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Original article

Multimodal management of primary adenocarcinoma of the female urethra: About four cases

Prise en charge multimodale de l'adénocarcinome uréthral féminin : à propos de quatre cas

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ABSTRACT

Purpose. – To retrospectively analyse female patients treated for urethral adenocarcinoma, modalities of treatment and long-term outcomes.
Patients. – Four cases of primary female urethral adenocarcinoma were treated in the departments of urology and radiation-oncology at Georges-Pompidou and Necker hospitals (France) over a 7-year period.
Results. – All of them underwent surgery, with three presenting stage pT3-pT4 and one a positive cytology on inguinal node. Three patients received adjuvant cisplatin-based chemoradiotherapy up to 60 Gy, and one preoperative chemoradiotherapy at 45 Gy. Two recurrences were observed: one local relapse occurred at 9 months from the diagnosis and was treated by anterior pelvic exenteration followed by chemoradiotherapy, with no recurrence. One tumour relapsed both at the local level and on distant metastatic sites at 9 months from the diagnosis, and died 21 months after this progression. Median survival and progression-free survival are respectively 4.2 years and 13 months. Three patients are alive at 7, 4.5 and 3 years from diagnosis.
Conclusion. – Female urethral adenocarcinoma is a very rare entity and often present in locally advanced stages. Initial extensive surgery with pelvic exenteration should be considered, followed by chemoradiotherapy according to the surgical margins and lymph nodes involvement.

Mots clés :
Adénocarcinome de l'urèthre féminin
Exénteration pelvienne
Chimioradiothérapie
RCMI

RÉSUMÉ

Objectifs de l'étude. – Analyser rétrospectivement des dossiers de patientes prises en charge pour un adénocarcinome primitif de l'urètre, les modalités thérapeutiques et leurs résultats à long-terme.
Patientes. – Quatre patientes ont été prises en charge pour un adénocarcinome urétral dans les départements d'oncologie-radiothérapie et d'urologie et des hôpitaux George-Pompidou et Necker sur une période de 7 ans.
Résultats. – Toutes les patientes ont été opérées, trois tumeurs ont été classées pT3-pT4N0 et une adénopathie inguinale a été confirmée histologiquement (cN1). Une chimioradiothérapie adjuvante à base de cisplatine de 60 Gy a été délivrée à trois patientes et une chimioradiothérapie préopératoire de 45 Gy à une autre. Deux récidives sont survenues, une récidive locale à 9 mois du diagnostic, qui a

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été traitée par exentération pelvienne suivie d'une chimioradiothérapie, avec un contrôle local ultérieur, une locale et métastatique synchrone à 9 mois du diagnostic. Les durées médianes de survie globale et de survie sans progression étaient respectivement de 4,2 ans et 13 mois. Trois patientes étaient en vie à 7, 4,5 et 3 ans du diagnostic.

Conclusion. – L'adénocarcinome urétral féminin est une entité rare et est souvent localement évolué. Une chirurgie initiale de type exentération pelvienne devrait être envisagée pour ces formes localement évoluées, suivie d'une chimioradiothérapie selon les marges chirurgicales et l'envahissement ganglionnaire.

1. Introduction, epidemiological aspects

With an incidence of less than 1 per million women, primary carcinomas arising in the female urethra are a rare entity, mostly occurring above 65 years. These carcinoma accounts for 5% of all urethral malignancies, and represent 0.02% of all female carcinomas.

According to recent epidemiological studies, the most common found histologic subtypes in women are transitional (urothelial) cell carcinoma in 45% to 55%, squamous cell carcinoma in 19% to 21%, adenocarcinoma in 16 to 29% and unknown or undifferentiated carcinoma in 6% [1–3]. Thus, primary adenocarcinoma of the female urethra is among the rarest and most pejorative histology [1], while most patients present with advanced stages pT3–T4, accounting for 50% of all cases [3]. Survival outcome of urethral carcinoma has been associated with T stage, node involvement, non-squamous histological features, as well as the length of invasion along the urethra. In a recent population-based analysis reported by Champ et al., median survival reported for 359 women was 42 months, and 5-year and 10-year overall survival rate were respectively 43% and 32% [3].

The available published data consist mainly on small series or case reports. Given the paucity of patients, there is no standardized therapeutic strategy for the management of adenocarcinoma of the urethra, but the increasing reports of single-institution series tend to show that a multimodal strategy – combining extensive surgery and chemoradiotherapy – is likely to improve both local control rate and distant metastasis.

We report herein four cases of female urethral adenocarcinoma, three of them developed from known diverticula. Therapeutic strategy, success in preserving the bladder, patterns of failure, and outcomes are described, as well as a discussion on the optimal surgical and radiotherapy modalities.

2. Patients and methods

Based on ARIA software (Varian®) and the diagnosis encoded in the database, we searched the files for female patients who had been irradiated for urethral carcinoma in our department, in the last ten years. This matched with the data recorded by urologist surgeons; all of the cases of urethral adenocarcinoma operated the last years were colligated.

We retrospectively analysed the files of four female patients treated in the department of urology and radiation-oncology at Georges-Pompidou and Necker hospitals (Paris, France) over a 7-year period.

The patients' characteristics are summarized in Table 1.

The radiological aspects are shown in Fig. 1.

3. Results

3.1. Patient no. 1

This patient aged 61 years old complained of dysuria, suspubic pain, recurrent cystitis and a urinary retention, and had a past history of urethral diverticul removed 30 years ago.

A pelvis digital examination found an irregular induration of the anterior vaginal wall, occupying the totality of the anterior vaginal wall, guiding several biopsies of the urethra and vagina. Cystoscopy found a normal bladder, and clinical examination showed a depression of the anterior wall of the vagina, at 2 cm below the urethral meat. Repeated core biopsies were performed through an endovaginal approach. A supracentimetric inguinal adenopathy was also noted.

A primitive lesion measuring 25 × 20 mm, developed on the posterior wall of the urethra, on the vaginal urethra bulkhead, without lymph nodes involvement nor parametrial invasion was detected by magnetic resonance imaging (MRI). A hypermetabolism located on the primitive tumour, without metastatic dissemination was confirmed by (^{18}F)-fluorodeoxyglucose (FDG) positron emission tomography (PET).

A preoperative pelvic and inguinal chemoradiotherapy was performed, delivering 46 Gy in five weeks, with 5-fluorouracile 400 mg/m^2/day on day 1–5 and cisplatin 20 mg/m^2/day on week 1 and 5, leading to a partial radiological response.

Surgery was performed six weeks later by anterior pelvectomy, ureterectomy and transileal ureterostomy (Bricker).

Pathological examination found a white and firm tumoral infiltration developed from the urethra to the anterior vaginal wall. Microscopic examination revealed an adenocarcinoma embedded in a fibrous stroma with a glandular atypical proliferation admixed with a mucinous adenocarcinoma invading the urethral and anterior vaginal wall, the muscular wall of the bladder neckband. Urethral and vaginal distal margins were tumour free, as well as bladder urothelium, uterus and lymph nodes.

In the postoperative setting, complications occurred with an abdominal wall abscess and a urinary fistula treated conservatively by transient bilateral percutaneous nephrostomy and repositioning of urethral stents. At a follow-up of 4.5 years from the diagnosis, the patient was free of any recurrence, with a functional Bricker derivation.

3.2. Patient no. 2

Patient no. 2 reported a past history of pollakiuria, mictional leakages for one year. MDCT urography found a voluminous lesion,