Primary squamous cell carcinoma of the male posterior urethra: a rare urogenital malignancy

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SUMMARY
Primary urethral cancer is an extremely rare and aggressive malignancy. Due to its rarity and the lack of large prospective trials, no standardised treatment protocols are currently available, and treatment decisions are most often made on a case-to-case basis. We present the case of a 62-year-old male with squamous cell carcinoma of the posterior urethra treated at our institution followed by an in-depth discussion on presentation, diagnosis and treatment of this rare cancer.

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INTRODUCTION
EPIDEMIOLOGY
Primary urethral cancer represents <1% of urogenital malignancies with a median age at diagnosis of 60. Incidence increases with age and is higher in black race.1,2 The most common histological subtypes of primary urethral carcinoma are urothelial carcinoma (54-65%), followed by squamous cell carcinoma (SCC; 16-22%) and adenocarcinoma (10-16%).1,3

RISK FACTORS
Risk factors for male primary urethral carcinoma include urethral strictures, chronic irritation due to intermittent self-catheterisation, history of urethroplasty, external beam radiotherapy, radioactive seed implantation and chronic urethritis caused by sexual transmitted disease (e.g., human papilloma virus).4-7

CASE REPORT
A 62-year-old male with a childhood history of long-term urethral catheterisation after a skull fracture and subsequent recurrent urethral strictures for which he underwent multiple internal urethrotomies presents with a 6-month history of perineal pain and swelling. Urethroscopy during a recent internal urethotomy procedure reveals necrotic tissue in the bulbar urethra, which is identified on pathology as SCC.

Magnetic resonance imaging (MRI) of the pelvic floor confirms a bulbar mass reaching into the corpus spongiosus. Clinical examination and inguinal ultrasound show a left-sided adenopathy of which a core needle biopsy is taken revealing a metastasis of the urethral SCC. Subsequent positron emission tomography/computed tomography (PET/CT) confirms the urethral mass and left-sided adenopathy without any other distant metastatic locations. The tumour was thus staged as cT2N1M0.

After multidisciplinary oncological consultation, the patient underwent radical surgical excision under the form of total urethrectomy with radical prostatectomy and pelvic lymph node dissection (PLND) as well as left-sided radical inguinal lymph node dissection (ILND) and right-sided modified...
ILND. A continent catheterisable stoma was created for urinary diversion. Surgical margins were negative, however, SCC reached up to the dorsal urethral margin. Twenty-eight pelvic nodes and ten right-sided inguinal nodes were excised, all negative for malignancy. Of the twelve left-sided inguinal nodes resected, one was positive for SCC and did not show extracapsular extension.

After a multidisciplinary case discussion involving experts from Christie’s Manchester, St. Geoges Hospital London and University College London Hospital (UCLH) on the Clinical Patient Management System (CPMS) via the European Reference Network for rare urogenital diseases (eUROGEN), the patient underwent adjuvant treatment under the form of concomitant radiochemotherapy. This consisted of a 28x1.8 Gy dose to the tumour bed and inguino-pelvic lymph node areas and six cycles of cisplatin. Chemotherapy had to be discontinued after four cycles due to neutropenia. Oncological follow-up with PET/CT at five and eight months was completely negative. The patient developed mild radio-rectitis complaints that were treated symptomatically and is still alive at time of publication. He is catheterising via an umbilical stoma and has complaints of overactive bladder with low bladder capacity and sometimes urinary leakage via the stoma. Botox injections in the detrusor have recently been administered. If not sufficiently effective, we will plan ileal augmentation cystoplasty when he is recurrence-free for at least one year.

DISCUSSION

CLINICAL PRESENTATION AND DIAGNOSIS

Urethral cancer typically presents late with aspecific symptoms. Voiding and irritative lower urinary tract symptoms as well as haematuria or urethral bleeding are most frequent. Other symptoms include urethral discharge and penile or perineal mass. Clinically enlarged lymph nodes in patients with urethral SCC most often represent metastatic lymphatic spread. However, it is notable that where lymphatics from the anterior urethra drain into the superficial and deep inguinal lymph nodes and subsequently into the pelvic lymph nodes, the posterior urethral lymphatics drain directly into the pelvic lymph nodes.

IMAGING

Magnetic resonance imaging has become the new gold standard for clinical staging and evaluating local tumour extent, thus facilitating surgical planning, whereas whole body PET/CT is an excellent screening tool for distant metastases. Ultrasonography with fine needle aspiration or core needle biopsy where possible is recommended for the detection of malignant lymph nodes.

MULTIMODAL TREATMENT

Surgery or radiotherapy alone could be sufficient for distal and low stage urethral tumours. Treatment of advanced stage posterior SCC, however, should be multimodal and include radical surgery. Total urethrectomy with urinary diversion after bladder neck closure is usually required. For patients with advanced disease at presentation and/or nodal metastases, neo-adjuvant cisplatin-based chemotherapy is recommended as this improves overall survival and recurrence-free rates after consolidating surgery. Gakis et al. reported improved survival of locally advanced (cT3 and/or cN+) patients who received neo-adjuvant chemotherapy with or without radiation therapy compared to those
FIGURE 2. Surgical specimen. En bloc resection of urethra with corpus spongiosum, prostate and bladder neck.

who underwent upfront surgery with or without adjuvant chemotherapy. Dayyani et al. reported an overall survival rate of 50% at 42 months for patients with locally advanced disease and treated this way with curative intent (i.e., ≥cT3 and/or N+, but M0). Wide negative surgical margins should intraoperatively be confirmed, and reconstruction of defects with pedicled myocutaneous flaps can be needed after such radical surgery.

NODAL DISSECTION
Although clear evidence supporting prophylactic bilateral inguinal and/or pelvic lymphadenectomy is lacking, which increases postoperative morbidity, regional lymphadenectomy should strongly be considered in the initial treatment approach of patients with clinical enlarged or histologically proven malignant nodes since complete nodal control could still be possible in these patients.

ADJUVANT THERAPY
Data on adjuvant therapy is very scarce, but adjuvant chemotherapy has a role in locally advanced disease and is possibly associated with improved outcomes. Neo-adjuvant therapy, however, is often preferred with the intent of tumour downstaging prior to radical surgery. External beam radiotherapy to the pelvis has been used as adjuvant treatment after surgery as well as for local recurrence in selected cases.

OUTCOME
Outcome after radical treatment is highly variable. Negative predictors of overall survival in all primary urethral cancer are the presence of metastatic lymph nodes, posterior urethral localisation, higher tumour stage and SCC histology. This means that proximal urethral SCC is one of the most
aggressive urethral tumours. Owing to its usually late presentation and aspecific symptomatology, it mostly presents as advanced disease at diagnosis. Muneer et al. reported on one of the largest series of proximal urethral SCC in an expert centre and described a one-year overall survival rate of 34%. This is in line with the series by Dalbagni et al. who described a five-year overall survival rate of 26% for posterior urethral carcinoma versus 69% for anterior urethral carcinoma. Salvage surgery or radiation therapy in patients who underwent primary surgical treatment and developed recurrent local disease results in similar survival rates as those of patients who never developed recurrent disease.

**CONCLUSION**

SCC of the male proximal urethra is a very rare and aggressive urogenital cancer that often presents late with aspecific symptoms. Standardised treatment protocols are lacking but we believe that a multidisciplinary approach based on radical surgery combined with (neo)-adjuvant chemotherapy and radiation therapy provides the highest therapeutic benefit as represented by this case.

**REFERENCES**