Prostate cancer metastasis to calcaneus: a solitary lesion at an atypical site, dormant for more than 10 years

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Lesson
In prostate cancer patients, if bone scan demonstrates a solitary lesion in atypical area, this is possibly an indication of metastatic disease. Therefore, biopsy confirmation is required to determine the nature of the abnormality and therefore dictates further staging investigations and treatment options.

Keywords
Prostate cancer, solitary metastasis, bone scan

Introduction
This case demonstrates that atypical solitary uptake in the peripheral skeleton on an isotope bone scan at diagnosis of prostate cancer can represent metastatic disease, and diagnostic biopsy should be considered in this setting.

Case report
Mr X, an 82-year-old man with castrate resistant prostate cancer, presented to the outpatient clinic with a painful, swollen, erythematous left foot.

Eleven years previously, Mr X was diagnosed with localised prostate cancer. At this time, a staging isotope bone scan revealed isolated radiotracer uptake in his left ankle (Figure 1(a)). This was determined to represent degenerative change, because of the solitary atypical location. A magnetic resonance imaging scan of pelvis revealed a clinical stage 3 prostate cancer, with no local lymphadenopathy. Mr X was treated with radical radiotherapy to his prostate at a dose of 74 Gray, with three years of adjuvant luteinizing hormone–releasing hormone agonist therapy. All treatments were stopped at this point.

Six years later, Mr X presented to the clinic with a rising prostate-specific antigen. A staging computed tomography scan of thorax abdomen and pelvis revealed localised bladder wall thickening, but no evidence of metastatic disease. Mr X was treated for relapsed prostate cancer with combined androgen blockade. Eight months later, Mr X had a further prostate-specific antigen progression and was commenced on abiraterone and prednisolone along with continued luteinizing hormone–releasing hormone agonist treatment. Eleven months later, his prostate-specific antigen rose again, at which point Mr X presented to the clinic complaining of left foot pain.

An isotope bone scan demonstrated significantly increased radioisotope uptake at his left ankle (Figure 1(b)). A plain film of Mr X’s left foot showed a worsening bone abnormality (Figure 1(c)). A computed tomography (Figure 1(d)) and magnetic resonance imaging scan (Figure 1(e)) of the symptomatic area were inconclusive but suggested metastatic disease affecting the left calcaneus.

A computed tomography-guided biopsy of the left calcaneus was positive for metastatic adenocarcinoma of prostate (Figure 2). Mr X was treated with palliative radiotherapy to the left ankle, with good symptomatic relief.

Discussion
Prostate cancer is common, with an incidence rate of 157.3 per 100,000 per year in Ireland (National Cancer Registry of Ireland). While the overall 5-year survival is 98.9%, this drops to 28.2% in individuals diagnosed with metastatic disease (SEER database), with a 10-year survival of 7% with best current treatment.¹

Bone is a common site for metastatic disease in prostate cancer. Although only ~9% of men with prostate cancer have a positive isotope bone scan at the time of diagnosis,² approximately 85%–90% of individuals with metastatic prostate cancer have bone involvement.³

The spread of prostate cancer to bone occurs by hematogenous dissemination. While hematopoietic stem cells can be found in the calcaneus of younger adults,⁴ active bone marrow in adults predominantly occurs in the axial skeleton.⁵ Functional imaging
Figure 1. Change in left calcaneal metastatic deposit over 10 years. Mr X had an isotope bone scan carried out at the time of his diagnosis of localised prostate cancer in 2004, showing isotope uptake in his left ankle (a). When Mr X returned to the clinic complaining of left foot pain and swelling in 2015, the isotope bone scan was repeated demonstrating a further increase in uptake (b). To further evaluate the findings on isotope bone scan, Mr X had plain film (c), computed tomography (d) and magnetic resonance imaging (e), each of which was consistent with a metastatic deposit.

Figure 2. Prostate cancer immunohistochemistry. A bone biopsy of the affected calcaneus demonstrated an infiltration of malignant epithelial cells on haematoxylin and eosin staining (a). The cells stained positively with the pan-cytokeratin antibody AE1/3 (b) and also for prostate-specific antigen (c), confirming the diagnosis of metastatic prostate cancer.
techniques show that in adult cancer patients, active bone marrow is concentrated in the pelvis and vertebrae. Post-mortem and ante-mortem metastatic prostate cancer case series show that prostate cancer bone metastases occur predominantly in this distribution, affecting the pelvis, vertebrae and ribs. Fewer than 1% of prostate cancer bone metastases found outside of the axial skeleton occur in the absence of co-existing axial skeletal metastases. Solitary haematogenous prostate cancer metastases have been reported in manubrium, radius, tibia, clavicle, lung, brain and testis. To our knowledge, isolated metastasis to the calcaneus has not been reported previously.

Several case series describe the significance of solitary lesions on isotope bone scan imaging in individuals with established cancers. Isolated lesions occurring in the vertebrae are found to represent a malignant process in 43% of cases. In the case of solitary rib lesions, the rate of malignancy is variably reported between 10% and 43%. At atypical sites, a malignant cause is found in 11.1% of all cancer cases, and in none of 16 cases of metastatic prostate cancer.

In summary, our case describes a unique site of solitary prostate cancer metastasis, with a long and ongoing survival following a six-year period without treatment. We highlight the fact that solitary lesions on isotope bone scan may represent metastatic disease, and biopsy may be appropriate even at atypical sites.

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