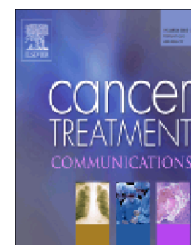




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Stabilization of bone marrow infiltration by metastatic breast cancer with continuous doxorubicin

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Abstract

Complete bone marrow infiltration with profound pancytopenia is very uncommon in breast cancer. Bone marrow metastasis can frequently occur following development of metastatic breast cancer. However, bone marrow failure as the herald of this disease is not typically seen. Very limited data exists as to the safest and most efficacious manner to treat patients with profound pancytopenia due to metastatic solid tumor involvement. In this case, the patient's thrombocytopenia was particularly worrisome, requiring daily platelet transfusions. There was also concern that cytotoxic chemotherapy would exacerbate the patient's thrombocytopenia and increase bleeding risk. The patient's dramatic response to chemotherapy with full platelet recovery is also highly unusual. For our patient, continuous doxorubicin successfully "unpacked" the bone marrow despite a low baseline platelet level, and without increasing the need for more frequent platelet transfusion or risk of catastrophic bleeding. Given the rarity of this presentation, it is currently unknown if the majority of similar patients experience near full recovery of hematopoietic function after initiation of appropriate systemic treatment for metastatic disease.

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1. Introduction

Breast cancer is the most common malignancy in women and number one cause of death in women between the ages

of 45 and 55 in the United States [1]. Although metastatic disease, considered incurable, is rarely seen at the time of initial diagnosis, approximately 20% of women with operable breast cancer eventually relapse, with about 70% of the relapses as distant metastases [2-5]. Approximately 80% of women with metastatic breast cancer have skeletal metastases, which are often the result of bone marrow infiltration of malignant cells with subsequent progression and invasion of the skeletal cortex [6-9]. The most common complications of skeletal metastases are pathologic fractures, spinal cord compression as the result of vertebral compression fracture or extension of the tumor beyond the epidural space, and hypercalcemia [7-9]. Furthermore, skeletal metastases sometimes require surgery or radiation therapy to treat pain or an impending fracture. Bone marrow metastases result in the invasion and destruction of the bone tissue matrix by tumor cells [6]. Although bone marrow infiltration by metastases is commonly present among breast cancer patients, total bone marrow infiltration resulting in profound pancytopenia is extremely rare [6,10].

2. Case report

A 62 year-old female presented with increased fatigue that was interfering with her activities of daily living. Her previous medical history was remarkable only for hypertension. Her family history included lung cancer in her mother. On physical exam, she was ill-appearing and fatigued. Sclera were anicteric. Lips were dry and oral mucosa was notable for blood tinged secretions. Lungs were clear to auscultation bilaterally. Cardiovascular exam was normal, with no murmurs, rubs or gallops appreciated. Abdomen was soft and nontender without organomegaly. Her breast exam was

notable for a fixed, 1 cm left axillary lymph node. Neither breast had a palpable mass or skin changes. Peripheral blood laboratory tests indicated severe pancytopenia. Her white blood cell (WBC) count was 3.2 K/ μ L, hemoglobin (Hgb) was 6.8 g/dL, and platelet count was 3 K/ μ L. Multiple imaging studies, including computed tomography (CT) of the chest, abdomen and pelvis, as well as a bone scintigraphy were completed as part of the initial diagnostic work up. Chest CT revealed left axillary adenopathy and a medial, nodular left breast lesion. The bone scintigraphy scan showed diffuse skeletal metastatic disease involving multiple vertebrae and the pelvis. A mammogram had also been performed and showed an irregular spiculated nodule in the upper inner left breast. The patient subsequently underwent a core needle biopsy of an enlarged left axillary lymph node. The biopsy revealed a metastatic lobular carcinoma strongly positive for both estrogen and progesterone receptors (ER and PR) and negative for HER2 and E-cadherin by immunohistochemical staining.

To further evaluate the patient's profound pancytopenia, which required frequent transfusion of packed red blood cells (pRBC) and platelets, the patient underwent a bone marrow biopsy. The pathology showed that the metastatic carcinoma had entirely replaced the bone marrow (Figure 1). The tumor cells were positive by immunohistochemical staining for cytokeratin AE1/AE3, ER and PR, but were negative for HER2, consistent with metastatic breast cancer.

After much discussion of the risks and benefits of therapy in view of profound pancytopenia, the patient initiated systemic therapy with doxorubicin administered as a continuous three day infusion (20 mg/m²/day) on a 21 day cycle in the inpatient setting. A continuous infusion of doxorubicin was selected based on small, prior studies suggesting that acute and chronic toxicities, including bone marrow suppression, may be lessened when doxorubicin is administered as a continuous versus bolus

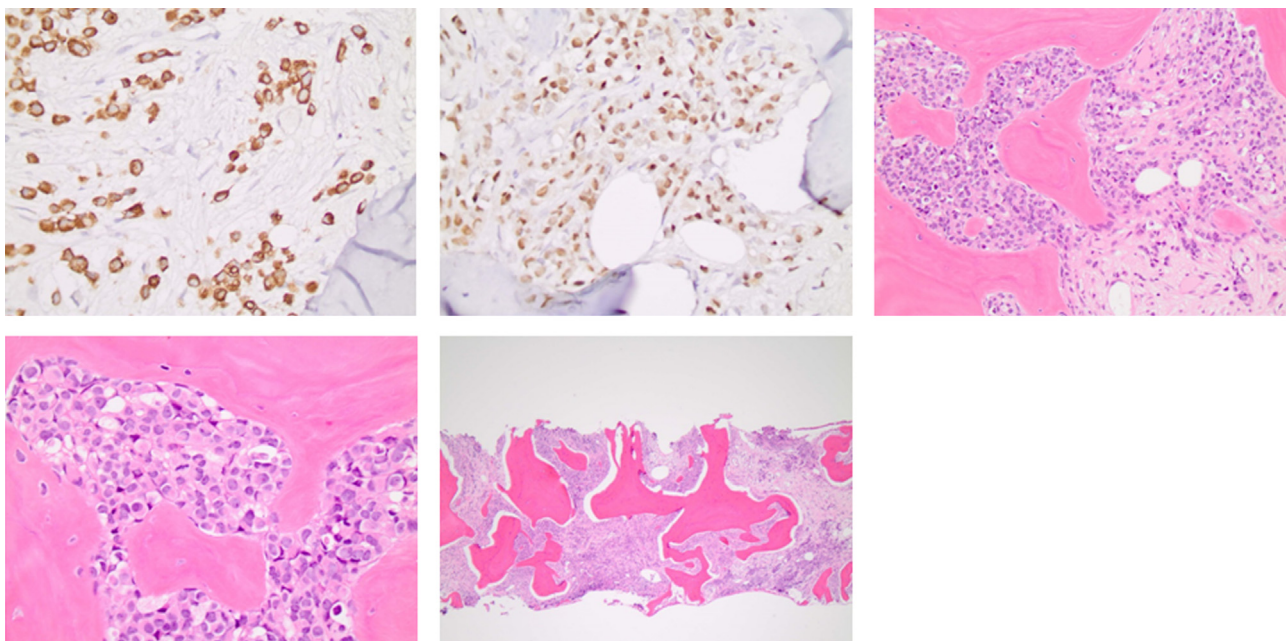


Figure 1 The bone marrow biopsy shows that the hematopoietic elements are entirely replaced by fibrosis and metastatic carcinoma infiltrating individually and in small clusters, and comprised of intermediate sized cells with round to ovoid nuclei, a thin rim of cytoplasm and occasional intracytoplasmic vacuoles.

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