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CDK4/6 Inhibitors after Chemotherapy for Patient with HR+ve, HER2-ve Metastatic Breast Cancer Presented with Visceral Crisis: A Case Report

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Abstract

Palbociclib is an oral drug that inhibit cyclin-dependent kinases 4 and 6(CDK4/6) which play a critical role in cell cycle proliferation and regulation, approved in the treatment of hormonal receptor (HR) positive HER2 negative metastatic breast cancer in combination with letrozole in postmenopausal women. In this study, we report a premenopausal woman presented with HR +ve HER2 -ve metastatic breast cancer with visceral crisis. This patient started chemotherapy by paclitaxel for six cycles then shifted to palbociclib and letrozole combination with ovarian suppression by GnRH agonist. Patient tolerated treatment very well and showed marked response at the initial and subsequent assessment without significant treatment related side effects.

Keywords: CDK4/6; Breast cancer; Palbociclib; Visceral crisis; Letrozole

Introduction

Breast cancer is the most common cancer among women and one of the common causes of cancer related mortality especially those with metastatic disease, where the tumor metastasizes to other organs, such as the bone, liver, lung and brain [1,2]. As known, Palbociclib is an oral drug that inhibit cyclin-dependent kinases 4 and 6(CDK4/6) which play a critical role in cell cycle proliferation and regulation [3]. Currently, this drug has been approved in the treatment of advanced hormone receptor (HR) positive and human epidermal growth factor receptor 2 (HER2) negative breast cancer [4]. Nowadays, Palbociclib have acted as star drug for reversing ET resistance with improvement of the prognosis of cases with HR+/ HER2 - ve advanced breast cancer (ABC) [5]. This case report showed the efficacy and tolerability of Palbociclib after chemotherapy in premenopausal woman with advanced breast cancer presented with visceral crisis

Case History

48 ys old female pre-menopausal, married and had 8 offspring's the youngest is 10 years old, she is a teacher, declared no special habits. there is no positive family history, there is no med or surgical history of chronic diseases. She came to ER one year back as a case of breast mass complained from marked SOB, with marked hypoxemia. At this period there was COVID 19 epidemic so pt admitted in isolation room as a case of suspected COVID12 till the results became negative then patient admitted in oncology ward for further investigation and management. In the oncology ward, patient was distressed with de-saturation in room air corrected with O_2 therapy. Breast examination showed diffuse enlargement of Lt breast with ulceration and complete erosion of the nipple. Chest showed bilateral crepitations, CT chest showed multiple bilateral pulmonary variable sizes nodules Q mets. discussion with the patient and her husband regarding the conditions and expected outcome and they agree to go for biopsy and subsequent treatment. True cut biopsy from breast and LNs, showed IDC, grade 2, ER, PR strongly positive, HER2 negative, Ki 67 low, we asked for metastatic workup, CT CAP, bone scan, tumor markers, that revealed multiple scattered bilateral pulmonary nodules mostly metastatic in nature abdomen and pelvis free. Bone diffuse multiple bony mets, tumor markers CA15-3 high. So, the final diagnosis was a pre- menopausal case of HR +ve HER2 –ve met CA breast with visceral crisis.

Case discussed in the tumor board and final decision to go for chemotherapy then according to the response patient will be shifted to further treatment with CDK 4/6 inhibitor + AI+ GnRH agonist. Patient started chemotherapy in the form of paclitaxel 175mg/^{m} every 3 weeks. she received 6 cycles during which there is marked improvement in pulmonary symptoms, after 6 cycles patient shifted to letrozole 2.5 mg OD+ Zoladex 3.6 monthy+ palpociclib 125mg od for 21 Ds then week rest. The initial and subsequent radiological assessment showed marked resolution of previously seen breast mass and pulmonary lesions (Figure 1). Till now patient tolerated treatment very well without any treatment side effects and without any treatment holding or dose reduction.

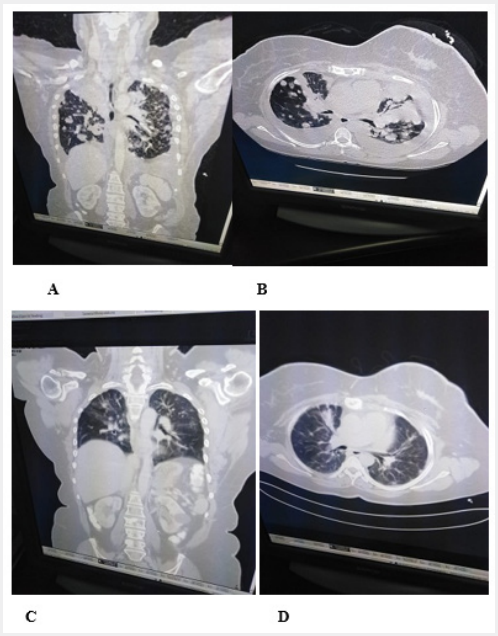

Figure 1: CT chest with contrast, Pre-treatment (A,B) and post treatment (C,D).

Discussion

It is noted that, Palbociclib showed a critical role in cell cycle regulation by phosphorylation of the retinoblastoma protein (Rb) and can inactivate Rb function as a tumor suppressor [6]. Many studies comparing Palbociclib plus aromatase inhibitors (AIs) to AIs alone as first-line therapy for postmenopausal women with ER+/HER2- advanced breast cancer showed improvement in progression-free survival [4,6-8]. It is noted in Turner et al study, endocrine therapy alone showed significant poor response in patients with disease progression on previous exposure to endocrine monotherapy [9]. The outcome from preliminary results of part 1 of a phase II trials showed that palbociclib plus letrozole are superior to letrozole monotherapy in postmenopausal cases and that combination was associated with an improvement in the objective response and disease control rates suggest a benefit in premenopausal women better than AIs combination with capecitabine [10,11]. In our case, palpociclib + letrozole + Gn RH agonist were used as after chemotherapy in a pre-menopausal young patient with metastatic breast cancer and showed marked response after initial assessment and expected to give complete response during continuation of the treatment. The patient in our study tolerated treatment very well without any reported treatment related side effects.

Conclusion

Although all trials of palbociclib used it mainly in postmenopausal cases with HR +ve, HER2-ve advanced breast cancer without visceral crisis, its role in premenopausal state also evidenced, the results of current study strongly support the use of palbociclib with letrozole after chemotherapy for young patient with HR+ve, HER2 -ve advanced breast cancer presented with visceral crisis.

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