Cyclophosphamide	Docetaxel+Carboplatin
Second line treatment	Tamoxifen	Gemcitabine	Gemcitabine
Third line treatment	Not receive	Not receive	Bevacizumab
Immunihistochemical profile	ER/PR/ P53 and Ki67: positive HER2;negative	ER/PR/ P53 and Ki67: positive HER2;negative	ER/PR/ P53 and Ki67: positive HER2;negative
Time to recurrence	December 2015	November 2013	December 2013
Metastasis site	Skull/Vertebral	Bones	Liver
Oral therapy for metastasis	Ibarnce + Letrozole	Ibrance+Exemestane+Capecitabine	Ibarnce + Letrozole
Death	No	No	No
Treatment outcomes	Stop the progression of cancer	Promising	Relatively stable

6. Conclusions

The importance of reviewing this article is from the perspective of oral treatments that have been used after metastasis in patients with breast cancer which have relatively good responses. Also, in comparison with intravenous therapy, this treatment can be helpful in the remedy protocols.

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