CASE REPORT

UROLOGICAL ONCOLOGY

Squamous cell carcinoma of the prostate following treatment with an LHRH–agonist: a rare case of transformation of adenocarcinoma of the prostate

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Squamous cell carcinoma (SCC) is a rare variant of prostate cancer. We report a case of a patient who was diagnosed with metastatic adenocarcinoma of the prostate, treated with leuprorelin and subsequently found to have SCC 18 months later. We have found one case in the literature with a similar scenario of possible transformation of adenocarcinoma to SCC secondary to luteinizing hormone–releasing hormone (LHRH) treatment. We found interesting similarities between the two cases, which raise the possibility of the transformation of tumour type and highlights the importance of the clinical picture in the follow–up, even with low prostate specific antigen (PSA) value.

Key Words: prostate ‹› adenocarcinoma ‹› squamous cell carcinoma ‹› LHRH

CASE REPORT

A 65–year–old Caucasian male presented with lower urinary tract symptoms and a PSA level of 84.5 ng/mL. A diagnosis of Gleason 4+5 adenocarcinoma of the prostate (Figure 1) was made on biopsies. He had a positive bone scan and was placed on LHRH analogue leuprorelin. He achieved a PSA nadir of 0.4 ng/mL.

Two years later he underwent transurethral resection of the prostate for worsening lower urinary tract symptoms. There was a wide–spread necrotic tumour extending from the verumontanum proximally involving the bladder neck, trigone and both ureteric orifices. Histopathology confirmed widespread infiltration of more than 90% of the chips with moderate to poorly differentiated keratinising squamous cell carcinoma (SCC) (Figure 2). There was no evidence of adenocarcinoma in the prostate chips this time. His new CT and bone scans restaged the disease as T4 N0 M0.

DISCUSSION

SCC of the prostate accounts for less than 1% of all cases of prostate cancers [1]. It tends to affect men in the seventh decade of their life and generally carries a worse prognosis than adenocarcinoma with early metastasis to bone liver and lungs. PSA and the Gleason grading system are of limited value in the diagnosis of SCC and the median post–diagnosis survival time is estimated to be 14 months [2, 6, 8–11].

While metastatic disease is fatal, organ–confined disease may be cured with radical cysto–prostatectomy [7]. Other treatment modalities such as radiotherapy and chemotherapy have been considered without being able to achieve long–lasting results [12].

We have found 23 reported papers on SCC of the prostate on PubMed using the key words: prostate, adenocarcinoma, squamous cell carcinoma, LHRH. There was one case reported describing a patient with an original diagnosis of prostate adenocarcino-

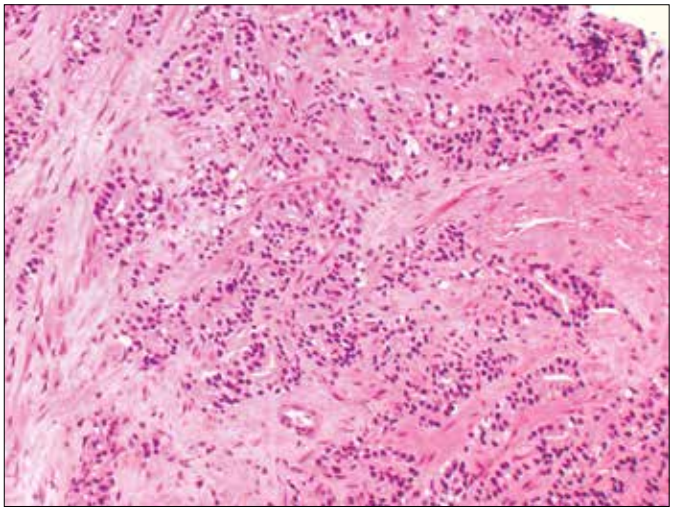

Figure 1. *Initial trans rectal prostate biopsies showing Gleason 4+5=9 adenocarcinoma of the prostate.*

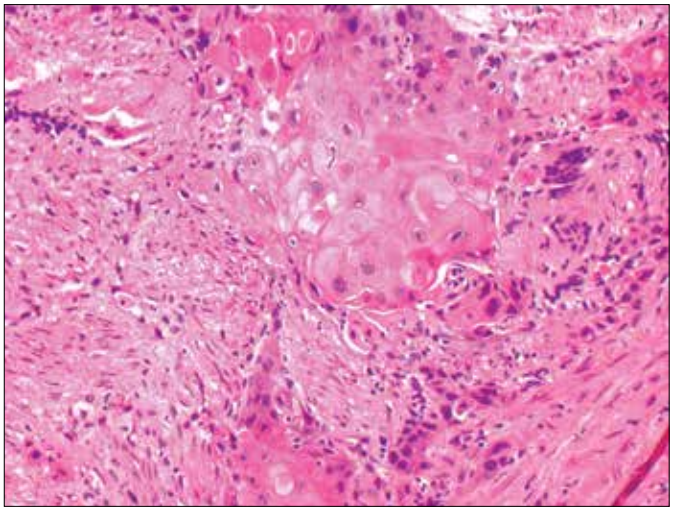

Figure 2. *Later (post LHRH treatment) trans urethral resection of the prostate chips showing new moderate to poorly differentiated keratinising squamous cell carcinoma with no evidence of adenocarcinoma.*

ma transformed after LHRH treatment (Braslis KG, et al.).

The origin of SCC of the prostate is not entirely clear [5]. It is proposed to be either of pure prostatic origin, prostatic or bladder urothelial squamous cell metaplasia, or a concomitant squamous metaplasia found within a primary adenocarcinoma [4]. While the concomitant type could still be an isolated new SCC, it has been proposed in the literature that it could be an adenocarcinoma modified by hormonal treatment [5]. Oestrogen–treated adenocarcinoma is commonly found to have elements of squamous differentiation [2, 4]. Another reported transformation of adenocarcinoma to SCC occurred secondary to radioactive seed implantation [3].

Table 1. *Similarities between our case and that of Braslis et al.*

Criteria	Our case	Braslis's case
Age	65	57
Initial Gleason score of AC	4+5=9	4+4=8
Hormone treatment	Leuprorelin	Leuprolide + flutamide
PSA nadir	0.4	<4.0
Presentation of SCC	TURP for worsening LUTS	TURP for worsening LUTS
TURP histology	SCC, no AC	SCC, no AC
Cysto–prostatectomy histology	N/A	SCC with small areas of AC
Duration of transformation	1–2 years (2010–2012)	2–3 years (1990–1992)
Prostatic Urethral Biopsy	N/A	Well differentiated SCC
Bone scan	Negative	Negative

In 1995, however, KG Braslis et al. reported the first and only case we found in the literature of SCC developing after treatment with LHRH for a high Gleason score adenocarcinoma. The SCC developed after treatment with leuprolide and flutamide. In a comment on the Braslis paper, MS Soloway from the University of Miami mentioned that a review of 113 radical prostatectomy specimens of patients who received neo–adjuvant LHRH treatment showed that 53% have squamous metaplasia in the prostatic ducts and glands as well as the prostatic urethra, and 13% had the same change in the malignant gland. He suggested that the transformation of the malignant gland is not expected to be a frequent event [2].

We have found very close similarities between our case and that reported by Braslis. These are summarized in Table 1. The prostatic urethral biopsy in the Braslis case was positive for well–differentiated SCC. It is difficult to explain how the proposed transformation has occurred in response to LHRH. It can still be argued that the development of SCC in both cases was purely incidental. The SCC in either case was found in more than 90% of the transurethral resection of the prostate (TURP) chips. The LHRH may affect both the benign and malignant gland. Could squamous metaplasia, or dysplasia, be an isolated event from the neoplastic process of the original adenocarcinoma?

Larger studies are required reviewing cases of the neo–adjuvant LHRH–treated prostate cancers undergoing radical prostatectomies to clarify the effect of LHRH on both the benign and the malignant component of the gland. Meanwhile, worsening lower

urinary tract symptoms and clinical progression on digital rectal examination are important parts of the follow–up of prostate cancer treatment, even when the PSA remains stable.

Abbreviations: adenocarcinoma (AC), squamous cell carcinoma (SCC), prostate specific antigene (PSA), transurethral resection of the prostate (TURP).

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