European Review for Medical and Pharmacological Sciences 2014; 18: 846-850

Multidisciplinary approach to uncommon, widely metastatic breast cancer

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Abstract. – Worldwide, breast cancer represents the most common malignancy in women. Most diagnoses can be made relatively early. However, aggressive metastatic disease is still possible. We report an unusual case of a neglected 69-year-old woman with an intensely malodorous right breast, back pain, and shooting pain in both of her legs. After obtaining history, clinical examination, magnetic resonance imaging and CT scan, she was found to have widely metastatic breast cancer (ER/PR positive, HER-2 negative, 43% Ki-67), with metastases in vertebral bodies of T1/T4, pleura, lungs, liver, mediastinal and axillary lymph nodes, compression pathological fractures of T12/L3, and an expansive, destructive sacral metastasis. She underwent a thoracolumbar surgical fixation for her lower spine and radiotherapy for the T1 metastasis. She received aromatase inhibitor therapy followed by palliative mastectomy. Here, we reviewed the diagnostic steps, management, multidisciplinary approach and the relevant literature of this rare presentation of a destructive, multi-metastatic breast cancer.

Key Words:
Metastatic breast cancer, Bone metastases, Palliative surgery, Radiation therapy.

Introduction

Breast cancer represents 22.9% of all cancers diagnosed in women. Worldwide, it is the most common cause of cancer-related death in females (13.7%)[1]. In the United States, it is the second most common cause of cancer death in women after lung cancer. The U.S. also has the highest prevalence rate of breast cancer in the world (128.6 per 100,000 Caucasian women)[2]. The main histological type is adenocarcinoma, which originated from glandular epithelial tissue[3]. The invasiveness of breast carcinoma is determined by a number of clinical and pathologic risk factors including the size of primary tumor, the presence of basal lamina invasion, endocrine receptor profiles, and nodal status; the most common type (75%) being invasive ductal carcinoma (IDC, also called infiltrating ductal carcinoma)[4]. Molecular typing classifies breast cancers into categories according to the presence or absence of estrogen (ER), progesterone (PR), and/or HER-2 receptors[5].

Metastases of breast cancer can develop in various organs including bones (most common, 70%), lungs, lymph nodes, liver, or brain[4]. Although the frequency and presentation of metastatic breast cancer are well recognized, the simultaneous presence of pulmonary parenchymal, visceral and thoracic lymph node metastases, along with wide-spread, structurally threatening skeletal metastases in a patient with an uncontrolled primary breast tumor is rare. Active palliative interventions are often required. Here, we report the case of a tragic presentation of a 69-year-old Russian woman with breast cancer. This woman presented with an excoriating breast mass and was unable to walk for the past two days; she was found on the floor of her apartment, having lied down there for a day without eating. Her metastatic extent included the spine, lungs, pleura, lymph nodes, sacrum and mediastinum. Her lower spine was surgically fixed by pedicle screws and rods, and palliative options were undertaken. Her case required special consideration in management strategies – the prognosis of late-discovered metastatic breast cancer remains poor, with a 5-year survival rate of 7-9%[6].

Case Report

A 69-year-old woman was brought in by ambulance to the Emergency Room of our hospital. The ambulance had been called by a neighbor who had

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Figure 1. ***A,*** Large fungating ulcerating mass arising from the right breast, coronal view. ***B,*** Large fungating ulcerating mass arising from the right breast, oblique-lateral view.

not seen her for ten days, and a malodorous smell was detected from her apartment. She was tachycardic and hypotensive. In the Emergency Department, she complained of back pain for approximately a week, inability to walk for two days, and shooting pain in both legs without episodes of fever or chills. However, she did complain of bladder distention. On physical examination, the patient appeared to be oriented, but very fatigued and malnourished. She had a blue-blackish, malodorous inflammatory exudate coming from an excoriating lesion in the right medial breast, with associated extensive tissue necrosis (Figure 1a/b). Her right breast tissue was indurated, disfigured, and markedly enlarged. She also complained of bilateral weakness in her legs, with pain in her left pelvic area. She denied sensory changes or anesthesia in the pelvic saddle area or lower extremities, and urinary or bowel incontinence. The motor strength and sensory testing of the distal lower leg muscles were within normal limits, and rectal tone was intact. Trauma survey and resuscitation were immediately performed. Then, laboratory tests, urinalysis, ECG, chest X-ray, and CT of the chest, abdomen and pelvis were obtained which revealed multiple suspicious metastases from a presumed breast primary cancer including vertebral body of T1, posterior part of T4 with epidural space involvement (Figure 2a), compression pathological fracture of T12 and L3 (Figure 2b), destructive sacrum metastasis (Figure 2c/d), axillary lymph nodes, pleura, both lungs, and mediastinum (Figure 2e). The T12 and L3 lesions were causing clinical cord compression. The sacral metastasis was extensive, with focal involvement of the mid-lower right paramedian sacrum including involvement of sacral foramina from S2 caudally. At this point, high dose steroids and emergent palliative surgery were necessary. Moreover, due to severe back pain, extreme weakness in the proximal lower extremities and urine retention, an emergent thoracolumbar magnetic resonance imaging was performed.

Due to the complexity and rarity of the clinical presentation encountered in the western society, a multi-disciplinary approach was the key in this case. The patient was admitted to the medical floor. Multiple services were involved including internal medicine, general surgery, neurology, neurosurgery, orthopedic, urology, pain service, medical oncology, radiation oncology, palliative medicine, psychiatry, nutrition, and chaplain service. After resuscitation, pain control and an extensive work-up, she was offered neurosurgical procedures for spinal stabilization and tumor debulking. She initially refused the procedure. However, after proper education and addressing all her concerns, she finally accepted surgery. Bilateral costal transversectomies with T11, T12, and L1 laminectomies were performed. Large areas of vertebrates of T9 thorough L4 were fixed posteriorly with pedicle screws and rod instrumentation (Figure 3). Arthrodesis with methyl methacrylate of T11 to L1 was also performed. Post-operatively, the patient recovered appropriately, with gradual returns of her neurological functions and had a better control

of her pain. The surgical specimen was examined pathologically, which confirmed adenocarcinoma with breast as its origin. Regarding her breast cancer, additional lymph node biopsies showed an estrogen receptor (ER) positive, progesterone receptor (PR) negative, and HER-2 negative carcinoma. The Ki-67 proliferation index was 43%. The patient was started with an aromatase inhibitor (anastrazole) for attempting to shrink her tumor burden in multiple metastatic foci, with the hope that it may stop progression for a while. Palliative mastectomy was discussed with the patient. The patient completed a course of radiotherapy (30 Gray in 10 fractions) to her epidural metastasis at vertebrae T4, which was above the operative area for spinal cord fixation. The patient will also receive a postoperative course of external beam radiotherapy to her operated lower spine as well, in addition to her expansive sacral metastasis which is still symptomatic. Unfortunately, considering the aggressive nature of her multi-metastatic cancer, multi-organ involvement and cancer dissemination, and a high Ki-67 proliferation index of her tumor, even though she may temporarily respond to aromatase inhibitors and alkylating chemotherapy, her prognosis remains very poor.

Discussion

Breast cancer is the most common cancer in women and causes 300,000 deaths per year worldwide[1]. However, multi-metastatic breast cancer is actually a relatively rare presentation in the United States, due to our success in screening programs and accessibility to general medical care.

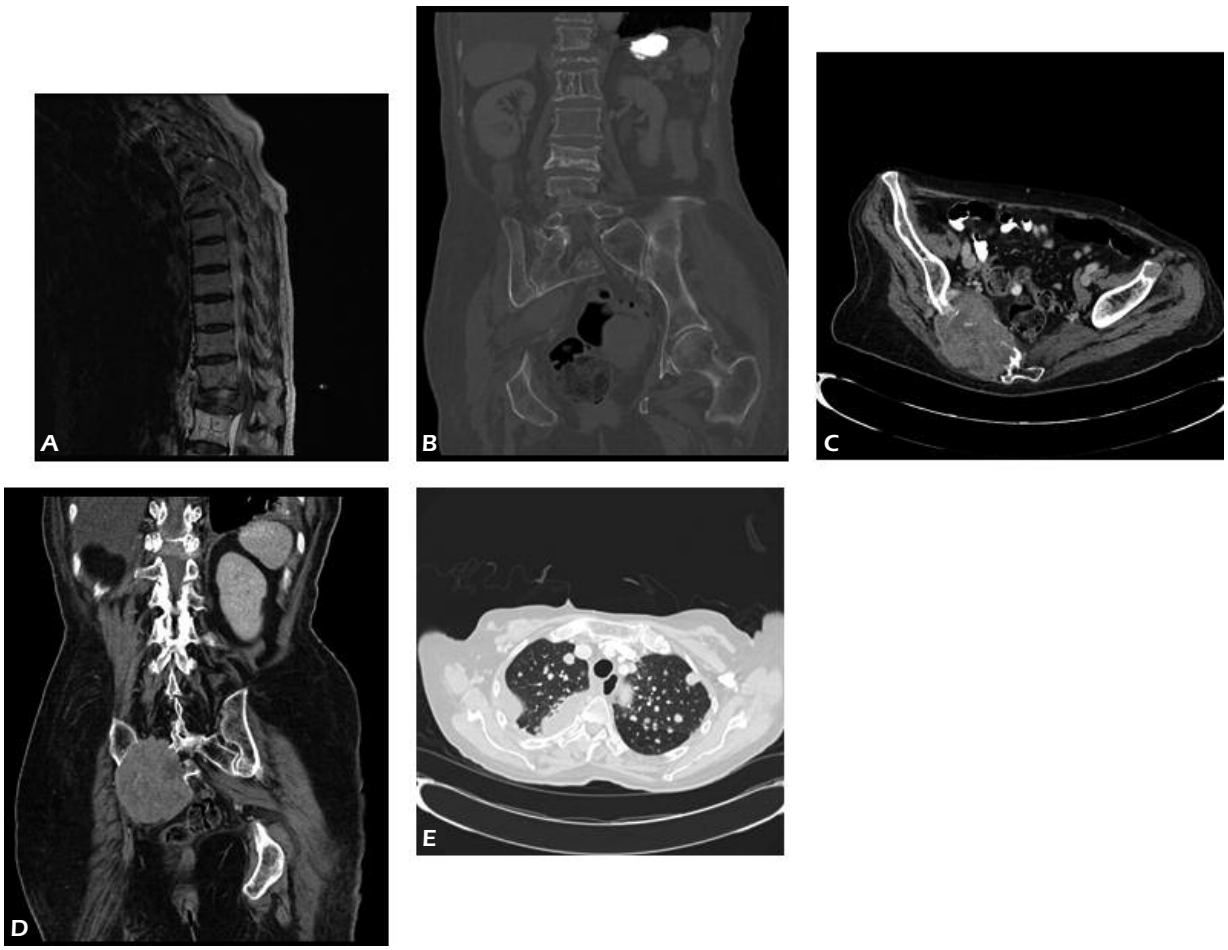

Figure 2. ***A,*** MRI of the spine showing the multiple vertebral metastases. ***B,*** Pathologic compression fractures of the T12 and L3 vertebral bodies. ***C,*** Large destructive metastatic lesion involving the right side of the sacrum with neural involvement, axial view. ***D,*** Large destructive metastatic lesion involving the entire right side of the sacrum with neural involvement. ***E,*** CT-scan of the chest showing numerous lung metastases and the presence of malignant pleural effusion.

Figure 3. Postoperative MRI of the spine (coronal view, fixation of T9 through L4 vertebras with pedicle screws and rods).

Metastatic breast cancer can most commonly involve bones (70% of breast cancer metastases), lungs, lymph nodes, liver, gastrointestinal tract, or brain[4]. Bone metastases usually have a predominant attraction for axial skeleton, which was thought to be related to the presence of red bone marrow. Bone invasion can present as osteonecrosis, fracture, or osteolysis, which significantly impacts the patient's quality of life[7]. Bone metastases can also induce bone lysis and hypercalcemia via PTHrP secretion. They can also secrete paracrine factors (cytokines) which stimulate the osteoclasts and inhibit the osteoblasts[8,9]. Osteolytic lesions can induce pathological fractures, pain, nerve compression, and most severely a spinal cord compression which happened in our patient. In breast cancer patients with uncontrolled bone metastases, the five-year survival is lower than 20%[10].

Options for palliative treatment of disseminated breast cancer include mastectomy, chemotherapy, radiotherapy, hormonal therapy, symptom-based palliative care, and supportive care[11]. General palliative options for bone metastases of a breast cancer include radiotherapy or pharmacological bisphosphonates[12]. For vertebral metastases, radiotherapy coupled with neurosurgery for unstable pathological fractures are indicated. In our patient's case, the most emergent problem was spinal cord compression, which caused bilateral leg weakness and urine retention. High dose steroids and surgical fixation of the spine followed by radiotherapy were the treatments of choice[13]. After her lower spine fixation, the medical team reflected on the available options for her T4 epidural metastasis which continued to threaten her spinal cord, in addition to her primary cancer. After a multidisciplinary discussion, radiotherapy was started for the T4 lesion, and aromatase inhibitors were given for her primary breast cancer with an evaluation for a possible palliative mastectomy in four to six weeks.

This case report details a late discovery of a multi-metastatic breast cancer and the importance of swift multidisciplinary managements in stabilizing a quickly deteriorating patient with uncontrolled, widely disseminated breast cancer.

Even though efficacious screening programs are well-established in high-income countries and have demonstrated their efficiency, a certain percentage of women are still found to be diagnosed with metastatic disease; this case also emphasizes the importance of prevention and early intervention especially in the socioeconomically vulnerable populations.

New biologic studies have shown that, as a proof of concept, gene expression profile can be obtained to delineate various tumor molecular patterns which have different sensitivities to chemotherapeutic agents. This latter assertion gives hope for more targeted and individualized cancer management in the treatment of multi-metastatic breast cancer[4,14-17].

Conclusions

Widespread, multi-metastatic breast cancer is not a frequent presentation, but a certain portion of women still get diagnosed at this late stage. Palliative treatment options are typically used; however, this rare, clinically challenging case remains one of the worst clinical presentations in the spectrum – the patient presented with an excoriating large mass in her right breast with rapid apparition of paraparesis, and the decisive use of depressive spinal surgery and radiation therapy has lengthened the patient's survival.

The main goals of treatment of metastatic breast cancer are to increase the survival time and delay cancer progression, while maintaining good quality of life and improving the symptomatology. With the development of new therapies and potential aid with gene expression profiling, it is hopeful that the survival for metastatic breast cancer can be improved. Clinically, a multi-disciplinary approach is paramount.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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