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CASE REPORT – OPEN ACCESS

Response and Tolerability of Palbociclib Plus Fulvestrant in Breast Cancer Patient with Bone Marrow Metastasis and Cytopenia: A Case Report

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ABSTRACT

Background: Palbociclib is a potent cyclin-dependent kinase (CDK) 4/6 inhibitor that impairs cell cycle progression. It has recently been approved for patients with hormone receptor positive metastatic breast cancer.

Case Report: We report the response achieved palbociclib plus fulvestrant therapy in a 68-year-old female breast cancer patient with bone marrow metastasis. She treated with paclitaxel weekly chemotherapy, but no response was obtained. Then, with dose reduction palbociclib 75 mg/day, plus fulvestrant treatment was administered. After 6 cycles, thrombocytopenia resolved and the palbociclib dose was increased to 125 mg/day. Cytopenia completely resolved after the eight cycle treatments. She is still going on treatment without progression and side effects.

Conclusion: The efficacy and safety of CDK 4/6 inhibitors in patients with bone marrow metastases have not been clarified. However, palbociclib treatment can be given with close follow-up and dose reduction in breast cancer patients with bone marrow metastasis.

Keywords: Bone marrow metastasis, breast cancer, palbociclib, fulvestrant, CDK 4/6 inhibitors

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INTRODUCTION

Palbociclib is a potent cyclin-dependent kinase (CDK) 4/6 inhibitor that impairs cell cycle progression (1). It has recently been approved for first-line therapy in combination with an aromatase inhibitor or fulvestrant in patients with hormone receptor positive, epidermal growth factor receptor negative (HER2-) metastatic breast cancer. Palbociclib is a drug with neutropenia side effects and dose adjustment may be required if severe neutropenia develops (2). There is insufficient clinical experience in the use of palbociclib in breast cancer patients with bone marrow metastases and cytopenia. Here, we report the response achieved by 8 months of palbociclib plus fulvestrant therapy in a breast cancer patient with bone marrow metastasis and cytopenia.

CASE REPORT

In October 2003, a 68-year-old female patient was diagnosed with Stage 2 left breast infiltrative lobular carcinoma. After she was operated, she received adjuvant cyclophosphamide 600 mg/m^2 plus doxorubicin 60 mg/m^2 plus 5-fluorouracil 600 mg/m^2 combination chemotherapy every 3 weeks for six cycles. In immunohistochemical (IHC) testing of tissue biopsy after surgery, the hormone receptor status was not evaluated due to technical incompetence and the patient did not receive adjuvant hormone therapy, because hormone receptor status was unknown. Subsequently, in October 2015, the patient was diagnosed with Stage 2 right breast infiltrative lobular carcinoma and she was operated. Estrogen receptor (ER) 96% (+), progesterone receptor (PR) 80% (+), and HER2 (–) detected in IHC evaluation. Adjuvant letrozole 2.5 mg/day was given to the postmenopausal patient. After 46 months of use of letrozole 2.5 mg/day in July 2020, thrombocytopenia and anemia were detected in the patient. Hemoglobin (Hgb) value was 8.2 g/dL and platelet (Plt) value was 30 000/µL. Fluoro-18 fluorodeoxyglucose (18-FDG) positron emission tomography/computed tomography (PET/CT) was performed for metastasis screening. In 18-FDG PET/CT, increased moderate hypermetabolism (SUV max: 4.0) of the bone marrow, was detected in the vertebral column (Fig. 1a). Magnetic resonance imaging (MRI) was performed, because bone metastasis was suspected. No bone metastases were detected in MRI (Fig. 1b). Bone marrow biopsy was performed due to unexplained cytopenia and suspicion of bone marrow metastasis. Bone marrow biopsy result was reported as breast carcinoma metastasis with ER 90% (+), PR (–), and HER2 (–). After red blood cell and platelet transfusion, paclitaxel 80 mg/m^2 weekly chemotherapy was started to patient. Before each chemotherapy, red blood cell and platelet transfusion were performed to the patient also neutropenia developed after each chemotherapy administration. No response was obtained with paclitaxel chemotherapy for 7 weeks, cytopenia continued (Hgb: 7 g/dL, Plt: 33 000/µL). In September 2020, with dose reduction

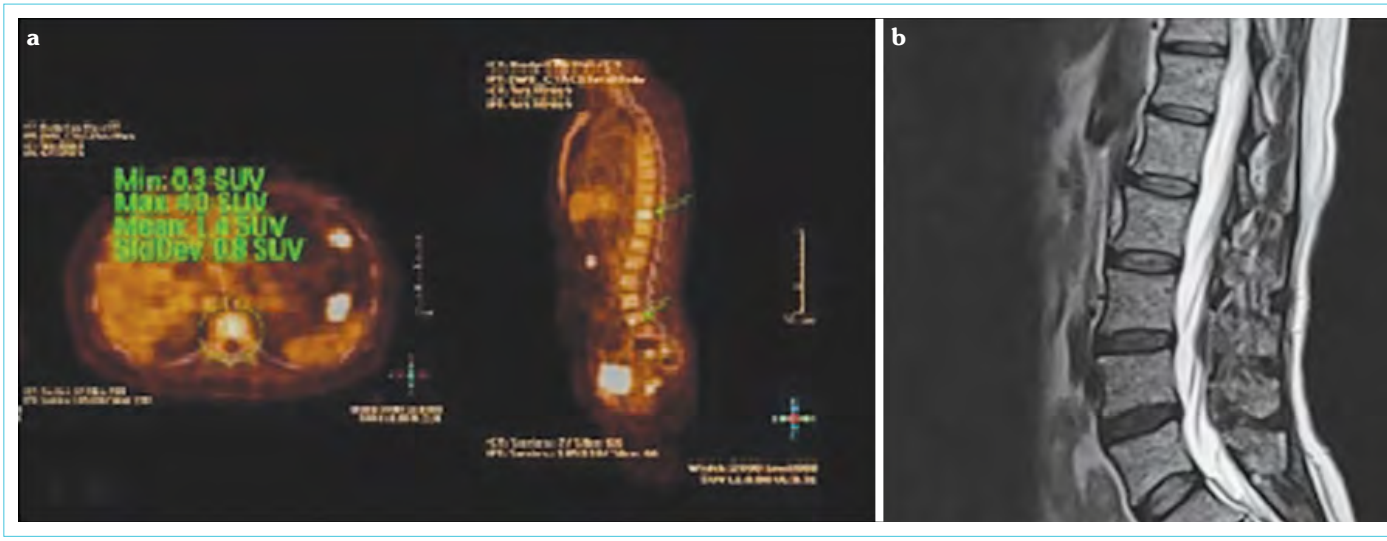

Figure 1. 18-FDG PET/CT with suspected bone and bone marrow metastases (a) and MRI with normal bone structure (b) in July 2020

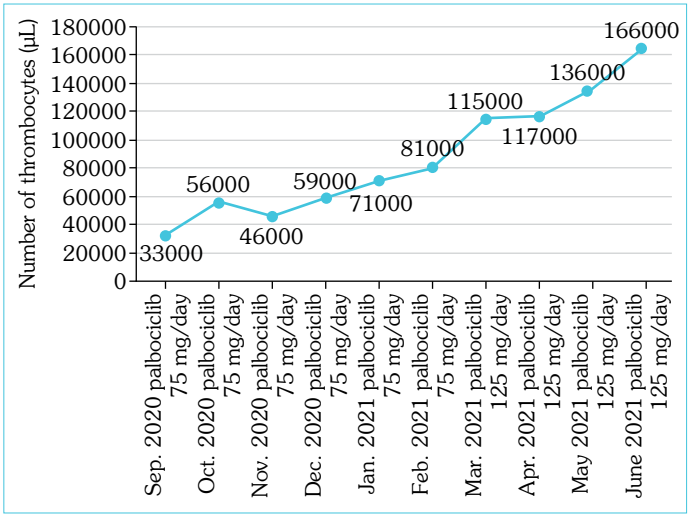

Figure 2. Number of thrombocytes before each palbociclib plus fulvestrant cycle

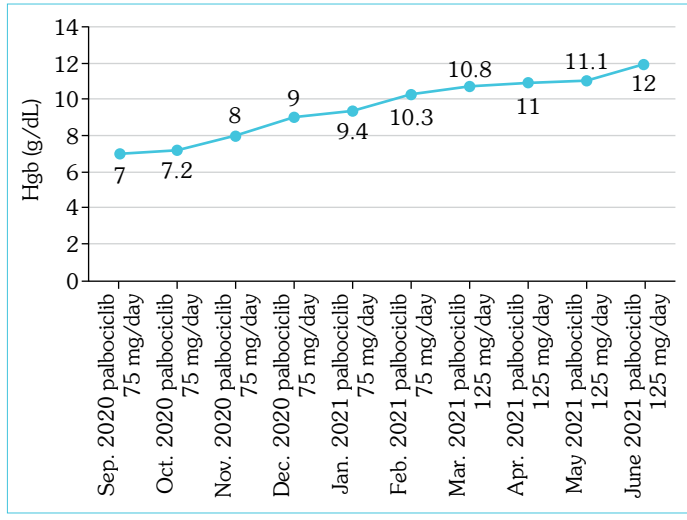

Figure 3. Hemoglobin value before each palbociclib plus fulvestrant cycle

palbociclib 75 mg/day (at a dose of 75 mg, administered orally, once daily for 21 consecutive days, followed by 7 days off, to comprise a complete cycle of 28 days) plus fulvestrant (at a dose of 500 mg, administered as an intramuscular injection according to standard of care, every 14 days for the first three injections and then every 28 days), the treatment was administered. After three cycles of treatment, regression in bicytopenia was observed. During the use of palbociclib plus fulvestrant, the patient did not need transfusion support and the patient's treatment was continued. After six cycles, the patient's thrombocytopenia completely resolved (Plt: 115 000/µL), but Grade 1 anemia (Hgb: 10.8 g/dL) continued. As the patient's thrombocytopenia improved, the palbocycline dose was increased to 125 mg/day. The patient received two additional cycles of palbociclib 125 mg/day plus fulvestrant. In the evaluation after the eight cycle treatments, the blood values were completely recovered Hgb: 12 g/dL, Plt: 166 000/µL). No tolerance problems or side effects were observed in the patient during the treatment.

The thrombocyte values of the patient observed during the treatment are given in Figure 2 and the Hgb values are given in Figure 3. The patient is still on nine cycles of palbociclib 125 mg/day plus fulvestrant without progression. All blood values of the patient are normal and there is no other sign of metastasis.

CONCLUSION

Systemic chemotherapy is usually recommended for patients with bone marrow metastases, but most patients cannot tolerate chemotherapy due to cytopenia (3). Endocrine agents have little myelotoxic effect. However, adequate response may not be obtained due to hormonal resistance and tumor heterogeneity. CDK 4/6 inhibitors plus fulvestrant is a treatment option in patients who develop metastases under adjuvant aromatase inhibitor therapy. The PALOMA-3 study demonstrated the efficacy of fulvestrant plus palbociclib for progression-free survival in metastatic first-line therapy. However, the efficacy and safety of CDK 4/6 inhibitors in patients with bone marrow metastases have not been clarified. Because patients with bone mar-

row metastases are often excluded from clinical trials (2). Abemaciclib is the agent with the lowest myelotoxicity among CDK 4/6 inhibitors (4). However, access to Abemaciclib is not possible in our country. Case series in which a breast cancer patient with bone marrow metastases was treated with palbociclib is limited in the literature. Yamaguchi et al. achieved response with palbociclib plus fulvestrant therapy in a patient with breast cancer with bone marrow metastases (5). Although bicytopenia was present in our case report, we observed that dose reduction and palbociclib plus fulvestrant treatment were effective in our patient. Since most patients with bone marrow metastases cannot tolerate chemotherapy, we think that CDK 4/6 inhibitors can be given to these patients with close follow-up and dose reduction.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – MÖ; Design – EM; Supervision – MÖ; Resource – STF; Materials – RC; Data Collection and/or Processing – EM; Analysis and/or Interpretation – STF; Literature Search – EM; Writing – EM; Critical Reviews – RC.

Conflict of Interest: The authors have no conflict of interest to declare.

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