Primary squamous cell carcinoma of the urethral diverticulum mimicking prostate cancer: Case report and review of the literature

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Abstract

Primary urethral carcinomas are uncommon, with urothelial carcinoma as the most common subtype. Urethral diverticulum is also rarely seen in men. A 44-year-old male presented with voiding symptoms. Abdominoperineal resection, prostatectomy, bladder neck excision, and proximal urethral excision were performed. A pathological examination revealed a well-differentiated squamous cell carcinoma (SCC) located inside an urethral diverticulum. We report this unusual case because primary SCC of the male urethral diverticulum is extremely rare. To our knowledge, our patient is only the second reported case.

Introduction

Primary urethral carcinoma (UC) is rare and accounts for less than 1% of all cancers.[1,2] UC is the most common subtype. Generally, UCs are seen in the 5th decade.[1,2] Patients presented with non-specific and overlapping clinical signs and symptoms.[1,3] Management of UC is still controversial and challenging due to lack of experience.[3] The surgical approach depends on the location and extent of the tumour. In advanced urethral squamous cell carcinoma (SCC), a combination of surgery, radiotherapy, and chemotherapy is recommended.[3-6] The 5-year overall survival in patients with UC is about 50% to 55%.[2,3,5]

Case report

A 44-year-old male presented with voiding difficulty and constipation for 3 months. He had a history of right nephrectomy for non-functional kidney secondary to a kidney stone. Although digital rectal examination revealed a hard, fixed mass on the anterior rectal wall, his prostate-specific antigen level was 0.61 ng/mL. A transrectal prostate biopsy was performed, and the pathological examination revealed a well-differentiated SCC. The patient was referred to our urology clinic with a preliminary diagnosis of primary SCC of the prostate. A magnetic resonance imaging (MRI) showed a 6 × 7.2 × 8.1-cm round mass with smooth margins and heterogeneous internal enhancement. The mass abutted the rectum and bladder, and extended to the apex of the prostate and the levator ani without sign of invasion (Fig. 1). The prostate and lymph nodes were normal. For the purpose of a differential diagnosis, a colonoscopy was performed and the mucosa was normal. The patient underwent a cystourethroscopy and biopsy under anesthesia. We demonstrated a large wide-mouthed urethral diverticulum and tumour growth in the bulbomembranous urethral diverticulum. The prostate was normal and the dimensions of the prostate were compatible with the patient's age. The bladder mucosa was intact, with external tumour compression. A histopathologic examination revealed a well-differentiated SCC with an inverted and warty growth pattern, keratinization with keratin pearl and dyskeratotic cells.

The patient was informed about the radical cystoprostatectomy and abdominoperineal resection if organ preservation was unfavourable, and informed consent was obtained. Abdominoperineal resection, prostatectomy, bladder neck excision, and proximal urethral excision were performed. On gross examination of the excision specimen, there was the prostate, bladder neck, tumoral mass, rectum, descending, and sigmoid colon. The tumour was located between the rectum and prostate. The cut surface of the tumour was a solid, grayish-white nodule, containing cysts and clefts. The diameter of the tumour was 13 cm. The tumour grew out of the urothelial lumen. It extended into the perirectal fat and rectum, which was ulcerated by the tumour (Fig. 2). On microscopic examination, the tumour included a well-differentiated SCC (Fig. 3, parts A, B). The urethral diverticulum was thick-walled, and included all layers of urethra. The epithelium of the diverticulum demonstrated

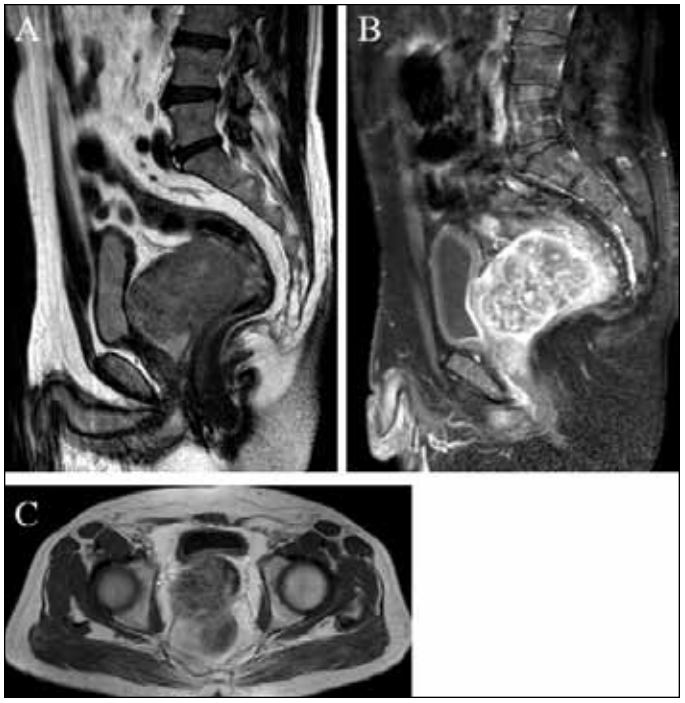

Fig. 1. Magnetic resonance imaging of the tumour. A: Sagittal T2-weighted image demonstrates tumour adjacent to the rectum and bladder. B: Sagittal T2-weighted post-contrast image demonstrates a 6 × 7, 2 × 8.1-cm round mass with smooth margins and heterogeneous internal enhancement. C: Axial T1-weighted image demonstrates tumour abutting the bladder.

Fig. 2. Gross appearence showing a large grayish-white tumour invading perirectal fat. The urethral diverticular wall depicted by arrow-heads. Tumour was seen inside the urethral diverticulum. The rectal mucosa depicted by stars.

foci of squamous metaplasia and dysplasia (Fig. 3, part C). No malignant prostatic glands were identified (Fig. 3, part D). The tumour extended into the left seminal vesicle and perirectal fat (Fig. 3, parts E, F). It infiltrated the rectum and the rectal mucosa was ulcereted (Fig. 3, part F). Immunohistochemically, the peritumoral area and epithelium of the diverticulum were CK7-positive. The tumour was p16-negative and P63-positive. Consequently, SCC seemed to arise from the squamous metaplasia of the diverticular epithelium.

No additional treatment was carried out due to the patient's other conditions. There was no evidence of disease recurrence after 9 months, in either the thoracic computed tomography or abdominal MRI.

Discussion

Primary UC is a rare urogenital cancer. In the European Union and the United States, the age-standardized rate is 1.6/million and 4.3/million for men, respectively.[2,3] The age-standardized rate for aged <55 years is very infrequent and negligible.[3] For male UC, the main predisposing factor is chronic inflammation.[1,5] Urethral strictures, urethroplasty, intermittent catheterization, history of radiotherapy, urethritis, and human papilloma virus 16 have been associated with primary UC.[3,5] It has been associated with many types of SCC, and confers a better prognosis, especially in the head and neck.[1,5] In our case, neither coilocytosis nor an expression of p16 was shown. Although no risk factor could be identified in our patient, a history of kidney stone might have led to chronic inflammation.

Urethral diverticular carcinoma (UDC) is another entity. UDC accounts for 5% of all female urethral carcinomas.[1,5] This cancer may arise from the urethral diverticulum.[5] Most urethral diverticulum do not include all the layers of urethra. Therefore, Ahmed and colleagues believe that a separate classification system for UDC is required.[5] Despite this, in the latest guideline for primary UC, UC and UDC are assessed together.[3] The first patient with UDC was reported by Hamilton in 1951, and since then about 100 female cases and only 1 male case have been reported.[5,7] Liew and colleagues reported first male UDC case, and the histological subtype was SCC.[7] Urine in the diverticulum led to symptoms, such as infection, stone formation and even carcinoma.[1,5,8] Although UC is the predominant subtype of primary UC (54%–65%), histologically, the most common subtype of UDC is adenocarcinoma, followed by SCC and UC in females.[1,3,5] In the literature, 10 females and 1 male SCC of urethral diverticulum have been reported (Table 1).[5] Our patient is therefore only the second reported case of male UDC, to our knowledge.

Diagnosis of UC is often delayed because of the non-specific and diverse symptoms.[3,5] The bulbomembranous urethral disease has a worse prognosis than distal disease due to diagnostic difficulty. The optimal treatment of UC has not yet been determined.[3] For proximal urethra, surgery alone achieves 5-year disease-free survival rates from 0% to 15%.[1,3,5,9] In advanced disease, the overall response rate

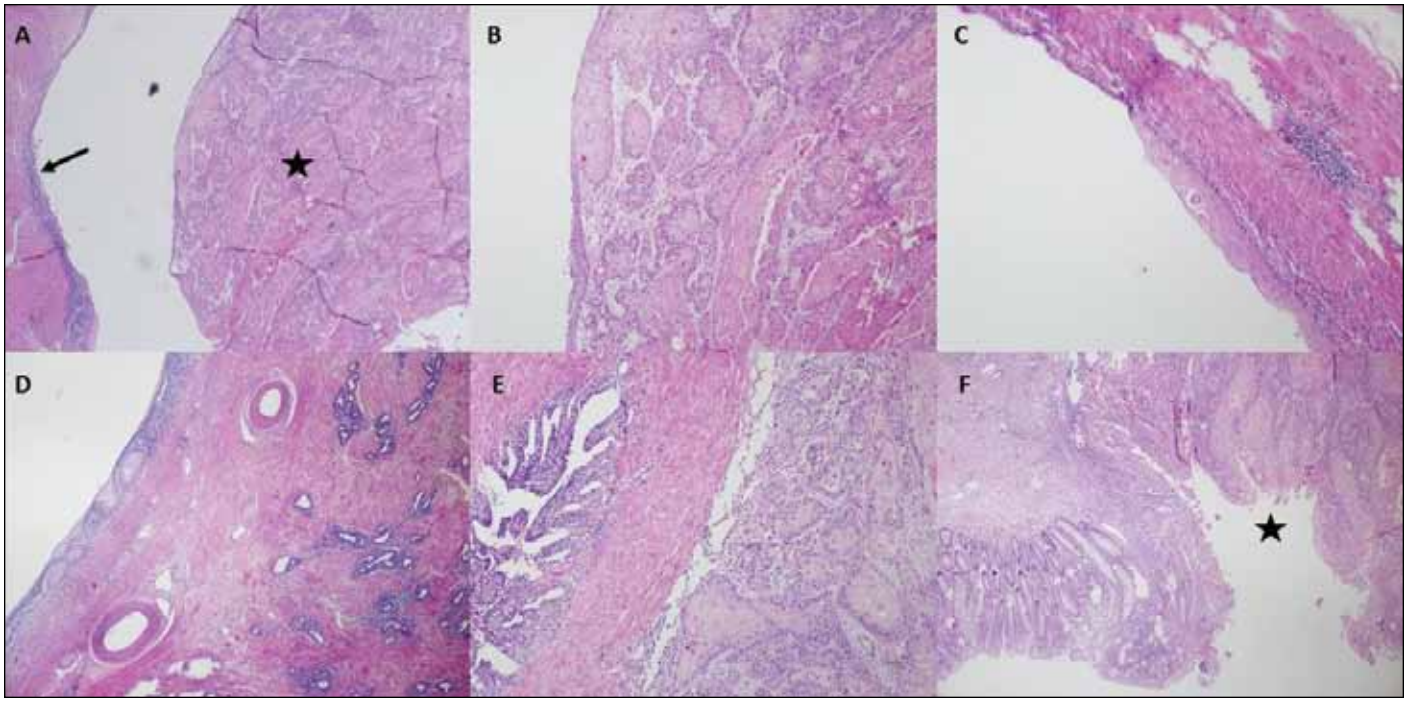

Fig.3. A: Section showing a well-differentiated squamous cell carcinoma and urothelium which depicted by star and arrow, respectively (hematoxylin and eosin stain [H&E] ×100). B: Section showing islands of squamous cell carcinoma with areas of keratinization forming keratin pearls (H&E ×200). C: Section showing foci of squamous metaplasia and dysplasia in epithelium of the diverticulum (H&E ×200). D: Section showing prostatic gland without sign of invasion (H&E ×100). E: Section showing invasion of left seminal vesicle which depicted by arrow (H&E ×200). F: Section showing infiltration of the rectum and ulcer of rectal mucosa which depicted by star (H&E ×100).

to cisplatinum-based chemotherapy alone and chemoradiotherapy are 72% and 83%, respectively.[3,4,6] Multimodal treatment with chemoradiotherapy and salvage surgery is recommended in advanced UC to improve local control and survival.[3-5] Salvage surgery alone improves 5-year disease-free survival rates from 54% to 72%.[3,10] Multimodal treatment was planned for our patient. In spite of this, no additional treatment was carried out due to the patient's request and his other conditions.

Conclusion

To our knowledge, this is the second reported case of SCC of the male urethral diverticulum. However, additional experi-

Table 1. Cases of urethral diverticular squamous cell carcinoma

Authors, year	Age	Gender	Location	Symptoms	Stage	Treatment
Thompson and Bivings, 1962[11]	46	Female	Unknown	Mass	T3	Radiotherapy
Wishard et al, 1963[12]	43	Female	Proximal	Bleeding	T3	Diverticulectomy
Huvos et al, 1969[13]	58	Female	Proximal	Mass	T3	Radiotherapy
Torres and Quattlebaum, 1972[14]	59	Female	Unknown	Unknown	Unknown	Diverticulectomy
Gonzales et al, 1985[15]	48	Female	Distal	Obstruction	Unknown	Diverticulectomy + adjuvant radio/chemotherapy
Gonzales et al, 1985[15]	36	Female	Middle	Mass	Unknown	Diverticulectomy + adjuvant radio/chemotherapy
Clayton et al, 1992[16]	44	Female	Middle	Hematuria	T3	Neoadjuvant + cystecomy
Clayton et al, 1992[16]	47	Female	Middle	Hematuria	T3	Cystectomy + neoadjuvant + adjuvant
Clayton et al, 1992[16]	63	Female	Middle	Urgency	T2	Diverticulectomy + adjuvant radio/chemotherapy
Shalev et al, 2002[17]	38	Female	Unknown	Irritative symptoms	Unknown	Cystectomy
Liew et al, 2003[18]	55	Male	Middle	Frequency	Unknown	Diverticulectomy + urethectomy + urethroplasty

ences are required for evaluation, differential diagnosis, and treatment of locally advanced UDC. Both the patient and the physician should be aware of the complicated operation involved and the additional chemoradiotherapy regimens.

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This paper has been peer-reviewed.

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