Breast cancer metastasizes to skeletal muscle. Moreover, skeletal muscle is a rare site of metastasis for any type of cancer. In this study, we report an unexpected finding of an enlarged mass in the gluteus maximus of an asymptomatic patient with a distant history of breast cancer. The mass was observed during computed tomography evaluation in preparation for a non-oncologic procedure. Biopsy and pathological investigation confirmed breast cancer metastasis. An increased awareness of rare metastatic sites is important so that such lesions are critically evaluated during early imaging examination.

**Key Words:** Breast neoplasms, Drug therapy, Metastasis, Radiotherapy, Skeletal muscle

**INTRODUCTION**

Considerable progress has been made in early diagnosis and treatment of breast cancer, which is one of the most common cancers. However, understanding of late diagnosis or recurrent disease leading to distant metastases is yet to be established. Knowledge of the frequent sites of breast cancer metastases can help clinicians during their search for atypical findings and narrow the differential diagnosis of patient’s lesions. In addition, clinicians once aware of rare metastatic sites, may recognize and respond properly to the atypical findings.

**CASE REPORT**

An 86-year-old female was evaluated preoperatively for a transcatheter aortic valve replacement. Computed tomography (CT) angiography of the chest, abdomen, and pelvis showed an infiltrating, enlarged mass within the right gluteus maximus (Figure 1A). The patient denied any clinical symptoms in the right gluteus.

The patient had a history of stage IIIA invasive lobular breast carcinoma and had undergone prior therapy including mastectomy with lymph node dissection. The primary cancer was a 4 cm invasive lobular carcinoma, histologic grade II with focal signet ring cell feature. Eight of the 19 lymph nodes were positive for metastatic invasive lobular carcinoma. The pathological specimen showed negative margins; however, a focal region of 0.2 cm existed from the excised surgical margin. The tumor was classified as IIIA – pT2, pN2a, and G2. The tumor was 100% estrogen receptor (ER) positive, 10%–15% progesterone receptor (PR) positive, human epidermal growth factor-2 (HER2) negative, and Ki-67 negative in the primary cancer pathological specimen. Consistent with invasive lobular carcinoma, cytoplasmic staining was observed with p120 catenin but not with E-cadherin. The patient’s comorbidities included hypertension, hyperlipidemia, type II diabetes mellitus, congestive heart failure, aortic stenosis, hypothyroidism, gastroesophageal reflux disease, obesity, and anxiety. Her Eastern Cooperative Oncology Group (ECOG) performance status score was 2. She had two siblings with breast cancer; however, genetic testing was never performed. The patient was treated with surgery and radiation therapy, and had been maintained on letrozole antihormone therapy for 5 years. The patient was recommended to continue antihormonal treatment for 10 years; however, letrozole was discontinued prematurely because of worsening musculoskeletal symptoms. Given the patient’s history of breast cancer, tissue sampling of the enlarged mass was recommended.

During our examination, an ultrasound-guided biopsy of the enlarged mass in the right gluteus maximus was performed. The mass appeared hypoechoic when compared to the surrounding normal musculature (Figure 1B). Multiple core needle samples were obtained to maximize tissue sampling as well as for adequate histological analysis. Histology showed that the tumor cells were positive for AE1/3 and GATA3, and partially positive for GCDFP-15, consistent with primary lobular carcinoma. The pathological specimen showed negative margins; however, a focal region of 0.2 cm existed from the excised surgical margin. The tumor was classified as IIIA – pT2, pN2a, and G2. The tumor was 100% estrogen receptor (ER) positive, 10%–15% progesterone receptor (PR) positive, human epidermal growth factor-2 (HER2) negative, and Ki-67 negative in the primary cancer pathological specimen. Consistent with invasive lobular carcinoma, cytoplasmic staining was observed with p120 catenin but not with E-cadherin. The patient’s comorbidities included hypertension, hyperlipidemia, type II diabetes mellitus, congestive heart failure, aortic stenosis, hypothyroidism, gastroesophageal reflux disease, obesity, and anxiety. Her Eastern Cooperative Oncology Group (ECOG) performance status score was 2. She had two siblings with breast cancer; however, genetic testing was never performed. The patient was treated with surgery and radiation therapy, and had been maintained on letrozole antihormone therapy for 5 years. The patient was recommended to continue antihormonal treatment for 10 years; however, letrozole was discontinued prematurely because of worsening musculoskeletal symptoms. Given the patient’s history of breast cancer, tissue sampling of the enlarged mass was recommended.

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Metastatic cancer was found to be 5%-10% ER positive, PR negative, HER2 negative, and 20%−25% Ki−67 positive. Cytoplasmic p120 staining was also observed, consistent with metastatic lobular breast carcinoma (Figures 2, 3). Therefore, systemic chemotherapy was started to improve prognosis. This case report did not require Institutional Review Board approval.
DISCUSSION

The most common sites of breast cancer metastases are bone, lung, and liver [1-3]. Although metastasis to the skeletal muscle is rare, the rate of metastasis to unexpected areas is increasing [2]. Several case reports of breast cancer metastases to the skeletal muscle are now available [1-10]. Three cases of metastases to the rectus sheath are also known [4,7,9]. Interestingly, only one case of metastatic breast cancer of the gluteal muscle has been currently reported [4]. Other rare sites of metastases include the pectoralis [3], biceps [8], forearm, psoas, and quadratus lumborum [10].

Skeletal muscle is a rare site of metastasis for carcinomas of any origin. Previous studies have shown that the percentage of skeletal muscle metastases from breast cancer ranges from 3.3% to 14% [5,6]. Various theories exist regarding the low incidence of skeletal muscle metastases. Changes in blood flow during rest and exercise may alter the blood flow through the musculature; this, combined with mechanical contractile activity may reduce the adherence of cancer cells. Protease inhibitors present in the skeletal muscle basement membrane may disrupt enzyme-dependent pathways resulting in tumor cell invasion. Skeletal muscle cells are capable of metabolizing lactic acid, which plays an important role in neovascularization, as well as the activation of lymphocytes and natural killer cells [3,5,7]. Further studies are needed to identify the exact mechanism by which skeletal muscle evades tumor metastasis.

A previous case report of breast cancer metastatic to the gluteus maximus presented a 52-year-old female with invasive ductal carcinoma, classified as cT2N0M0 [4]. The tumor was ER positive, PR positive, HER2 negative. The patient received five cycles of cyclophosphamide, methotrexate, 5-fluorouracil chemotherapy followed by tamoxifen for 2 years for primary cancer. The patient showed subsequent metastases in the lymph nodes and received letrozole with a complete response. The patient later showed gluteus muscle metastasis, and the therapy was switched from letrozole to exemestane, resulting in a poor response. Docetaxel and epirubicin were initiated and showed a partial response. No other comorbidities were reported in above case report; however, given the patient’s relatively young age, it is likely that the patient had no significant comorbidities.

Our patient had biopsy-proven stage IV breast cancer despite receiving letrozole, therefore, systemic chemotherapy was recommended. Taxanes are the most commonly prescribed chemotherapy for breast cancer. In elderly patients, a single-agent chemotherapy regimen with a better safety profile is preferred. These agents include taxanes, doxorubicin, capecitabine, and vinorelbine. Determining the prognosis of patients with metastatic breast cancer also includes many other factors. Advanced age, obesity, poor performance status (ECOG ≥ 2), triple-negative cancer, and a greater number of metastatic sites are associated with poor prognosis. In addition, given the rarity of breast cancer metastasis to the skeletal muscle, it is difficult to recommend a specific antineoplastic agent for treatment.

Magnetic resonance imaging (MRI) and positron emission tomography (PET)/CT are widely used for the diagnosis of soft tissue metastases. MRI is considered the gold standard for the evaluation of muscle pathology [7] while PET/CT is more routinely used in the follow-up of cancer patients to assess metastatic lesions [1]. PET/CT shows FDG-avid lesions, such as breast metastases with a high tumor-to-background contrast ratio, facilitating the identification of abnormal lesions. Greater area coverage from the head to the thighs on PET/CT also provides an advantage in detecting metastasis compared to the limited field of view present in MRI or CT [5]. Imaging with a nuclear bone scan is useful for assessing additional sites of bone metastases.

In our patient, CT angiography of the chest, abdomen, and pelvis identified a metastatic lesion as it was enhanced in the arterial phase. The CT appearance of metastasis to the muscle can vary and may mimic other non-malignant pathologies. Five different types of such CT findings have been described, including intramuscular mass, abscess-like intramuscular lesion, diffuse metastatic muscle infiltration, multiple muscle calcifications, and intramuscular bleeding [6]. This case presented as diffusely enhanced muscle infiltration (Figure 1A). The infiltrating appearance may be observed in cases of invasive lobular carcinoma due to tumor cells presenting as small confluent nodules infiltrating and thickening the surrounding cell walls, unlike invasive ductal carcinoma which presents as nodular masses [3].

Finally, breast cancer that metastasizes to the gluteus muscle is rare. Being aware of the rare sites of metastasis can help clinicians search for atypical findings in patients. Consequently, this will help formulate more comprehensive recommendations for clinical team members.
CONFLICT OF INTEREST

The authors declare that they have no competing interests.

REFERENCES