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Authors: CPT Sally Corey, MAJ Andrew Delmas, Morakinyo Toney, Thomas Dykes, Randy Hamill, Craig Cameron

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AUTHORS:

CPT Sally Corey[1],

MAJ Andrew Delmas[2],

Morakinyo Toney[3],

Thomas Dykes[4],

Randy Hamill[5],

Craig Cameron[6]

AFFILIATIONS:

[1]DO, MC, USA, Orthopedic surgery resident, Dwight D. Eisenhower Army Medical Center;

[2]MD, MC, USA, Staff Hematology/Oncology, Dwight D. Eisenhower Army Medical Center;

[3]MD, Deputy Chief Radiology, Dwight D. Eisenhower Army Medical Center;

[4]MD, Chief of Urology at the Charlie Norwood VA Medical Center;

[5]MD, Staff Pathology, Dwight D. Eisenhower Army Medical Center;

[6]DO, Orthopedic oncology specialist, Dwight D. Eisenhower Army Medical Center

CORRESPONDING AUTHOR DETAILS

Sally Corey, DO

Department of Orthopedic Surgery, 300 East Hospital Road, Fort Gordon, GA 30905

Email: sally.a.corey.mil@mail.mil

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ABSTRACT

Introduction

Although the most common primary tumors with metastasis to bone are prostate, breast, kidney, lung, and thyroid cancer; metastasis to bone occurs in 30-40% of patients with muscle-invasive bladder cancer. The femur is the third most common location for bladder cancer metastasis to bone surpassed by the spine and pelvis. Treatment for metastatic lesions of the femur often requires orthopedic intervention with intramedullary stabilization. Identification of the lesion is regularly performed concomitantly with the stabilization procedure through the collection and analysis of intramedullary reaming.

Case Report

We present a case of muscle-invasive bladder cancer with metastasis to the proximal femur treated with intramedullary stabilization, in which intramedullary reaming were inconclusive for pathology and an open biopsy was required.

Conclusion

Intramedullary reaming is not always adequate to identify the primary tumor in cases of metastatic lesions. Management of metastatic lesions in bone requires an understanding of the characteristics, behaviors, and treatment of the primary tumor, as well as the management of the bony lesion

Keywords: Metastatic, Bladder, Cancer, Femur

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INTRODUCTION

Metastasis to bone occurs in more than half of cancer patients. The most common primary tumors that metastasize to bone include prostate, breast, kidney, lung, and thyroid [1]. Although bladder cancer encompasses only 4.5% of new cancer cases annually [2], 30-40% of patients with muscle-invasive bladder cancer will develop bony metastasis. The most common locations for bladder cancer to metastasis in bone include the pelvis, spine, and femur in descending order [3]. In situations of impending long bone fractures, management of metastatic lesions includes identification of the lesion and stabilization of the bone [1]. Both of these tasks can commonly be accomplished through the collection of reaming during intramedullary nail fixation. Intramedullary reaming is a common surgical technique, which involves introducing a reamer down the canal of long bones prior to the placement of an intramedullary nail in order to increase the biomechanical stability of the construct. In cases of pathologic fractures or prophylactic stabilization, the reamer passes the bony lesion and allows for the collection of a sample of the lesion to send to pathology for further evaluation [10]. The following case report describes a case when intramedullary femur reaming was insufficient to diagnose metastatic bladder cancer necessitating an open biopsy.

CASE REPORT

A 72-year-old male with a long smoking history presented to the urology clinic secondary to episodes of gross hematuria. He was diagnosed with bladder cancer and underwent a transurethral resection of bladder tumors, which revealed invasive high-grade urothelial (transitional) cell carcinoma (T2N0M0). He was treated with four cycles of neoadjuvant gemcitabine and carboplatin followed by a radical cystectomy with ileoconduit. A PET scan was performed at the patient's six-month follow-up appointment and revealed increased signal in his proximal femur (Figure 1). The patient related to a two month history of thigh pain at the time the scan was performed. Radiographs, CT, and bone scan confirmed a lytic lesion of the proximal

femur involving greater than two-thirds the diameter of the bone with an associated soft tissue mass and no other areas of metastasis (Figure 2-4). The patient elected to proceed with intramedullary stabilization of the lesion with reaming sent to pathology for further identification of the lesion. The reaming analysis returned inconclusive of the primary tumor and an open biopsy was performed, which revealed transitional cell carcinoma based on histologic comparison to the patient's previous bladder tumor and staining positive for CK7 (Figure 5). The patient was treated with monthly 120 milligrams (mg) of denosumab and 30 Gy of radiation therapy in 10 fractions to anterior and posterior port sites covering the mass and the distal tip of the intramedullary nail. At one-year follow-up, the patient had a metastatic lesion in his right pubic bone and the left lung and received palliative treatment.

DISCUSSION

An estimated 76,960 new cases of urinary bladder cancer are predicted in 2016 [2]. Metastasis has long been associated with bladder carcinoma. In fact, Prout et al described bladder carcinoma as "a systemic disease" due to the rate of metastasis [4]. Understanding the patterns and risk factors associated with metastasis aids in timely identification and treatment. The most common locations for bladder cancer metastasis include lymph nodes, (69-90%), liver (26-47%), lung (37-45%), bone (30-47%), and the peritoneum (16-19%). The frequency and timing of metastasis is associated with local tumor extension. Increased frequencies and decreased metastasis-free intervals are related to T4 tumors [5, 6]. Secondary malignancy in addition to bladder cancer has also been observed in up to 20% of patients with prostate, lung, colon, larynx, and stomach the most common secondary tumors [6].

Identifying the primary tumor in a metastatic bone lesion is essential for proper treatment even in the case of known muscle-invasive bladder cancer. Proper diagnosis begins with a thorough history and physical examination. Laboratory evaluation may reveal anemia and/or hypercalcemia. Bony lesions should be evaluated with plain radiography of the whole bone and chest, whole-body tchnietium-99m bone scintigraphy, and computed tomography of the chest abdomen

and pelvis in order to assess for other metastatic lesions and the source of the primary tumor [1].

Treatment of metastatic lesions in long bones often requires not only identification of the lesion, but also stabilization. Mirels created criteria for predicting impending pathologic fractures based on the size of the lesion, pain level, type of lesion, and location. A score of 9 or more indicates an impending fracture and aids in the decision to perform proper fixation [7]. Jenkinson et al showed that patients who are treated with prophylactic stabilization of the femur have better results than patients who sustain a fracture and need stabilization [8]. The goal of prophylactic fixation of impending fractures is to allow patients immediate weight-bearing, which is commonly accomplished with intramedullary nailing in the case of lesions in the femoral shaft [1]. Intramedullary nail fixation offers the benefit of a strong construct in addition to the opportunity to diagnose the lesion from intramedullary reaming. Clarke et al reported that intramedullary reaming are adequate to make a definitive diagnosis of a metastatic lesion [9]; however more recent literature argues that a definitive diagnosis can be made in only 60% of metastatic lesions when intramedullary reaming are used in isolation. Due to the inaccuracy of intramedullary reaming, other methods of tumor biopsy are recommended in addition to pathologic analysis of reamings [10].

CONCLUSION

Although metastatic bladder cancer was assumed the most likely cause of the bony lesion in our patient based on the histologic features of his primary tumor, proper identification of the lesion was necessary for his treatment. The proper diagnosis was unachievable on intramedullary reaming alone and required an open biopsy. Management of metastatic lesions in bone requires an understanding of the characteristics, behaviors, and treatment of the primary tumor, as well as the management of the bony lesion; thus necessitating a multi-disciplinary approach.

CONFLICT OF INTEREST

The authors have no financial disclosures or conflicts of interest. The views expressed in this article are those of the authors and do not necessarily reflect the

official policy of the Department of Defense, Department of Army, US Army Medical Department or the US Government. This work was prepared as part of their official duties and, as such there is no copyright to be transferred.

AUTHOR'S CONTRIBUTIONS

CPT Sally Corey, DO

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

MAJ Andrew Delmas, MD

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

Morakinyo Toney, MD

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

Thomas Dykes, MD

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

Randy Hamill, MD

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

Craig Cameron, DO

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

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FIGURE LEGENDS

Figure 1: PET scan of the proximal femur showing increased signal. (A) Sagittal (B) coronal (C) axial images

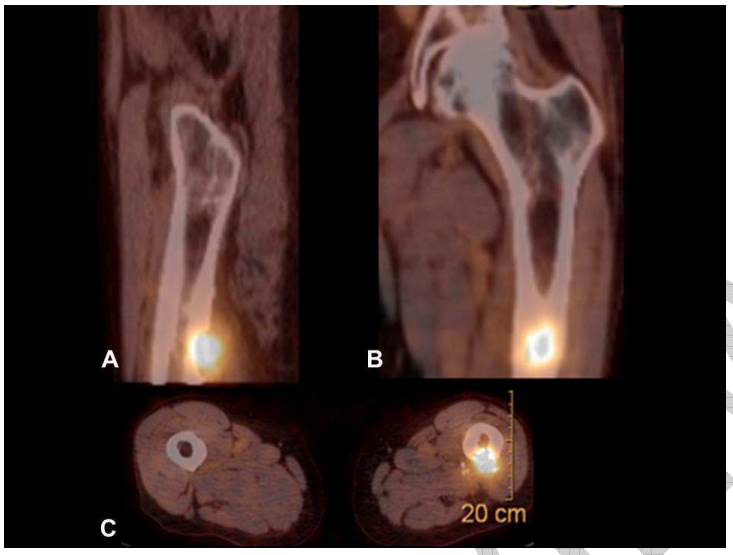
Figure 2: Radiographs reveal lucent lesion. (A)Anterior-posterior (B) lateral images

Figure 3: Select CT images reveal associated soft tissue reaction. (A) Coronal (B) sagittal (C) axial images

Figure 4: Bone scan reveals no other area of metastasis. Proximal femur uptake on the anterior-posterior (A) and lateral (B) images. (C) Increased uptake in abdominal region at area of ileoconduit.

Figure 5: (A) Histology of mass at 400x view shows nested malignant cells consistent with transitional cell carcinoma (TCC) invading bone (B) TCC staining positive for CK7

FIGURES



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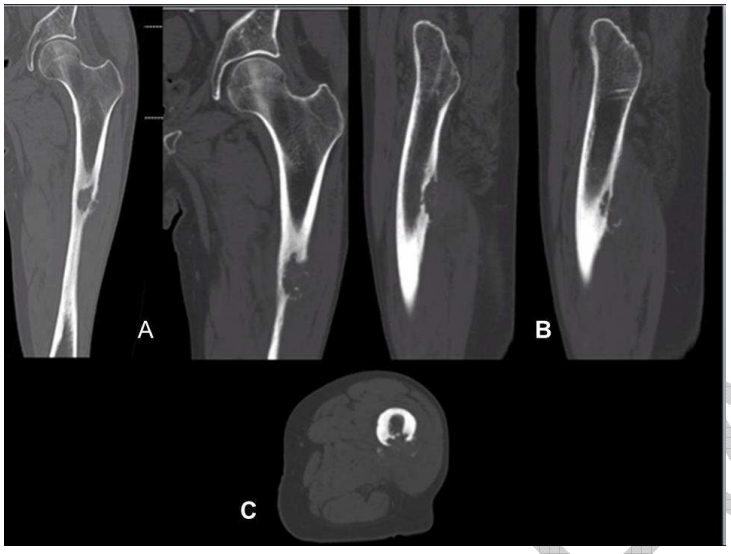
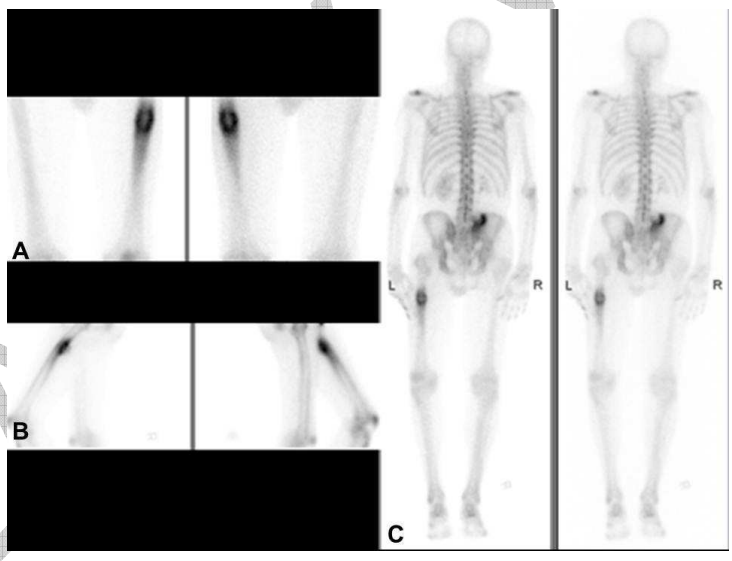


Figure 3: Select CT images reveal associated soft tissue reaction. (A) Coronal (B) sagittal (C) axial images



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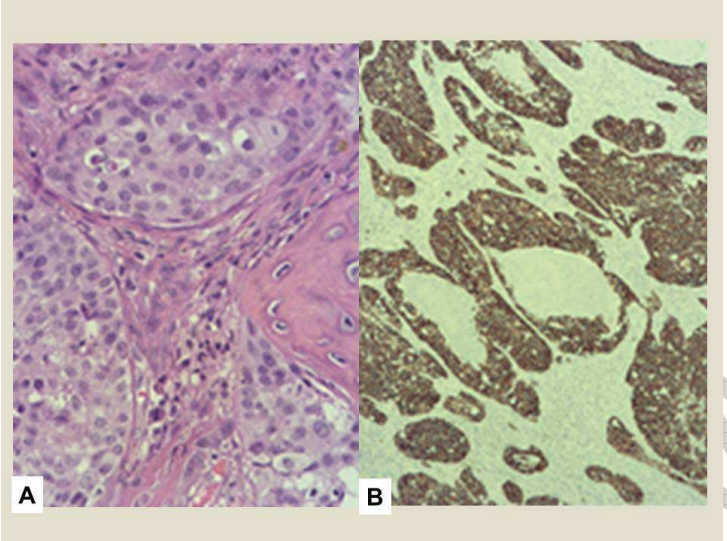

Figure 5: (A) Histology of mass at 400x view shows nested malignant cells consistent with transitional cell carcinoma (TCC) invading bone (B) TCC staining positive for CK7