A tale of four prostates

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Four urologists relate their personal experiences of prostate cancer and highlight some important learning points.

During the past two years, rather ironically, all four authors of this article, each a busy urologist in practice with an interest in prostate cancer, have themselves been diagnosed and treated for prostate cancer. Rather than hush it up, as if it were a dark secret, we decided that there would be some merit in terms of education, debate and awareness, if we were to make public the presentation and treatment of each of our four individual cases.

LEARNING POINTS
There are more than 1000 urologists presently practising in the UK. As there is a one in nine lifetime chance of being diagnosed with prostate cancer, the fact that there are at least four working urologists currently afflicted by the disease is probably not surprising. The four cases summarised here illustrate several important aspects of the management of prostate cancer, an area of medicine that is currently changing very rapidly.1

The first case (RK) illustrates the value of early detection using serial PSA testing in terms of diagnosing prostate cancer, while it is still confined within the capsule of the gland, and therefore potentially still curable. The results of the European Randomised Study of Screening for Prostate Cancer (ERSPC)2 confirm that mortality from prostate cancer, the majority of patients with low-risk, Gleason pattern 3+3=6 prostate cancer are now managed by active surveillance rather than by surgery or radiotherapy.6

A second learning point from this case is the value of high-resolution 3-Tesla MRI scanning, with gadolinium enhancement, in identifying suspect areas within the gland that can be targeted by either transrectal or transperineal ultrasound-guided biopsy (see Figure 1). Comparison of the preoperative MRI scan with the prostate itself after robotic surgery confirms the accuracy of this technology in localising the tumour. This in turn aids the surgeon in achieving negative surgical margins.

CASE 1: ROGER KIRBY
Roger Kirby, aged 61, an otherwise fit, asymptomatic individual who had measured his prostate-specific antigen (PSA) for more than a decade, noticed a gradual rise in PSA to 4.4ng/ml. 3-Tesla magnetic resonance imaging (MRI; Figure 1) revealed a suspicious focus in the right peripheral zone adjacent to but not penetrating the capsule. Transrectal ultrasound (TRUS)-guided biopsy confirmed Gleason 3+4=7 adenocarcinoma in three out of 12 cores. A bone scan was negative. A robotically assisted radical prostatectomy was performed, by Professor Dasgupta, without complications. Pathology confirmed complete excision of a Gleason 4+3=7 1.3cc tumour with invasion of the capsule but negative surgical margins. Recovery has been uneventful.

Go to the Trends website to view a video debate on this subject with Roger Kirby, Damian Hanbury and John Anderson: [URL to be added when available]
The second case (DH) illustrates the not uncommon dilemma of whether to use external beam radiotherapy in addition to androgen ablation when there are equivocal skeletal or soft tissue lesions, which may or may not represent metastatic disease. In this case there was a biopsy-proven locally advanced disease involving the prostate, which was responsible for the lower urinary tract symptoms, and a lesion within the pelvic bones, which may or may not have represented a metastasis. Fortunately, this area could be encompassed in the external beam radiotherapy field, which was used to treat the primary lesion.

Case 3 (JA) is most unusual in presenting with liver metastases, in spite of a normal PSA only a few months before and no other evidence of disease elsewhere. It does illustrate how the PSA level can be misleading, in spite of quite large-volume metastases, especially in very poorly differentiated tumours. Hormonal therapy produced a useful but relatively short-lived response, and fortunately taxane-based chemotherapy seems to be producing a second remission.

The final case (SV) illustrates the not uncommon presentation of locally advanced disease with lymph node metastases and the subsequent development of symptomatic bone metastases requiring local radiotherapy to resolve. A combination of androgen ablation with taxane-based chemotherapy and additional abiraterone has produced a prolonged response. The new oral agent enzalutamide, which has produced impressive results in clinical trials, and the encouraging clinical profile of the alpha-pharmaceutical Alpharadin are likely to be the next therapeutic options.

DISCUSSION

Anxieties about overtreatment of low-risk, low-volume Gleason 3+3=6 prostate cancers have fostered the myth that prostate cancer is somehow a toothless tiger. Consideration of the four clinical situations above, drawn from the ranks of actively practising urologists, clearly illustrates that this is not always the case.

Progress with treatment is being made with kinder, minimally invasive, robotically assisted surgery and better targeted, more powerful radiotherapy. Androgen ablation therapy still provides the mainstay of therapy for metastatic disease, but abiraterone, enzalutamide, Alpharadin and chemotherapy...
with taxotere or cabazitaxel are all now useful, evidence-based, second-line options when hormone relapse occurs.\textsuperscript{10}

One key question is whether or not we should all carefully monitor our own, and our patients’, PSA levels over time, and respond to a rise by organising a 3-Tesla MRI and a targeted biopsy of the prostate to achieve early detection. In one of the four cases (JA), the PSA was negative only a few months before presentation; in another (SV), the PSA rose from 1.4 to 78ng/ml over an 18-month time frame. Clearly, annual PSA testing would not have been helpful in either of these situations. New, better ways are needed to identify poorly differentiated, aggressive prostate cancers as they often do not manufacture and secrete PSA in their early, potentially curative stages.

The debate about screening for prostate cancer seems likely to run and run, especially since the ERSPC\textsuperscript{2} reported a positive result, while the US-based Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial\textsuperscript{11} produced a negative one. To compound the problem, while a Scandinavian study of radical prostatectomy versus watchful waiting revealed a survival advantage for patients treated surgically,\textsuperscript{12} the US-based Prostate Cancer Intervention versus Observation Trial (PIVOT) showed no benefit.\textsuperscript{13}

There is at last a realistic prospect for more targeted screening of those most susceptible to the disease.\textsuperscript{14} More than 30 prostate cancer susceptibility genes have been identified and it seems possible that men unlikely to develop prostate cancer could be excluded from screening protocols and instead attention focused on those most likely to develop the disease.

Much remains to be done to improve awareness about the risks of prostate cancer, among not only urologists, but also family practitioners and the general public. Although screening is still controversial, better treatments for hormone-relapsed disease are now becoming available. We sincerely hope that the openness about our own diagnoses and management will help to dispel the taboo that still haunts this most common of cancers of men.

REFERENCES