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Adenocarcinoma of the urethra: A rare subtype of urethral cancer

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ABSTRACT

Urethral adenocarcinoma (UA) is a rare type of urethral cancer with a poor prognosis. We present a case of UA of intestinal subtype in a 57-year-old patient who initially had lower urinary tract symptoms and was subsequently found to have a urethral lesion in a urethral diverticulum on pelvic MRI which was confirmed on biopsy. She had neoadjuvant chemotherapy followed by open anterior pelvic exenteration, complete urethrectomy and ileal conduit urinary diversion. She required adjuvant chemotherapy for local invasion and a metastasis in the uterus but developed progressive metastatic disease and succumbed to the disease 13-months after surgery.

Introduction

Urethral adenocarcinoma (UA) is rare type of urethral cancer which accounts for less than 5% of urethral carcinoma cases.[1] Histologically, UA is further subclassified into two other subtypes: clear cell and columnar/mucinous (intestinal).[1] Several risk factors for UA have been postulated, including pelvic radiation therapy, urethroplasty, intermittent catheterisation, chronic urinary tract infection and sexually transmitted infection, all of which trigger chronic inflammation of the urethra.[1] Patients with UA typically present with haematuria, lower urinary tract symptoms and occasionally a palpable mass.[1] Unfortunately, since patients with UA tend to present later in the disease, survival outcomes for UA is poor with a 5-year survival rate of 31%.[2] Furthermore, women with UA tend to have poorer survival outcomes than men.[2] The literature surrounding UA is scarce and there are no guidelines regarding its management.

We present a patient initially presenting with lower urinary tract symptoms who was found to have UA, of the intestinal subtype.

Case presentation

Patient A (57-year-old female) was referred to the emergency department (ED) at a tertiary hospital after failing a trial of void the day after she had an indwelling catheter (IDC) inserted for urinary retention. This was on a background of a 4-week history of dysuria, poor urinary stream, urgency, suprapubic pain. Patient A denied dyspareunia or post-void dribbling. She had a background of ulcerative colitis and previously underwent a pan proctocolectomy and end ileostomy. Her other medical history included asthma and depression. She was on regular dothiepin 37.5mg and Seretide 125/25mcg daily.

On examination, her vital signs were within normal limits. Her abdomen was soft, non-tender and her stoma was healthy. She had an IDC in situ. Blood tests revealed normal inflammatory markers and kidney function. An ultrasound of her renal tract performed 2 weeks prior showed an elevated post void residual of 300ml with no hydronephrosis. Urine collected at the time of presentation grew Citrobacter koseri and she was treated with a 5-day course of oral Augmentin Duo Forte. Patient was discharged from the ED and further elective follow-up was arranged.

A flexible cystoscopy showed extrinsic compression of the bladder neck anteriorly without any sinister bladder lesions. Pelvic MRI showed a urethral diverticulum at the mid-urethra with an enhancing filling defect and evidence of anterior vaginal wall involvement (Fig. 1). Urine cytology showed atypical cells. Patient A proceeded with a cystoscopy and urethral biopsy. Examination under anaesthesia revealed a large, firm anterior vaginal mass extending from bladder neck to distal urethral.

Histopathology revealed moderately differentiated UA of intestinal type (Fig. 2). The case was discussed at the uro-oncology multi-disciplinary team meeting, and the possibility of metastasis of an

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adenocarcinoma from another site such as the colon was discussed and excluded clinically and radiologically. Staging with flurodeoxyglucose-position emission tomography (FDG-PET) scan showed no nodal or distant metastases on FGD-PET. Due to the lack of treatment guidelines for UA, management was extrapolated from colorectal adenocarcinoma treatment guidelines. Patient A proceeded to neoadjuvant chemo-radiotherapy with capecitabine due to anterior vaginal wall involvement. She then had open anterior pelvic exenteration, complete urethrectomy (CU) and ileal conduit urinary diversion (ICUD).

Final pathology confirmed the diagnosis of primary UA of intestinal type. There was some chemoradiotherapy response. Patient A's specimen showed direct tumour invasion into the anterior vagina and urinary bladder wall with a metastatic deposit in the uterus, though margins were negative. She went on to have adjuvant capecitabine and oxaliplatin chemotherapy but developed further metastatic disease despite this. She was then switched to folinic acid, flurouracil and irinotecan chemotherapy of palliative intent. An initial repeat FDG-PET showed favourable partial response but subsequent scans showed further progression of metastatic disease and she died 13 months after surgery.

Discussion

Diagnosis of UA can be challenging as several differential diagnoses must be considered including secondary UA from the colorectum, pancreas, prostate, cervix and other sites, as well as benign mimics such as developmental heterotopia and urethritis glandularis. To confirm the diagnosis, numerous investigations are required, ranging from histopathological, immunohistochemical analysis of biopsy samples taken on cystoscopy; gastroscopy; colonoscopy; FDG PET; to tumour markers such as CA 19-9, CA 125, alpha-fetoprotein, and CEA. Histopathologically, UA of the intestinal subtype, as in our case, show malignant cells with evidence of gland formation and production of both intracellular and extracellular mucin.[3] Distinguishing primary versus secondary UA from the colon can be a diagnostic dilemma. However, immunohistochemical studies would aid in diagnosis with reactivity to CK-7 and CK-20, and non-reactivity to villin, suggesting primary rather than secondary UA from the colon.[4] Diagnostic confirmation of UA with intestinal subtype requires integrating all the aforementioned investigation findings.

Establishing the diagnoses for UA is critical as treatment for the other differential diagnoses is different. Based on the limited data available, management of UA is generally dependent on tumour stage with single and multimodality therapy offered for low-stage and high-stage disease respectively.[5] For the relatively uncommon small, superficial, distal UA local excision alone may be sufficient. However, for advanced UA typically involving proximal urethra and surrounding organs, OAPE in female or cystoprostatectomy in male with CU and ICUD with or without neoadjuvant and adjuvant chemotherapy and/or radiation therapy is favoured, as in our case.[5] There are no prospective trials studying chemotherapy use in UA. However, recent reports of UA patients who underwent chemotherapy with 5-fluorouracil, cisplatin or mitomycin C

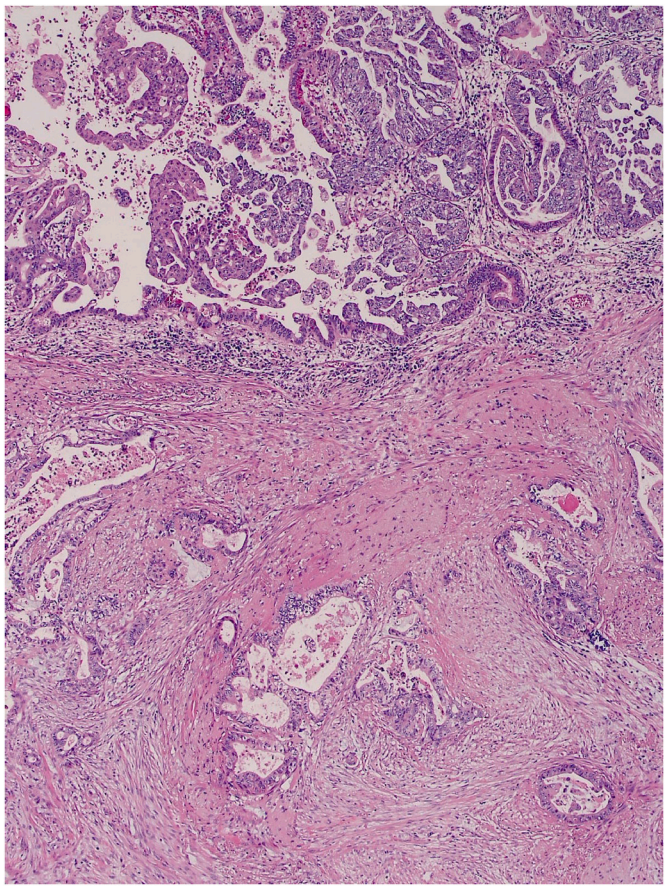

Fig. 2. H&E, x4 magnification. Complex villous processes, micropapillary arrangements and cribriform structures protrude into the lumen of the urethra, lined by malignant cells with intracytoplasmic mucin. Angulated glands lined by similar malignant cells infiltrate into the stroma below.

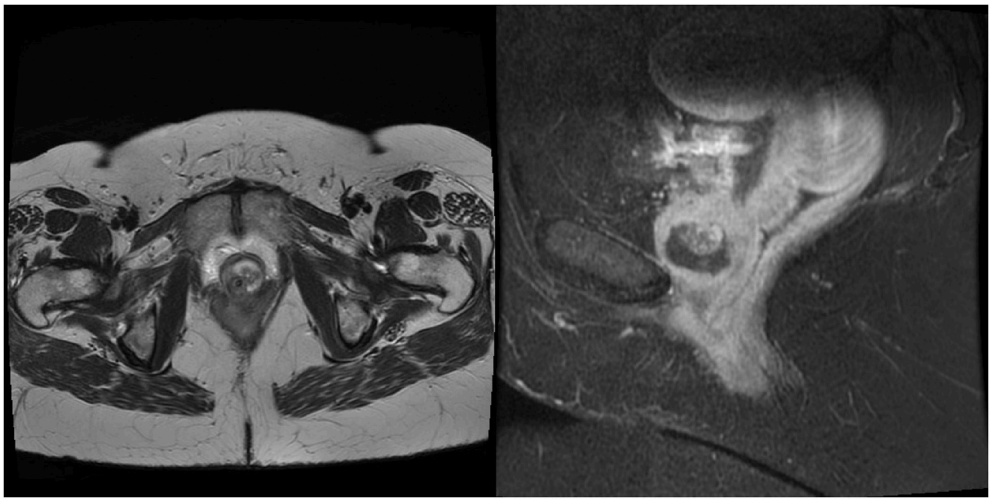

Fig. 1. MRI pelvis of Patient A. Urethral diverticulum with an enhancing filling defect representing urethral adenocarcinoma.

as primary management revealed a 60%–100% disease-free survival rate.[5]

Conclusion

In conclusion, our case reflects the poor prognosis of UA despite appropriate surgery combined with neoadjuvant and adjuvant chemotherapy. It also reflects the variable management options and the poor outcomes demonstrated in the literature. Data on chemoradiotherapy use in UA remains based on case reports and single institution experience. Due to the rarity of the condition the desirable trials may not be forthcoming.

Consent

Verbal and written informed consent was obtained from the patient's next-of-kin for publication of her de-identified clinical details and images.

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Author contributions

Drafting of the manuscript and case presentation - Pravin Viswambaram; Literature review and discussion: Oliver Oey; Histopathology image – Nicole Swarbrick; Revision of the manuscript: Pravin Viswambaram, Oliver Oey, Nicole Swarbrick, Dickon Hayne; Supervision: Nicole Swarbrick, Dickon Hayne. All authors have read and approved the final manuscript.

Declaration of competing InterestCOI

No authors have any conflicts of interests to report.

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