## CASE REPORT

## Fistulization in a locally advanced case of squamous cell carcinoma of the prostate

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Squamous cell carcinoma of the prostate gland is very rare, constituting 0.5%-1% of all prostatic malignancies. Though it has a similar clinical presentation to prostate cancer, the tumor is more aggressive, spreading to

Case report

A 74-year-old Caucasian male presented to a university hospital with frank painless hematuria for 1 week and subsequently developed acute urinary retention on a background of bladder outlet obstruction symptoms. His past medical history included hypertension, hypothyroidism and chronic obstructive airway disease. Clinical examination demonstrated a palpable bladder. In addition, a markedly enlarged, rock hard nodular prostate gland, estimated at 60 grams was

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Address correspondence address to Dr. Omer Raheem, Department of Urology, St James's Hospital, James's Street, Dublin 8, Ireland bone, liver and lung. The median survival time is approximately 14 months. Diagnosis is exclusively by histology. Therapeutic options may include radical surgery, radiotherapy, chemotherapy, hormonal therapy or a combination of these treatments. We present a case of locally advanced squamous cell carcinoma of the prostate and comment on its management and subsequent disease related complication.

**Key Words:** squamous cell carcinoma, prostate, fistula

palpated on digital rectal examination and clinically staged as T3 prostate cancer on both lateral lobes.

On admission, the patient's hematological and biochemical profile was performed. Hemoglobin level was 13.3 gm/dl (normal range 13.5 gm/dl-18 gm/dl), creatinine was 166 µmol/l (normal range 62 µmol/l-106 µmol/l) and prostatic specific antigen (PSA) was 19 ng/ml (normal range 0 ng/ml-4 ng/ml). An indwelling urinary catheter was subsequently inserted to decompress the urinary bladder which immediately drained a residual urine volume of 898 ml. On renal ultrasonography, a mild bilateral hydroureteronephrosis secondary to bladder outlet obstruction was identified. The patient proceeded to a channel transurethral resection of the prostate (TURP) of the lateral lobes (approximately 20 grams was resected).



**Figure 1a.** A high power (20x objectives) view of islands of well-differentiated squamous cell carcinoma of the prostate with intercellular bridges, central keratinisation and necrosis (Haematoxylin & Eosin stain).

Histology of the resected prostate specimens showed evidence of an invasive well differentiated squamous cell carcinoma (SCC) involving approximately 80% of the tissue examined with keratinization and necrosis. Perineural and vascular invasion was also identified, Figures 1a, 1b, 1c.

A staging magnetic resonance imaging (MRI) of the pelvis confirmed a locally invasive prostate cancer invading part of the mucosal layer of the anterior wall of the rectum, left neurovascular bundle and right seminal vesicle. In addition, bilateral iliac



**Figure 1b.** A high power (20 x objectives) of a focus of an invasive squamous cell carcinoma of the prostate, pleomorphic nuclei and prominent nucleoli (Haematoxylin & Eosin stain).



**Figure 1c.** Prostatic tissue, invaded by islands of welldifferentiated squamous cell carcinoma of the prostate (4x objective) (Haematoxylin & Eosin stain).

lymphadenopathy was also visualized confirming a radiological diagnosis of prostate cancer (T4N1M0), Figure 2. Additionally computerized tomography (CT) of the thorax, abdomen and pelvis revealed no evidence of metastatic disease. Technetium-99 (<sup>99m</sup>Tc) isotope bone nuclear scan did not show any evidence of bone metastases.



**Figure 2.** Axial T2 weighted high resolution Magnetic Resonance Imaging (MRI) of the prostate. 1, squamous cell carcinoma of the prostate breaching capsule of the prostate posterolaterally; 2, prostate gland and 3, invasion of the tumor into anterior rectal wall.



**Figure 3a.** Axial contrast enhanced Magnetic Resonance Imaging (MRI) of the prostate.1, necrotic tumor cavity/ abscess formation in continuity with prostatic urethra; 2, tract of the recto-vesical fistula.

This case was subsequently discussed at the urology/oncology multidisciplinary team meeting



**Figure 3b.** Axial contrast enhanced Magnetic Resonance Imaging (MRI) of the prostate. 1, prostate gland; 2, necrotic tumor cavity/abscess in continuity with prostatic urethra; 3, invasion of tumor into anterior rectal wall.

and given the locally advanced T4N1 disease, it was recommended to irradiate this patient with a palliative dose of external beam radiotherapy (RT) to pelvis. The early phase of RT was interrupted on several occasions by the development of hematuria, anemia and weight loss. Following the delivery of 18 Gy of the prescribed dose, the RT course was stopped after the development of a perineal discomfort associated with a discharging sinus. Subsequent pelvic MRI revealed the development of perineal abscess leading to the formation of prostatocutaneous and rectovesical fistula, Figures 3a, 3b.

The patient was initially managed conservatively; however he ultimately required a palliative ileal conduit and sigmoid colostomy diversion. Postoperatively, the patient made an uncomplicated recovery and subsequently received additional palliative RT to the pelvis at a dose of 15 Gy. A year after the completion of RT, this patient remains disease stable with PSA < 0.1 ng/ml with good stoma function and no additional management problems, apart from a single requirement for blood transfusion secondary to development of anemia.

## Discussion

Prostate cancer is the most common noncutaneous cancer and only second to lung cancer as a leading cause of cancer deaths in men in the western world.<sup>1</sup> Although, the vast majority of prostate cancer is adenocarcinoma, SCC of the prostate is very rare and constitutes only 0.5%-1% of all prostate cancer. The common age of presentation is the sixth decade.<sup>2</sup> Although, the clinical presentation of SCC of the prostate is much more aggressive and presents often with early disseminated disease, symptoms related to bladder outlet obstruction can be an early presentation.<sup>3</sup> SCC of prostate commonly metastasizes to bone (mainly with osteolytic lesions rather than osteosclerotic), liver and lungs more than local disease extension.

The median postdiagnosis survival is 14 months.<sup>2</sup> The first case report of prostate SCC was described in 1977 by Wenk et al.<sup>4</sup> Since then, approximately 130 cases have been reported in the medical literature indexed by PubMed service.

The diagnosis is confirmed on histological review by the presence of histological features of SCC differentiation such as keratinisation, squamous pearls and intercellular bridges.<sup>2,5</sup> Mott suggested histological criteria for the diagnosis of SCC of the prostate including 1) a clearly malignant neoplasm as judged by invasion, disordered growth and cellular anaplasia; 2) definite squamous features of keratinization, squamous pearls and/or numerous distinct intercellular bridges; 3) a lack of any glandular or acinar pattern; 4) no prior oestrogen therapy; 5) an absence of primary squamous cancer elsewhere, particularly within the bladder.<sup>2</sup> Primary seminal vesical SCC with prostatic extension must also be ruled out during the patient investigations.<sup>3</sup> The diagnosis of prostate SCC has been reported to be associated with schistosomiasis, chronic prostatitis, pelvic irradiation, prostatic infarcts and estrogen exposure although none of these appeared relevant in our patient.<sup>6-8</sup>

Several therapeutic approaches have been employed in prostate SCC management including radical surgery, radiotherapy, chemotherapy and hormonal therapy. None of these approaches have demonstrated significant survival benefit.<sup>5</sup> The lack of large randomized trials can be partly explained by the rarity of the diagnosis, the locally advanced nature of the disease, with rapid disease progression in many patients, thus limiting the opportunity to determine more effective treatment options for these patients.

Although, definitive treatment strategies for prostate SCC are limited, combined modality approaches including external beam radiation, systemic hormonal, chemotherapy and radical surgery have been suggested with questionable benefit.<sup>9,10</sup>

In contrast to adenocarcinoma of prostate, there is limited evidence in the literature to support prostate SCC express PSA. One theory proposes that SCC of the prostate results from dedifferentiation of prostatic adenocarcinoma and the presence of PSA staining in some neuroendocrine cells appear to support this hypothesis.<sup>11</sup> Some studies reported on low amounts of PSA found in patients with prostate SCC at diagnosis.<sup>9,10</sup> In our case report, PSA level was 19 ng/ml at diagnosis, this would suggest that PSA is secreted from the tumor and/or from destruction of the surrounding normal tissue. One would suspect that the PSA would respond to hormonal manipulation due to shutting down the prostate itself; however this needs to be proven immunohistochemically.

In a published case report, a 76-year-old man diagnosed with locally advanced nonmetastatic SCC of prostate, was treated with a concurrent chemoradiation approach (three courses of cisplatin 75 mg/m<sup>2</sup> on day 1 and continuous infusion 5-fluorouracil 750 mg/m<sup>2</sup> on day 1 to 5) and, subsequently, radiotherapy, with the delivery of a total dose of 46 Gy to the whole pelvis, with additional boost doses of 20 Gy to the prostatic bed and adjunctive 6 Gy to the prostate gland. This patient remained disease free for 5 years before finally experiencing local relapse and subsequently dying of acute renal failure secondary to bilateral hydroureteronephrosis.<sup>10</sup>

An earlier published case report has also commented on the potential benefit of combined chemoradiotherapy with regards to prolonged disease specific survival up to 18 months. A 65-year-old man received 50 Gy and 10 Gy of external beam radiation to the pelvis and prostate respectively, in addition to 15 mg of intravenous peplomycin was given weekly up to 150 mg and 80 mg/m<sup>2</sup> and cisplatin every 4th week for two cycles.<sup>8</sup>

In the context of a locally advanced SCC of prostate, external beam radiotherapy may be useful for symptom control, albeit with an increased risk of radiation related complications such as fistulization because of the locally advanced nature of disease. It is also hypothesized that combined chemoradiotherapy modality can diminish the probability of systemic spread. Data from recent clinical trials on other sites of SCC e.g. head and neck, cervix and non small cell lung carcinoma have recommended the use of the combined chemoradiotherapy approach with particular emphasis on its evolving standard of care.<sup>12-14</sup>

It is most probable that this patient's development of fistula primarily related to his late stage presentation and subsequent initial tumor response to the palliative radiation course. Despite improvements in the technical aspects, pelvic radiation related complications can occur in up to 20% of patients when high dose protocols are required to large treatment volumes. The most common serious pelvic radiation related complications are radiation enteritis and colonic stricture. Other less frequent complications include radiation proctitis, fistula formation and small bowel obstruction.<sup>15</sup> In a study published by Turnia et al,<sup>15</sup> the occurrence rate of visceral fistulization following radiotherapy for pelvic malignancy (25 colorectal carcinoma, 10 prostate cancer, 7 cervical carcinoma and 6 other tumors) was 17%, however fistula formation with modern 3D conformed or intensity modulated radiation therapy (IMRT) prostate protocols is very rare. Three were enterocutaneous, 3 were enterovaginal, 1 was enteroenteric, and 1 was rectourethral fistula. Four fistulas required stoma at initial admission. All patients required resections with successful fistula repair.<sup>15</sup> In our case report, poor general condition and performance status have prevented the patient from undertaking a formal repair of the rectovesical fistula. An earlier study by Perez et al noted a 0.4% occurrence rate of vesicosigmoid and rectovesical fistula in 738 patients with prostate cancer, all of which required colostomy.<sup>16</sup>

Management of the vesicosigmoid and rectovesical fistula is mainly achieved by colonic and/or urinary diversions.<sup>15,16</sup> As shown in this case report, symptoms

of fistulization can be alleviated by ileal conduit and sigmoid colostomy. No systemic therapy was given to this patient due to poor general condition.

In conclusion, this case report highlights the rarity and aggressiveness of SCC of prostate. The treatment options for locally advanced disease remain limited with poor outcome. Although radiotherapy can be a therapeutic option, the delay of this modality can be complicated following early tumor response in the context of locally advanced T4 disease and adjacent major organ/direct tumor extension. Randomized controlled trials will never likely be done on a rare population like this; the best that should be attempted is an effort at a large prospective registry to capture initial clinical and treatment as well as outcome data to try to make some conclusion regarding effective treatment(s).

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