Palbociclib Efficacy and Safety in Metastatic Breast Cancer with Spinal Cord Compression

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Abstract

Symptomatic Metastatic Spinal Cord Compression (MSCC) in Breast Cancer (BC) is clinically rare. MSCC represents an oncological emergency, thus necessitating prompt diagnosis and early treatment for local and systemic disease control.

Palbociclib, a potent cyclin-dependent kinase 4/6 inhibitor, has been recently approved in combination with Endocrine Therapy (ET) for treatment of hormone-receptor-positive, human epidermal growth factor receptor-negative metastatic BC. There is currently no evidence supporting palbociclib use in MSCC-BC. We report a 36-year-old pregnant woman presenting with a two-month history of middle thoracic back pain and one-week of leg weakness due to MSCC-BC. A prompt diagnosis led to an early caesarean section, followed by neurosurgical decompression plus radiotherapy for local tumor control. Subsequently, further local and systemic tumor control was attained with palbociclib plus ET, without any unexpected side effects.

To the best of our knowledge, this is the first case demonstrating the efficacy and safety of palbociclib in MSCC-BC.

Keywords: Palbociclib; Spinal cord compression; Metastatic breast cancer; Endocrine therapy

Introduction

Metastatic Spinal Cord Compression (MSCC) occurs in 5% to 14% of cancer patients during the disease course and represents an oncological emergency [1,2]. Although Breast Cancer (BC) is one of the most common malignancies to metastasize to the spine with the risk of developing MSCC, the optimal treatment for local and systemic tumor control remains controversial. To date, most recommendations for optimal MSCC treatment are based on studies on various primary malignancies, with limited data on single histological types. Additionally, different therapeutic strategies have been employed for MSCC treatment, including corticosteroids or Radiotherapy (RT) alone in patients with poor prognosis, and a radical multimodal approach, including surgical resection of the tumor metastasis followed by RT in suitable patients. This is based on two meta-analyses that concluded that decompressive surgery followed by RT is associated with improved ambulatory status and survival compared with RT alone in selected patients [3,4].

Selection criteria for surgery include the presence of mechanical instability, uncontrolled pain, neurologic dysfunction, along with patient age and performance status, number of disease sites, primary tumor, and disease-free interval [5].

There is currently no evidence supporting clinical decision making for distant disease control in different histological types [6]. While chemotherapy remains a valid option in highly chemosensitive malignancy, there is less evidence supporting hormonal manipulation in patients with Hormonal-
To the best of our knowledge, there are no data on the efficacy and long-term toxicity profile of CDK 4/6 inhibitors in luminal MSCC-BC.

This report describes the case of a young pregnant woman diagnosed with MSCC-BC, who greatly benefitted from a multidisciplinary approach for local tumor control and is still deriving benefit from the addition of palbociclib-based therapy [9,10].

Case Presentation

In August 2015, an irregular right breast nodule with a maximum diameter of 44 mm and ipsilateral axillary lymph node enlargement was revealed by diagnostic mammography in a 33-year-old woman. Both breast and axillary node biopsies revealed histopathological evidence of grade 2 infiltrating-ductal-carcinoma with HR+ and Human Epidermal growth factor Receptor-2 negative (HER2-) status.

After excluding distant metastasis, standard neoadjuvant chemotherapy based on the sequential use of anthracycline and taxanes was administered with radiographic partial response as the best tumor response. Modified right radical mastectomy with complete homolateral axillary dissection was performed on April 11th, 2016. Histopathological examination revealed residual disease in the breast and axillary nodes, with final stage ypT2 (25 mm) ypN2a, ER 90% PgR 90% Ki67 35% HER2 1+. Adjuvant radiotherapy to the chest wall and supraclavicular space was administered, and adjuvant ET based on ovarian suppression plus 20 mg/day tamoxifen for five years was prescribed. Due to her desire to have children, ET was willingly stopped after 18 months and the patient became pregnant 12 months later. Unfortunately, the patient presented to the emergency ward at 32 weeks of pregnancy, with a progressively increasing thoracic spine pain that started two months previously, and a sudden neurological deficit in the lower limbs (motor weakness and paresthesia). Based on neurological examination and Magnetic Resonance Imaging (MRI), severe spinal MSCC due to the tumor was diagnosed which exhibited circumferential epidural extension and obliteration of cerebrospinal fluid along with a bone fracture at T5 level (Figure 1). In view of the pregnancy, an emergency caesarean section was successfully performed in the 33rd week of pregnancy (May 2nd, 2019). The newborn was in good health and precautionary placed in an incubator for 24 h. After excluding distant metastasis, standard neoadjuvant chemotherapies were administered using a posterior approach through a laminectomy and facetectomy, and a transpedicular approach to free the ventral epidural space. Posterior segmental fixation was accomplished using screw-rod systems, including pedicle screws in the thoracic spine, from T3-4 to T6-7 spine (Figure 2 and 3).

Although the patient was in a poor clinical condition, complicated by the development of bilateral pneumonia and renal tubulopathy postoperatively, which were properly managed, active oncological therapies were recommended. Specifically, two weeks later RT from T4 to T7 was performed with a total dose of 30 Gy divided into 10 fractions, and first-line ET based on ovarian suppression plus 2.5 mg/day letrozole was concurrently prescribed. Due to the risk of cumulative bone marrow toxicity, palbociclib administration was postponed by one week from the end of RT. The patient began 125 mg/day palbociclib for three weeks on and one week off on June 11th, 2019, and systemic therapy with zoledronic acid every 28 days was introduced. Additionally, the patient was discharged home from the...
ward, and since she was still unable to walk independently, motor rehabilitation was recommended. Overall, the systemic therapy was well tolerated and no unexpected side effects were observed. During the first three months of treatment, the patient reported slight hot-flashes and arthralgias, along with dry skin and itching, which were promptly resolved by local therapy. Due to the development of G3 neutropenia on day 1 of the second and third cycles which resolved two weeks later, palbociclib dosage was reduced from 125 mg to 100 mg. By then, the patient’s clinical condition had progressively improved from ECOG 3 to 0 in less than six months, giving back the patient autonomy with regard to motor functions, self-, and baby-care. Currently, the patient is still receiving treatment with palbociclib at a dose of 100 mg in addition to ET and, as shown in Figure 3 and 4, the therapy seems to be contributing to tumor shrinkage at the thoracic spine level, and no other disease sites have emerged.

Discussion

MSCC is a major clinical problem that causes the onset of disabling symptoms and adversely affects the quality of life and prognosis of patients [1]. The most appropriate treatment, for local and systemic tumor control in MSCC, remains unclear.

This study reports the case of a young patient with MSCC arising during pregnancy, who successfully delivered a healthy baby and immediately after, benefited from a multidisciplinary approach based on surgery and radiotherapy in addition to palbociclib plus ET. Although no definitive conclusions can be made from a single experience, this is the first case supporting the efficacy and safety of CDK 4/6 inhibitors plus ET in luminal MSCC-BC. This case has two important messages. Firstly, physicians, particularly general practitioners, should highly suspect underlying malignancies in young and pregnant patients with back pain, especially in those with a history of previous malignancies. Previous studies have reported that patients who were ambulatory prior to treatment continued to ambulate after treatment [11]. In this case, the correct diagnosis was delayed due to pregnancy. Secondly, only rapid synergistic benefits were supported by internal funds.

REFERENCES

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