Prostate cancer metastasizing to bone with normal PSA level: a lesson to learn

Sir,

Prostate cancer is the second most common cancer diagnosed in men and is increasingly being diagnosed as a result of the widespread use of prostate specific antigen (PSA) testing and patient awareness. PSA has found a role also in monitoring the response to treatment. Some poorly differentiated prostate cancers do not, however, secrete PSA, and they are consequently diagnosed later with a high incidence of metastases (Sella et al, 2000) and are difficult to follow in the absence of a known marker. The authors describe a case with development of metastases despite a normal PSA and discuss cautions that should be considered.

A 66-year-old man underwent transurethral resection of the prostate (TURP) for bladder outflow obstruction. Before the operation he was noted to have a hard prostate on clinical examination and subsequently PSA was checked and noted to be normal at 1.5 µg/litre. He had a good result from the TURP but the histology of the prostatic chippings revealed a Gleason grade 4+5 adenocarcinoma in a large percentage of the chippings. He underwent a bone scan that was negative for metastases. He then underwent neoadjuvant hormone therapy followed by radical radiotherapy. His PSA dropped to a nadir of 0.2 µg/litre. Five years later he developed back pain but his PSA remained 0.2 µg/litre and there was no suspicion of metastases at this point. A few months later, in view of continuing back pain, the serum alkaline phosphatase (ALP) was checked, which was noted to be raised at 250 µg/litre – there was no baseline figure to compare with. He therefore underwent a further bone scan (*Figure 1*). This confirmed multiple metastases and he died a few months later. At no point had his PSA risen.

In this case the cancer was diagnosed after TURP with the PSA level having been normal and histology confirmed a poorly differentiated cancer. After hormone manipulation, however, the PSA did respond and fell to an almost undetectable level. With the development of bone pain his PSA remained at this nadir. Therefore, the thought that he may have developed metastases was not considered until the ALP was noted to be raised.

Metastases may still occur even with PSA that has decreased to an undetectable level after therapy as evidenced by a report by Chow et al (1998) of two cases. In a series by Oefelein et al (1995) of 394 patients, 2.3% developing recurrence post-radical prostatectomy had an undetectable PSA level.

The authors would therefore suggest a cautious approach in the follow-up of patients with prostate cancer, even when the PSA is low. This may suggest dedifferentiation of tumour where PSA is no longer secreted. If the initial cancer was poorly differentiated or the patient develops symptoms then ALP should be checked as an alternative marker being produced and the possibility of bony metastases considered.

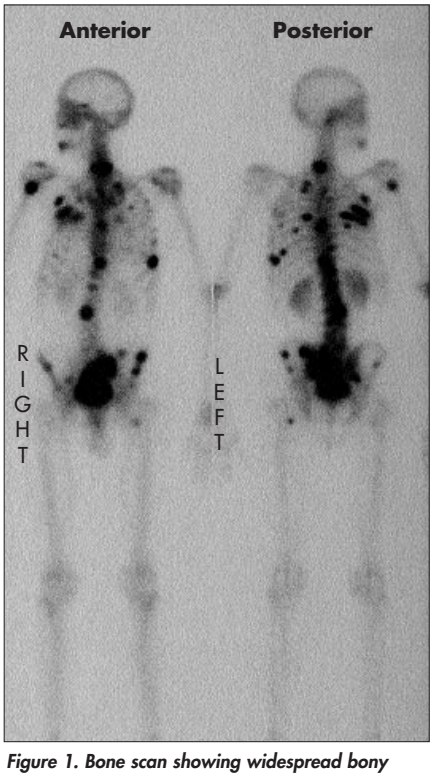

Figure 1. Bone scan showing widespread bony metastases.

Mr P Kumar,
Research Registrar in Urology
Email: kumardoc1@yahoo.co.uk
Miss J Pati
Consultant Urologist
Department of Urology
Homerton University Hospital
Homerton Row
London E9 6SR

Chow E, McLean M, Patterson B, Bayley A, Goldberg R (1998) Progression of prostate cancer despite undetectable serum prostate specific antigen. *Can J Urol* **5**: 620–2

Oefelein MG, Smith N, Carter M, Dalton D, Schaeffer A (1995) The incidence of prostate cancer progression with undetectable serum prostate specific antigen in a series of 394 radical prostatectomies. *J Urol* **154**: 2128–31

Sella A, Konichezky M, Flex D, Sulkes D, Baniel J Low (2000) PSA metastatic androgen-independent prostate cancer. *Eur Urol* **38**: 250–4