MULTIPLE FOOT BONE RENAL CELL CARCINOMA METASTASES: FEASIBILITY OF SIMULTANEOUS CT-GUIDED MICROWAVE ABLATION

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ABSTRACT

Renal tumor has a high incidence of bone metastasis (BM). BM are burdened by a considerable morbidity and are the most common cause of cancer-related pain. Local treatment of metastases remains controversial despite showing promising results for pain control. We would like to report our experience with a patient who developed foot bone metastasis 3 years after a left nephrectomy for a renal cell carcinoma. Metastasis were treated in two session of CT-guided microwave ablation. One lesion in the first session and three, simultaneously, in the second one. Cement augmentation was performed in all cases. No complications were noticed in the first session, while a wound infection developed in one of the needle insertion points of the second session.

The patient showed good pain control immediately after the procedure and on follow-up at six months.

KEYWORDS: Renal Cell Carcinoma Metastases; Foot Bone Metastases; Simultaneous Microwave Ablation; CT Guided Microwave Ablation; Pain Therapy.

Introduction

The growth of malignant cells in the bone tissue has been recognized as a complication of cancer dating to 1889 by Paget.[1]

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Even if the axial skeleton is the most common site of bone metastases (BM) due to the highly vascularized anatomy, cancer could potentially spread in all the bones. Renal tumor represents one of the five cancer sites with the higher incidence of BM, presenting an incidence rate of 35% of bone metastases.[2-3] BM are burdened by a considerable morbidity, complex demands on health care resources [4] and are the most common cause of cancer-related pain. The pathophysiologic mechanisms of this pain is poorly understood but probably include tumor-induced osteolysis, direct infiltration of nerves and local tissue production of prostaglandins.[5] Local treatment of metastases such as metastasectomy or radiotherapy remains controversial in the treatment of metastatic renal cell carcinoma.[6] Stereotactic body radiotherapy (SBRT) represents a significant advance; utilization varies institutionally and geographically and reduces the risk of serious adverse events compared with conventional radiotherapy.[7] Minimally invasive procedures such as radiofrequency ablation (RFA), microwave ablation (MWA) and cement augmen-

tation is emerging as a promising therapeutic regimen because of the short process time, minimally invasive nature, and ability to be performed on an ambulatory basis.[7-8] We would like to report our experience with a patient who developed foot bone metastasis three years after a left nephrectomy for a renal cell carcinoma.

The patient underwent two microwave thermal ablation of 3 metastases with cement augmentation.

Case presentation

We would like to report our experience of a 63-year-old Caucasian diabetic male patient presenting multiple metastases of the left foot treated with CT-guided microwave ablation. Three years earlier, the patient underwent left nephrectomy for a Clear Cell Renal Cell Carcinoma (RCC), Fuhrman $G_{3,}$, $T_{4,}$ for the infiltration of the ipsilateral adrenal gland, without any pathological finding of node metastasis ($N_{0,}$) and imaging findings of distant metastasis ($M_{0,}$). So patients began immune-therapy using Sunitinib and follow-up. At one year from the nephrectomy, a CT scan revealed the presence of a fifth left rib metastasis. So the patient underwent a single session of radiotherapy and continued therapy with Sunitinib. The patient presented a progressive disease with the developing of new metastasis.

Two years after the nephrectomy the patient complained of pain at the left foot when walking. A plain X-ray showed multiple osteolytic lesions, the biggest being: the calcaneal tuberosity, the I metatarsal base, the talus and the scaphoid.

After a percutaneous US guided biopsy of the talus lesion confirmed the BM, the multidisciplinary oncologic group decided to perform a palliative surgical treatment with cementoplasty and a fixating screw followed by a SBRT (30 months after the nephrectomy) of the foot (Figure 1). In the same period, the

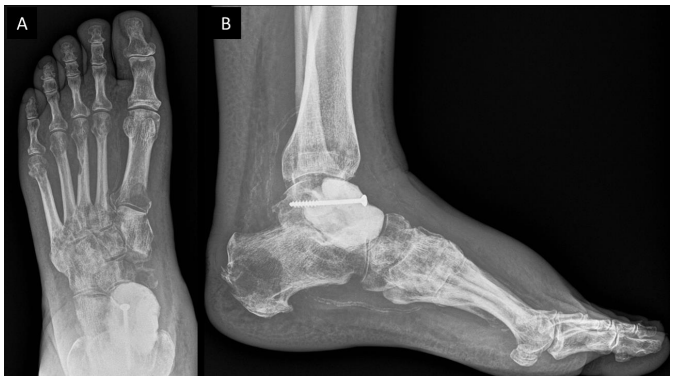


Figure 1: Plain X-ray in two views showing multiple bone osteolytic metastasis. Note, the outcome of the surgical cementoplasty and the fixating screw of the talus.

patient developed a cardiovascular toxicity to sunitinib, characterized mainly by hypertension, so he began a second line of therapy with Pazopanib, without any assumption of bone modifying agents (considering the hypercreatininemia in monorenal patient).

The scans showed stable disease and the patient experienced a partial relief of pain that lasted for few months.

Three years after nephrectomy, the patient stopped ambulating experiencing pain on foot even out of load, and with a poor drug control even using morphine and NSAIDs. A CT scan (figure 2A) and a whole body scintigraphy (figure 2B) confirmed the activity of the calcaneal lesion.

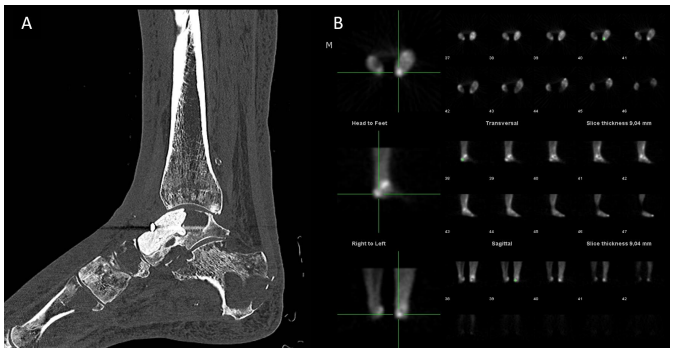


Figure 2: A) CT sagittal scan showing the multiple bone metastasis; please note the major BM in the calcaneus, navicular and I metatarsal.**B)** left foot focused reconstruction of the whole body scintigraphy showing a significant uptake of the calcaneus and the talus BM.

Due to the radiation dose exposure limit reached by SBRT, we decided to treat the calcaneal BM with microwave thermal ablation. Under CT guidance a Kirschner thread was positioned in the middle of the calcaneal lesion to have a line for positioning microwave probe. After the positioning of an 11 G Coaxial had introduced with a fish mouth like tip (Trap Drill, HS Amica, HS Hospital Service S.p.A., Aprilia, Italy), a 14-gauge x 150mm minichoked, water-cooled interstitial antenna (HS Amica, HS Hospital Service S.p.A., Aprilia, Italy) was inserted into the tumor. The introducer was then retracted before energy delivery so not to interfere with microwave emissions by the active probe tip (Figure 3A). With the use of a 2.45-GHz generator delivering energy a power of 60 W was applied for 5 minutes.

Than cement augmentation with 3 ml of high viscosity polymethylmethacrylate (Confidence spinal cement system, DePuy Spine, Raynham, Massachusetts) was performed without fluoroscopic guidance (Figure 3B). The technical result was good, without peri-procedural complication. The patient experienced a prompt relief of pain and was able to load on the left foot two days after the procedure.

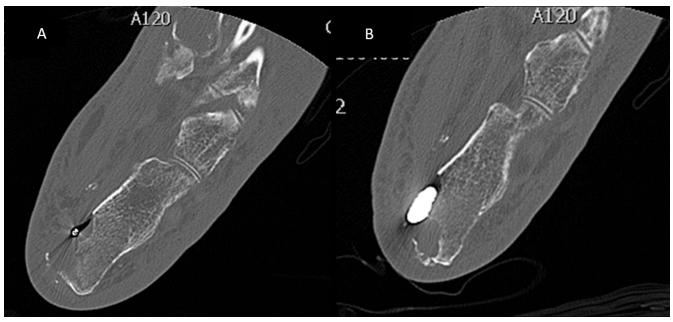


Figure 3: CT axial scans are showing the needle positioning in the calcaneus **(A)** and the final result after cement augmentation **(B)**.

One month later, the patient complained of recurring pain and two weeks later stopped walking again. We decided to perform the ablation of the two other lesions (navicular bone and base of I metatarsal bone; figure 4A) and to complete the ablation of calcaneal tuberosity (Figure 4B) BM in the same session using the previous mentioned technique (Figure 5, 6A and B) with three ablations sequentially.

Cement augmentation was performed without fluoroscopic

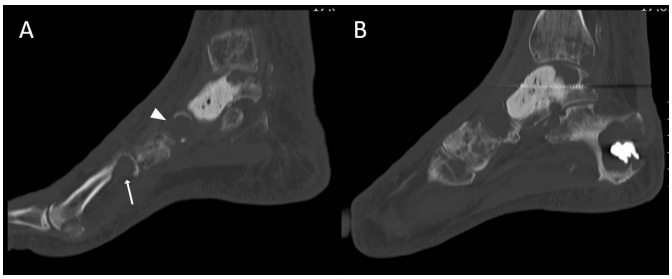


Figure 4: A) CT sagittal scan showing the metatarsal (white arrow) and navicular (white arrowhead) lesions. **B)** CT sagittal scan showing the calcaneal bone metastasis, note the result of the first treatment.

guidance using 1 ml, 1,5 ml and 2 ml, respectively for the calcaneal, navicular and metatarsal metastasis, of high viscosity cement using a single polymethylmethacrylate vial (Confidence spinal cement system, DePuy Spine, Raynham, Massachusetts).



Figure 5: Triple access to calcanear, navicular and I metatarsal metastasis using introducers and Kirschner wires.

The absence of fluoroscopic control during the release of the augmentation caused a small leak of cement out of the bone, more evident at the puncture site of the metatarsal base (Figure 7A and B). Three days after the procedure, the patient was discharged without symptoms providing a therapy with amoxicillin-clavulanic acid (875 mg+125 mg bid os) and levofloxacin (500 mg die os) for 10 days. The patient started walking using Lofstrand crutches with partial load. At one month follow-up, the patient presented swelling of the foot, mild fever in the absence of leukocytosis and mild oozing from the wound of the metatarsal ablation, which did not heal. A wound swab was negative for infection. However, we scheduled a broad-spectrum antibiotic therapy, with gentamicin and teicoplanin

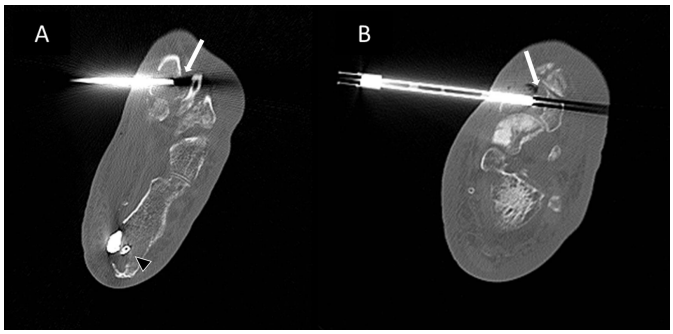


Figure 6: CT scans showing the needle positioning in the I metatarsal base (white arrow) and in the calcaneus (black arrow head) near previous cementoplasty **(A)**, and in the navicular bone (white arrow; **B)**.

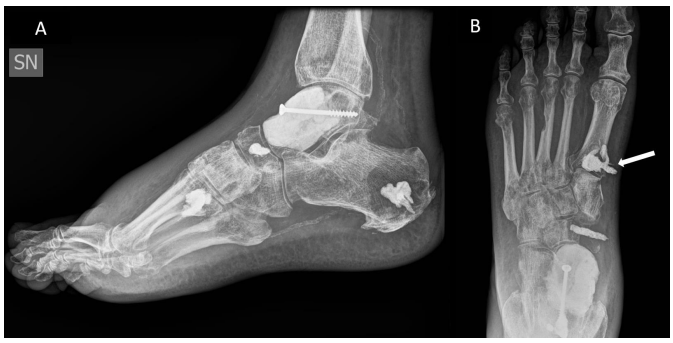


Figure 7: Plain X-ray in two views showing the final result after the multiple ablations with cement augmentation. Please note the cement leakage at the metatarsal base (white arrow).

for ten days in association with corticosteroids. The patient did not improve so an extended period antibiotic treatment was set up and a second swab demonstrated an S. aureus infection. Consequently, the patient interrupted immune-therapy experiencing metastasis progression. After two months, the patient started a third line immunotherapy with nivolumab and at six months after the ablation is still experiencing good pain control without clinical evidence of osteomyelitis as confirmed by a contrast-enhanced MR (Figure 8), even if the wound on the forefoot near the I metatarsal base cement leak still not healed. After the MW ablation procedure, the requirement of analgesic drugs progressive decreased, and now the patient has a satisfactory pain control using only NSAIDs.

Discussion

Bone metastasis are frequent in advanced stages of cancer. Most common primary tumors where metastases originate are the prostate, breast, lung, kidney, rectum, colon, and ovary.[109-101]

Complications from skeletal metastases include intractable pain, fracture, and decreased mobility, which may reduce patient's quality of life. Treatment of local disease may reduce pain in these patients, who, in most cases, have a short life expectancy. Such treatment has been shown to be fast, safe, effective and tolerable.[11-12]

BM pain can be difficult to treat, although a number of treatment options are available, ranging from radiotherapy and chemotherapy to thermal ablation and pain therapy. Thermal ablation shows promising results in several tissues and is currently

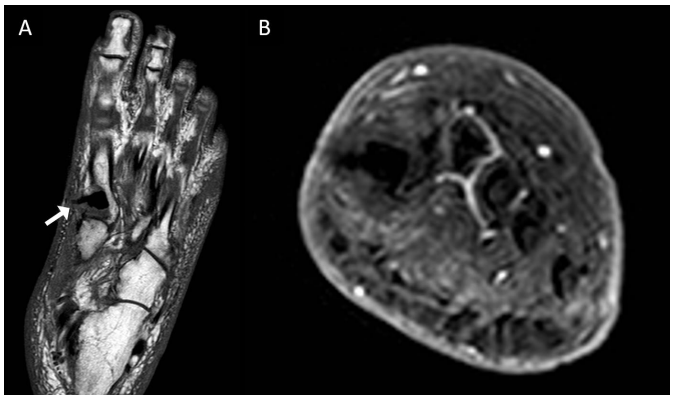


Figure 8: A) coronal T1 weighted MR scan of the left foot showing the result of I metatarsal base cement augmentation; note the leakage of the cement and the skin wound (white arrow); **B)** axial T1w contrast-enhanced MR scan showing the absence of contrast enhancement near the cementoplasty.

included in several treatment guidelines in oncologic patients not eligible for surgery or for palliative intent.[12-14]

Thermal ablative procedures developed from RFA and new therapies, such as cryoablation and MWA have emerged as viable options for the palliative treatment of musculoskeletal metastases,[15] even if the supporting evidence is still poor. Concerning the treatment of metastasis of limbs short bones using minimally invasive ablation, the evidence is even less. Even if MW ablative technique developed later than radiofrequency, it shows promising results, both alone and in combination with other treatments such as radiotherapy.[14] The present case reports the feasibility of MW ablation of RCC metastasis in small bones. Foot bones represent a tricky site to perform MW ablation due to the small dimension of bones and the closeness of many different tissues, particularly the skin. In our patient, the leakage of cement in the metatarsal base probably should be considered a contributory cause of wound delayed healing; diabetes and immunotherapy contributed worsening the foot perfusion and the angiogenesis to the wound, both essential for its healing.[16] At least, even the previous SBRT should be considered in delayed wound healing etiology. Anyway, the infection caused an interruption in immunotherapy which allowed metastasis progression, but the pain control significantly improved.

Immunotherapy demonstrated an excellent ability in disease control and the slow progression permitted the switch of different TKI, using Nivolumab as third line therapy; despite, the success in progression control patient's pain was the main issue conditioning the quality of life; therefore a multidisciplinary approach is essential in such patients.

The foot, even more than vertebrae, undergoes a severe mechanical distress due to weight bearing that explains the extreme difficulty in pain control; MW ablation and cement augmentation showed a satisfactory palliative effect. Even if there was no objective evidence, a reduction of pain and improvement in the quality of life was reported by the patient as early as a few days after the procedure and was maintained on follow-up at six months.

Future studies with extended clinical follow-up periods are needed, although these studies would be limited by the short life expectancy of these patients. However, given the promising palliative effects experienced in this case, MW seems a feasible treatment of multiple foot metastasis by RCC.

Aknowledgements

Authors' Statements

Competing Interests

All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

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