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Short Review on Doxorubicin Treatment Stabilizes Metastatic Bone Cancer

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Abstract

In breast cancer, complete bone marrow infiltration accompanied by severe pancytopenia is extremely uncommon. After metastatic breast cancer develops, bone marrow metastasis may frequently occur. However, it is uncommon to observe bone marrow failure as a sign of this disease. The safest and most effective way to treat patients with severe pancytopenia caused by metastatic solid tumor involvement is poorly studied. The patient's thrombocytopenia was particularly concerning in this instance, necessitating daily platelet transfusions. Cytotoxic chemotherapy was also feared to worsen the patient's thrombocytopenia and increase the risk of bleeding. The patient's remarkable response to chemotherapy, which resulted in a complete recovery of her platelets, is also extremely unusual. Even though our patient had a low baseline platelet level, continuous doxorubicin was able to successfully "unpack" the bone marrow without increasing the need for more frequent platelet transfusions or the risk of catastrophic bleeding. Due to the rarity of this presentation, it is currently unknown if the majority of comparable patients experience near-full recovery of hematopoietic function upon beginning the appropriate systemic treatment for metastatic disease.

Keywords: Pancytopenia; Metastatic bone Cancer; Doxorubicin;

Introduction

In the United States, breast cancer is the most common cancer among women and the leading cause of death among women between the ages of 45 and 55. Although metastatic disease, which is thought to be incurable, is uncommon at the time of the initial diagnosis, approximately 20% of women with operable breast cancer eventually relapse, with approximately 70% of these relapses occurring as distant metastases. Approximately 80% of women with metastatic breast cancer have skeletal metastases [1], which are typically the result of malignant cells invading the skeletal cortex and progressing into the bone marrow. Pathologic fractures, spinal cord compression as a result of a vertebral compression fracture or tumor extension beyond the epidural space, and hyperkalemia are the most frequent complications of skeletal metastases. In addition, in some cases, skeletal metastases necessitate surgery or radiation therapy to alleviate pain or prevent a fracture. Tumor cells invade the bone tissue matrix and destroy it in bone marrow metastases. Although metastasis-induced bone marrow infiltration is common in breast cancer patients, total bone marrow infiltration with severe pancytopenia is extremely uncommon [2].

Method

A woman in her 62s presented with increased fatigue that was hindering her daily activities. The only notable aspect of her previous medical history was hypertension. Her mother had lung cancer, which was in her family history. She appeared unwell and exhausted during a physical examination. Anicteric sclera existed. Lips were dry, and blood-colored secretions stained the oral mucosa. Both lungs were visible during examination. The cardiovascular exam was unnoticed, with no murmurs, rubs, or applauds. Without organomegaly, the abdomen was soft and non-tender. Her breast exam revealed a fixed, one centimeter-long left axillary lymph node. There were no visible skin changes or masses on either breast [3]. Laboratory tests on peripheral blood revealed severe pancytopenia. As part of the initial diagnostic workup, multiple imaging studies, including computed tomography (CT) of the chest, abdomen, and pelvis, as well as a bone scintography, were completed. Her white blood cell (WBC) count was 3.2 K/L, her hemoglobin (Hgb) was 6.8 g/dL, and her platelet count was 3 K/L. A chest CT scan revealed a medial, nodular left breast lesion and a left axillary adenopathy [4]. Multiple vertebrae and the pelvis were involved in the diffuse skeletal metastatic disease that was detected on the bone scintography scan. A mammogram had also been taken, and the upper inner left breast contained an irregular spiculated nodule. A core needle biopsy of an enlarged left axillary lymph node was then performed on the patient. By immunohistochemical staining, the biopsy revealed a metastatic lobular carcinoma that was strongly positive for both estrogen and progesterone receptors (ER and PR) but negative for HER2 and E-cadherin.

A bone marrow biopsy was performed on the patient in order to further analyze the severe pancytopenia that necessitated frequent transfusions of packed red blood cells (pRBC) and platelets. The pathology revealed that the bone marrow had been completely replaced by the metastatic carcinoma. Immunohistochemical staining revealed that the tumor cells were positive for cytokeratins AE1/AE3, ER, and PR, but negative for HER2, indicating that the disease was metastatic. The patient began systemic therapy with doxorubicin, which was administered as a continuous three-day infusion (20 mg/m2/day) on a 21-day cycle in an inpatient setting after extensive discussion of the risks and benefits of therapy in light of profound pancytopenia [5]. A small number of previous studies suggested that doxorubicin's acute and chronic toxicities, including bone marrow suppression, may be reduced when administered as a continuous rather than bolus. As a result, a continuous infusion of the drug was chosen.

Result

In the end, the patient received three cycles of this treatment. Due to elevated transaminases, the first cycle's dose of doxorubicin was reduced by 50%. These transaminases returned to normal in subsequent

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cycles of treatment. Full dose was used for the second cycle, but febrile neutropenia necessitated hospitalization. As a result, the dosage of doxorubicin was decreased by 25% during the third cycle. Since the patient's platelets had sufficiently recovered, monthly liposomal doxorubicin (40 mg/m2) was switched to continuous therapy after three cycles for ease of administration in the outpatient setting [6]. The patient's pancytopenia steadily improved after chemotherapy was started. Her WBC increased to 5.4 K/L, Hgb increased to 11.6 g/dL, and platelet count improved to 131 K/L approximately four months after beginning treatment. The patient experienced a near-full recovery from her pancytopenia approximately thirteen months after beginning treatment, with no evidence of anemia or thrombocytopenia.

At the time, her laboratory tests revealed a remarkable response to treatment, with a WBC of 4.8 K/, RBC of 4.00 M/L, Hgb of 12.8 g/dL, and platelet count of 160 K/L. The patient was transferred to endocrine therapy with letrozole, an aromatase inhibitor, after four cycles of liposomal doxorubicin. 43 months after beginning continuous doxorubicin treatment, her laboratory profile remained stable. Her disease progressed in the liver, bone, orbit, and brain over the course of her final year. She was given radiation to treat the brain and orbital metastases, but she declined systemic chemotherapy. Her platelets decreased to 15 in the final month of her life, but her white blood cell count and hemoglobin levels remained stable. 44 months after receiving her initial diagnosis, she succumbed to complications of metastatic breast cancer and passed away [7].

Discussion

In breast cancer, complete bone marrow infiltration with extensive pancytopenia is extremely uncommon. After metastatic breast cancer develops, bone marrow metastasis may frequently occur. However, it is uncommon to observe bone marrow failure as a sign of this disease. The safest and most effective way to treat patients with severe pancytopenia caused by metastatic solid tumor involvement is poorly studied.

The patient's thrombocytopenia was particularly concerning in this instance, necessitating daily platelet transfusions. Cytotoxic chemotherapy was also feared to worsen the patient's thrombocytopenia and raise the risk of bleeding. The patient's remarkable response to chemotherapy, which resulted in a complete recovery of her platelets, is also extremely unusual. Even though our patient had a low baseline platelet level, continuous doxorubicin was able to successfully "unpack" the bone marrow without increasing the need for more frequent platelet transfusions or the risk of catastrophic bleeding. Due to the rarity of this diagnosis, it is currently unknown whether the majority of similar patients experience near-full recovery of hematopoietic function upon beginning the appropriate systemic treatment for metastatic disease.

Conclusion

Patients with metastatic breast cancer rarely present with pancytopenia. Adjuvant chemotherapy with alkylating agents and topoisomerase II inhibitors was found to be the cause of pancytopenia in several studies, as opposed to metastatic disease. Although this association has not been completely established, some have suggested that the use of growth factor support medications like filgrastim or peg-filgrastim may also increase the risk of developing pancytopenia associated with myelodysplastic syndrome or acute myeloid leukemia. Saito reported on a patient with pancytopenia who had metastatic breast cancer and evidence of bone marrow metastasis and therapy-related acute myeloid leukemia concurrently. Pancytopenia was primarily brought on by metastatic breast cancer causing bone marrow infiltration in our case. This rarely appears in the literature and includes patients who have received therapy with both positive and negative outcomes. Patients who have responded to systemic therapy, such as low-dose capecitabine, endocrine therapy, and trastuzumab monotherapy, are highlighted in a number of reports. Therapy does not always work for all patients, as expected. Reported a case of a patient with breast cancer metastasis to the bone marrow. Disseminated intravascular coagulation (DIC) caused pancytopenia, so the patient received G-CSF injections and weekly paclitaxel therapy.

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