Metastatic prostate cancer to lung with normal prostate specific antigen levels

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INTRODUCTION

Prostate cancer remains the leading cause of internal malignancy in men and is the second most common cause of cancer death in men (Eastham and Scardino, 2002). With ageing populations in many developed countries, the incidence of prostate cancer and the number of deaths from this disease is expected to rise, so clinicians need to be aware of all its manifestations. Pulmonary metastases from prostatic carcinoma are known to occur in end-stage disease. However, pulmonary metastasis of prostate cancer in the absence of a prostate specific antigen (PSA) rise is a rare event. This article reports the case of a 77-year-old man diagnosed with prostate cancer in an unusual fashion by way of a solitary urethral polyp. He later presented with shortness of breath and had developed pulmonary metastases in the setting of a normal PSA level and no known osseous involvement. Pulmonary metastases should always be considered in patients with prostate cancer, even when no other evidence of metastatic disease is apparent.

DISCUSSION

In prostate cancer, clinical involvement of visceral sites is relatively uncommon, even in patients with hormone-refractory disease. The incidence of clinically apparent metastases is reported to be between 5 and 27%, whereas the incidence at autopsy has been reported as 23–74% (Eisenberger and Carducci, 2002). Such metastases are normally seen only seen clinically after bony or lymph node involvement is apparent.

In general, two basic radiological patterns occur with pulmonary metastases from prostate cancer. The most common radiological appearance on chest radiography is a lymphangetic pattern, presumably as a result of infiltration of pulmonary lymphatics (Apple et al, 1985). The less common finding, as in this case, is discrete nodular densities, either solitary or multiple, representing haematological spread (Apple et al, 1985; Hofland and Bagg, 2000). Pleural effusions and mediastinal metastases have also been reported (Apple et al, 1985). Diagnosis may be confirmed by fine needle aspiration and cytology, bronchoscopy with washings or biopsy, with the key feature being positive staining of the adenocarcinoma for PSA (Cusan et al, 1994).

Treatment of patients with pulmonary metastases is similar to that of metastatic disease in other sites. Hormonal ablation has been shown to have a good response and does not necessarily confirm a worse outcome than for metastases at other sites (Hofland and Bagg, 2000). In this case, intermittent hormonal ablation had been undertaken as first-line treatment for his prostate cancer. His response to further ablation appeared successful with his PSA falling from 22 to 1.5 μg/litre after 9 months, with no clinical evidence of further metastases.

The presence of pulmonary metastases without bony metastases or lymph node involvement is rare, with only 10 cases reported (Cusan et al, 1994; Hofland and Bagg, 2000). Of this small group, only one patient (Hofland and Bagg, 2000) had under-

CASE REPORT

A 77-year-old man presented with significant lower urinary tract symptoms, complaining of urinary frequency and poor flow. He had a normal feeling prostate. A cystoscopy was unremarkable apart from a polyp in the prostatic urethra that was biopsied. Histology revealed adenocarcinoma of the prostate, Gleason combined grade 8 (4+4). Transrectal ultrasound and biopsy was performed confirming adenocarcinoma in three of six cores. A bone scan and a computed tomography (CT) scan revealed no evidence of metastatic disease.

Several weeks post cystoscopy his prostate specific antigen (PSA) level was raised at 8.1 μg/litre (normal <4.0 μg/litre); however, this settled 2 weeks later at 3.3 μg/litre. After discussion, he was commenced on hormone ablation therapy (cyproterone acetate, a steroidal antiandrogen) because of ongoing voiding symptoms and a further normal cystoscopy. A biochemical response to treatment was achieved with his PSA falling to 0.6 μg/litre. This remained low 6 months later, so the antiandrogen was ceased, with a view to recommencing if symptoms developed or if his PSA rose.

He presented to his GP 6 months after cessation of therapy with shortness of breath. His PSA remained low at 0.2 μg/litre. A CT scan of his abdomen was normal but the chest X-ray (CXR) revealed multiple pulmonary nodules, with no pleural effusion or pulmonary oedema (*Figure 1*). A CXR performed at diagnosis of his prostate cancer was normal.

The thoracic unit was consulted, with the possibility of a new primary neoplasm raised, given his normal PSA and the fact that he was an ex-smoker. Bronchoscopy was performed with negative cytology and biopsy. A wedge biopsy of the right lung was then undertaken reporting positive histology consistent with metastatic prostatic adenocarcinoma, comparable to previous biopsies (*Figure 2*). Immunohistochemistry for PSA (*Figure 2*) and prostatic acid phosphatase were both positive, confirming the metastasis to be of prostatic origin. Upon review 1 month after his biopsy, a rapid acceleration was noted with his PSA climbing to 22 μg/litre. Hormone ablation treatment was commenced and a subsequent radionuclide bone scan revealed metastatic prostate cancer to his pelvis.

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gone hormone manipulation before the pulmonary involvement, and he had also had a radical prostatectomy and pelvic radiotherapy.

This case is notable because the patient first developed clinically apparent pulmonary metastases, after undergoing successful hormone manipulation alone as treatment for his prostate cancer. Further interesting features of this case were his original diagnosis, by way of a prostatic urethral polyp at cystoscopy done for voiding symptoms and the fact that his PSA was normal (0.2 μg/litre) in the presence of a distant metastasis. Distant metastases are normally accompanied by a significant rise in serum PSA. The normal serum PSA level may be explained by poor differentiation of the metastasis, and an inverse relationship between Gleason grade and the PSA content has been suggested (Aihara et al, 1994).

Figure 1. Chest radiograph demonstrating widespread nodular pulmonary metastases, characterized by the multiple, rounded opacities.

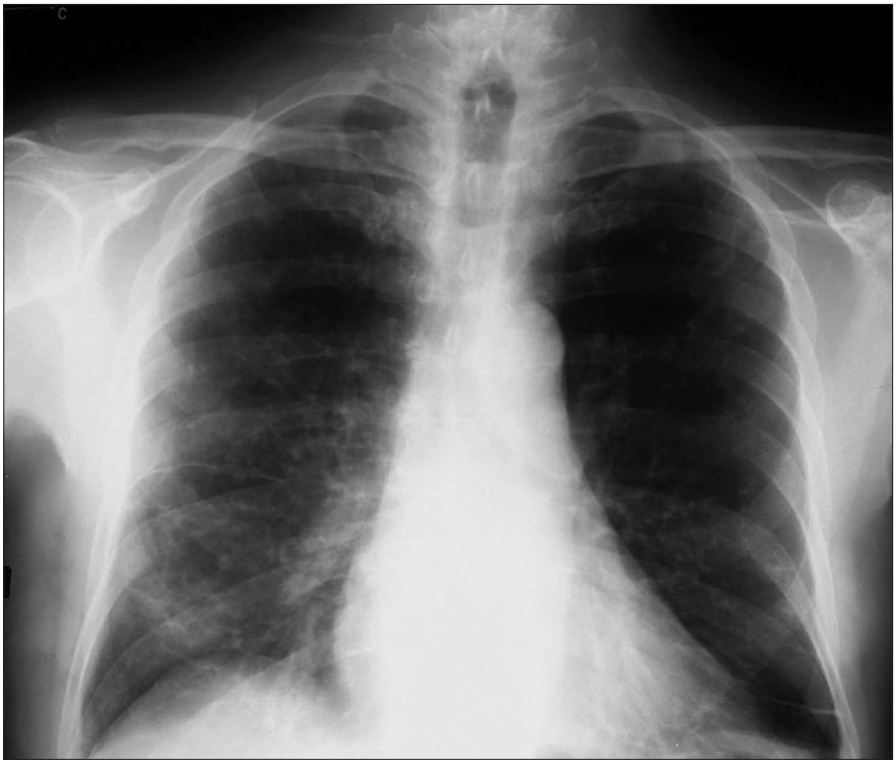
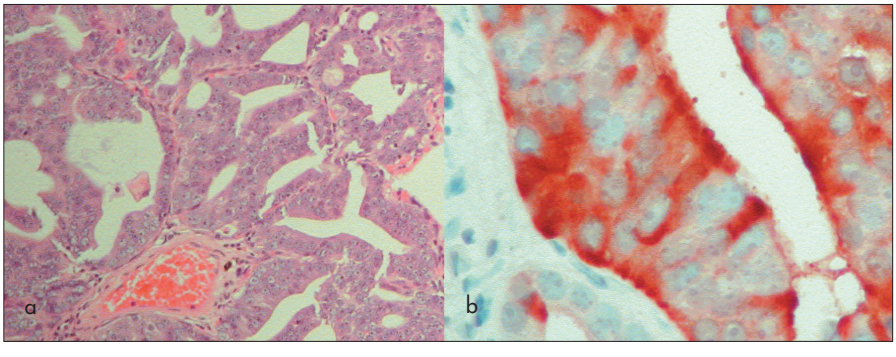


Figure 2. Histology of the metastatic pulmonary nodule (a) after standard haematoxylin and eosin staining with (b) positive prostate specific antigen staining confirming prostatic origin of the metastatic deposit.



CONCLUSION

This is an interesting case highlighting features of pulmonary metastatic prostate carcinoma and demonstrating that these may occur alone in the setting of a normal PSA level, even following apparently responsive hormonal manipulation. It may be worthwhile considering chest radiography in patients with a rising PSA level who have no other evidence of metastatic disease. The possibility of pulmonary metastases, even if other metastases are not apparent, should be considered, as early treatment will more than likely respond to hormonal manipulation. HM

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