Treatment of Metastatic Prostate Adenocarcinoma to the Calcaneus

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Abstract

Metastatic skeletal adenocarcinoma is an all too common and unfortunate complication of advanced oncologic states. Mortality rates are usually elevated when bony metastasis are evident, as this signifies advanced disease. The foot and ankle are uncommon sites for metastatic deposits, but may occur. As such, the foot and ankle surgeon must be aware of the potential for such disease, and be able to proceed with an imaging and medical work-up of the patient with foot and ankle skeletal metastasis. The goal of treatment is pain relief and the preservation of functional ambulation, which may greatly enhance the quality of remaining life for patients. A team approach is mandatory to manage the patients with metastatic disease. We present a case of an elderly male with a known history of prostate cancer, who presented with unrelenting heel pain, which upon diagnostic work-up, proved to be progressive calcaneal as well as axial metastasis after a brief period of clinical remission. Operative management coupled with palliative radiation and bisphosphonate therapy provided symptomatic pain relief and maintenance of functional ambulation.

Case Report

An 81-year-old white male was referred to the senior author (C.B.) with a several month history of progressive heel pain that had recently become unrelenting, severely exacerbated with weight-bearing ambulation, and now, unable to bear weight on his right foot. The patient’s medical history was positive for a previous diagnosis of prostate cancer (Gleeson grade 3 + 3, 6/10, Stage 1), diagnosed 2 years prior, by biopsy specimens from a transurethral prostate resection, performed for symptoms of urinary retention associated with an elevated prostate-specific antigen (PSA). At that time, because of his advanced age, and, in conjunction with the patient’s wishes, radical surgical therapy was not sought. Androgen suppressive therapy was initiated and maximized. During androgen therapy, the patient developed an upper extremity thrombosis with pulmonary embolism, and was started on chronic warfarin therapy. Two months prior to office referral, the patient developed heel pain and was evaluated in the emergency department, discharged with a diagnosis of pseudogout, with a follow-up rheumatology appointment. The rheumatology department ruled out pseudogout, and referred the patient to the foot and ankle service.

At presentation for his heel pain, the patient’s PSA level had risen to 7.18 ng/mL from a low of 0.07 ng/mL while on androgen suppression (normal range = 0.00 – 4.00 ng/mL). In addition, the patient complained of the new onset of rib and back pain. Physical examination revealed diffuse spinal tenderness in the thoracic/lumbar region, without neurologic deficit. The lower extremity exam revealed an intact neurovascular exam, with exquisite tenderness along the medial and lateral wall of the calcaneus. There was no swelling or redness, or palpable masses in the foot or ankle region. No regional adenopathy was appreciated. Plain radiographs revealed a mixed lytic/sclerotic lesion in the body of the calcaneus in proximity to the
posterior subtalar facet, without evidence of gross fracture (Figure 1).

In light of the patient’s medical history, metastatic prostate cancer was suspected. Confirmatory magnetic resonance imaging (MRI) was ordered, which revealed a low signal intensity lesion on T1 within the calcaneus, exhibiting erosive margins. T2 images were heterogeneous (mixed) signal intensity, with apparent erosion of the lateral wall of the calcaneus (Figures 2 and 3). A total body bone scan revealed lesions in the thoracic and lumbar spine and multiple ribs. A working diagnosis of metastatic prostate adenocarcinoma was rendered, with plans for open biopsy and resection of tumor from the calcaneus. The surgical goal was to provide pain relief and restore structural integrity of the os calcis for weight bearing.

Because of the patient’s history of pulmonary embolism, and being at a high risk of further thromboembolic events in association with metastatic disease, warfarin was not discontinued. General anesthesia, complemented by an ultrasound-guided popliteal pain catheter was used. The patient was positioned lateral with a thigh tourniquet. Loupe magnification was used to examine soft tissue planes during the surgical approach. A curvilinear lateral incision was used to gain access the lateral wall of the calcaneus, using the interval between the peroneal tendons and the lateral malleolus, avoiding the sural nerve as well as the lateral calcaneal branch of the peroneal artery. Inferior retraction of the peroneal tendons provided ideal access to the metastatic tumor; the lateral wall of the calcaneus was removed, exposing the tumor (Figure 4). Specimens from the lateral wall and from the intraosseous portion of the lesion were sent for frozen section. Frozen section confirmed the diagnosis of adenocarcinoma, with tumor extension through the lateral wall of the calcaneus. The bulk of the lesion was enucleated from the calcaneus, using fluoroscopic guidance as needed to reach and curette the far extents of the tumor within the calcaneus (Figure 4). A high-speed burr was used to completely debride the inner walls of the calcaneus. Next, intrallesional chemoablation was performed by directly instilling hydrogen peroxide ($\text{H}_2\text{O}_2$) into the calcaneus. After the effervescence

**Fig. 1.** Preoperative lateral plain radiograph of patient with metastatic prostate adenocarcinoma to the calcaneus. The mixed osteolytic/sclerotic appearance is subtle, best appreciated below the posterior facet of the subtalar joint (right panel).

**Fig. 2.** Sagittal T1 and T2 MRI images illustrating the extent of the tumor as well significant bony edema, best seen on the T2 image.
from the H$_2$O$_2$ subsided, the remaining H$_2$O$_2$ was evacuated with suction. The argon beam (Ar-beam) photocoagulator was then used to coagulate remaining tumor tissue lining the inside of the calcaneus. All surfaces inside the calcaneus were “sprayed” with the Ar-beam photocoagulator, as well as the soft tissue planes in contact with the outer wall of the calcaneus (Figure 5). This sequence of treatment modalities (H$_2$O$_2$/Ar-beam photocoagulation/high-speed burr) was considered one intraoperative treatment cycle. A total of 4 intraoperative treatment cycles were performed. Following a final saline irrigation and a thorough drying of the surgical field, polymethylmethacrylate cement (PMMA) was mixed under a vacuum, to maximize the structural integrity of the PMMA. The PMMA was inserted using mild pressurization into the calcaneal bone defect. A layered closure was performed after hemostasis. Meticulous hemostasis and the use of PMMA and a vascular plane interval obligated the need for a drain. Final radiographs revealed adequate filling of the calcaneus with PMMA (Figure 6). Permanent pathology section confirmed metastatic prostate adenocarcinoma (Figure 7).

Postoperatively, the patient’s pain decreased dramatically, and the patient was allowed immediate protected toe-touch weight bearing, and advanced to full weight bearing in a CAM boot over 4 weeks. The patient was referred to radiation oncology, with the need for soft tissue-sparing palliative radiation emphasized. In collaboration with the foot and ankle service, in order to minimize the potentially devastating soft tissue complications from radiation therapy, the patient was allowed to initiate radiation after complete healing and

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Fig. 3. MRI transverse images of metastatic prostate adenocarcinoma to calcaneus.

Fig. 4. Intraoperative appearance of tumor within calcaneus (left panel). Fluoroscopic-guided debridement to reach the far extent of the tumor (right panel).
early maturation of the surgical incision (8 weeks). Radiation oncology selected a 3000-cGy dose in 10 equal fractions. After completion of his lower extremity treatments, the patient continued to be ambulatory, with a vast improvement in foot pain. However, the patient declined further radiation or medical treatment for his spine lesions, but allowed hospice services to assist him with quality-of-life issues. To date, 8 months since his index musculoskeletal surgery, the patient has survived and remains ambulatory with an assistive device.

Discussion

Metastatic bone disease is a common occurrence with progressive malignancy, with metastatic bone disease ultimately occurring in 30% of patients with malignancy (3). Patients with metastasis to the appendicular skeleton have a poorer prognosis than their counterparts (10). Among the various sites in the appendicular skeleton, foot and ankle metastases are quite uncommon. In an analysis of 694 patients, Maheshwari and colleagues (3) demonstrated that only 2% of all bone metastases occur in the foot, most often arising from the genitourinary system (3–5), and most commonly lodging in the talus and calcaneus. Other primary tumor tissues that metastasize to the foot include the colon, lung, and breast (3, 4).

Bone is the third most common site for metastasis of adenocarcinomas (23%), only being surpassed by metastasis to the lung and liver (11). Thus, the presentation of a patient with progressive pain, especially persistent pain despite non-weight bearing, night pain, especially with a known history of a primary carcinoma that exhibits a tendency for bone metastasis, must elicit a vigilance for metastatic bone disease (Table 1). When such a patient history is accompanied by a lytic, or, a mixed lytic/sclerotic lesion on plain radiographs, the index of suspicion must be immediately elevated, and further imaging studies obtained. To better image the skeletal area in question, after plain radiographs, the senior author will obtain an MRI of the lower extremity region in question; on occasion, computed tomography (CT) of the foot and ankle may be helpful to assess architectural collapse that is not well visualized on plain radiographs or MRI. In the case of prostate carcinoma, MRI typically will demonstrate a mixed enhanced signal on T2 sequences (1). The senior author always also

Fig. 5. Intraoperative tumor chemoablation with H2O2 (left panel) and Ar-beam photocoagulation (right panel).

Fig. 6. Final intraoperative radiograph of PMMA reconstruction of calcaneus (left panel). Clinical appearance postoperatively (right panel). Meticulous hemostasis and the use of PMMA and a vascular plane interval obligated the need for a drain.
obtains a total body bone scan (technetium-99m methylene diphosphonate [Tc-99m]), as detection of additional sights of metastatic disease is mandatory. The reason behind this strategy is that occult metastatic lesions may be identified on a Tc-99 bone scan as early as 3 months earlier than on plain radiographs, because bone absorption of 30% to 50% from baseline values is often required to detect the presence of a lytic bone lesion (11). Follow-up spot MRI or CT of areas positive on the total body bone scan is then undertaken. Disease work-up by F-18 fluor choline-positron emission tomography/CT to detect occult metastases (12), or procollagen type 1 amino-terminal propeptide assay as a marker for bone metastases (13) are newer, promising investigative modalities that are yet to be implemented on wide-scale use. Body cavity CTs (chest, abdomen) are obtained as indicated to assess local primary site disease progression and further metastases. The PSA is also reevaluated, and oncology services consulted (general oncology and urology).

In one small series, 53% of metastatic foot lesions arose without a previously known primary source (4). This poses an especially difficult setting, in that a search for a primary locus implies advanced malignancy, and a poorer prognosis. Regardless of a known primary source, the discovery of metastatic bone globally imparts a poorer prognosis, with patients surviving only up to 14 to 20 months (3, 4). In this manner, the goals of treatment are simple and defined: the provision of pain control, and maximization of function as it pertains to the quality of the remainder of life. To this end, the mainstay of treatment of metastatic prostate adenocarcinoma includes debulking of the metastatic tumor and the provision of bony structural support, followed by medical therapies to decrease bone pain and control local tumor growth. In our reported case, because of advanced disease and patient age, the senior author preferred an “intralesional excision” of the metastatic tumor, with adjuvant Ar-beam and H2O2 chemoablation of residual tumor cells. Bony structural support was provided by void-filling with PMMA, which allows immediate protected weight bearing. Palliative radiation treatment may then follow, after the surgical wound is healed. Palliative radiation may be in the form of single- or multiple-fraction treatment, with a suggested trend toward single-fraction treatment for patients with a short life expectancy, and in cases where the effects of radiation therapy on the soft tissue envelope are less concerning (14). This is in contradistinction to primary musculoskeletal sarcomas, in which preoperative radiation (or chemotherapy) may be used to shrink the primary lesion before definitive surgical intervention.

Bisphosphonate therapy has been successfully used to ameliorate the pain of metastatic bone disease. Several prostate cancer cell–produced cytokines, such as transforming growth factor (TGF) alpha and beta, as well as changes in the expression of tumor cell ligands (ligand “switching”), that involve the Receptor Activator of Nuclear Factor-kappaB ligand (RANKL)/RANK/osteoprotegerin (OPG) molecular system, enhance osteoclastogenesis and bone destruction associated with the presence of metastatic prostate tumor cells (15–18). By virtue of the anti-osteoclastic activity of the bisphosphonates, bone resorption (lysis on radiographs) is inhibited, as well as the risk of subsequent microfracture, overt fracture, and pain. However, the use of bisphosphonates is not without risk, as the development of subtrochanteric insufficiency fracture has been observed with prolonged use of certain bisphosphonates, such as alendronate. In general, this is believed to be attributable to the long-term impairment of bone remodeling. However, in patients with metastatic bone disease with a short life expectancy, the benefit of palliative bisphosphonates may be judiciously weighed against the risks of long-term use.

In conclusion, metastatic bone disease is a common occurrence in cancer patients. Although metastases to the foot and ankle are
uncommon, the occurrence of such pathology is described in the literature (albeit in low numbers). Thus, in the appropriate clinical setting, metastatic bone disease must be included in the differential diagnosis. The foot and ankle surgeon must be aware of the potential for these metastatic bone tumors, as well as the most likely tissue types. The approach to patients with metastatic bone disease in the foot and ankle involves a team approach involving the musculoskeletal surgeon and the various oncology services. The goal for advanced disease states is control of pain and extremity function. A system of integrated medical treatment is required to provide optimum care for oncology patients, and, when such a care system is not locally available, referral to a musculoskeletal surgeon experienced in the management of such patients with disposal to a complete array of oncology and supportive medical services can assist with providing the metastatic cancer patient an improved quality of survivable life.

References