HMJ

OLGU SUNUMU/CASE REPORT

Primer Kadın Üretra Karsinomu: Bir Olgu Sunumu

Primary Carcinoma of the Female Urethra: A Case Report

Engin Kölükçü[1] ORCID: 0000-0003-3387-4428, **Doğan Atılgan**[1] ORCID: 0000-0001-8584-2124, **Murat Beyhan**[2] ORCID: 0000-0002-8630-4632, **Faik Alev Deresoy**[3] ORCID: 0000-0002-2243-9394

[1]Department of Urology, Tokat Gaziosmanpasa University, Faculty of Medicine, Tokat, Türkiye.
[2]Department of Radiology, Tokat Gaziosmanpasa University, Faculty of Medicine, Tokat, Türkiye.
[3]Department of Pathology, Tokat Gaziosmanpasa University, Faculty of Medicine, Tokat, Türkiye.

Geliş Tarihi/Received: 24.02.2021
Kabul Tarihi/Accepted: 06.05.2021
Yazışma Adresi/Address for Correspondence:
Engin Kölükçü
Department of Urology,
Tokat Gaziosmanpasa University
Faculty of Medicine 60300,
Tokat, Turkey.
E-posta: drenginkolukcu@gmail.com

Anahtar Sözcükler:
Kadın
Üretra
Üretral Karsinom

Key Words:
Female
Urethra
Urethral Carcinoma

ÖZ

Kadınlarda primer üretra kanseri literatürde son derece nadir karşılaşılan bir durumdur. Bu olgu sunumunda hematüri yakınması ile başvuran ve primer üretra kanseri tanısı konulan 79 yaşındaki kadın hastanın literatür bilgileri altında tartışılması amaçlanmıştır.

ABSTRACT

Primary urethral carcinoma in women is rare in the literature. The aim of the present case report was to discuss with literature the 79 years old female patient who presented with hematuria complaint and was found to have primary urethral cancer.

Introduction

Urethral cancers are rare in women. They account for approximately 0.02% of all cancers in women. As with other types of cancer in the urinary system, there are no specific diagnostic symptoms. Dysuria, hematuria, urethrorrhagia, weak urine stream, pollakiuria, acute urinary retention, recurrent urinary tract infections, perineal pain are major complaints with which patients apply to clinics. This nonspecific clinical presentation often leads to delays in diagnosis, and urethral cancers are highly aggressive for both sexes (1). An in-depth analysis shows that studies into female urethral cancers with large case series are quite limited. Unlike other urogenital system tumors such as kidney, bladder and prostate, there is no detailed information about risk factors, diagnosis, follow-up and treatment approaches (2). Aim of the present case report was to demonstrate clinical approach we used, with a literature review, for a 79 years old female patient who applied to our clinic with hematuria complaint and had primary urethral cancer diagnosis.

Case Report

Seventy-nine years old woman admitted to our clinic about three months ago with intermittent hematuria complaint. Our patient, who was in the postmenopausal period, had a 20-year history of smoking packs. She had no surgery, radiotherapy or chronic disease except for dementia. In the medical history of our patient, it was determined that urethral catheterization was not performed for any reason. Results of laboratory examinations were as follows: serum creatinine 1.01 mg/dl, urea 36.11 mg/dl, hemoglobin 11.14 g/dl and white blood cell count 9100/mm^3. Urine analysis confirmed gross hematuria (RBCs full number), albumin +1, white blood cells 6-11/high power field (HPF), negative nitrite and casts absent. Plain abdominal x-ray appeared normal. Renal ultrasonography showed normal kidney measurements and echogenicity and it excluded hydronephrosis, masses or stones. On axial contrast-enhanced computed tomography examination, the 2 cm size mass lesion showing predominantly peripheral contrast enhancement, with a slightly irregular border, soft

Kölükçü E, Atılgan D, Beyhan M, Deresoy FA. Primary Carcinoma of the Female Urethra: A Case Report. Hitit Med J 2021;3(3):92-95.
10.52827/hititmedj.885131

tissue density, which is indistinguishable from the muscle plans extending to the periurethral area by filling the urethra. No pathological lymph node was detected in the parailiac or inguinal region adjacent to the mass lesion (Figure 1a,b). Images were evaluated by two radiologists, and no finding was found indicating metastatic disease within the limitations of contrast-enhanced computed tomography. Detailed physical examination showed papillary tumor mass in external urethral meatus. In cystourethroscopy, tumors were observed throughout the urethra. On the other hand, no tumor was observed in both bladder neck and bladder. It was observed that the lesion was fragile and hyperemic in the endoscopic evaluation, however it did not cause complete obstruction in the urethra. Cold cup biopsy was taken from the mass during endourological evaluation. In pathological evaluation of specimens, malignant tumoral infiltration was observed in the form of trabecular, insular and solid areas, indicating invasiveness in large areas. Tumoral structures were found to consist of large hyperchromatic malignant cells with pleomorphic nucleus, unclear margins, narrow eosinophilic cytoplasm and high nucleus/cytoplasm ratio. These cells had solid trabecular development forming focal follicle-like structures in some places. It was observed that they had quite pronounced pleomorphism and bizarre nuclear forms in some places with frequent and atypical mitosis (Figure 2a, b). Pathologists of our clinic reported that the tumor was an invasive high-grade urothelial carcinoma. Radical cystourethrectomy was performed with bilateral pelvic lymph node dissection, hysterectomy, salpengectomy and anterior vaginal wall excision followed by ileal urinary diversion. In accordance with the results of the urethra biopsy examination, histological evaluation of radical cystourethrectomy material showed tumor cells with large hyperchromatic and pleomorphic nucleus, unclear margins and pale eosinophilic cytoplasm. These tumor cells were observed to have frequent and atypical mitosis (Figure 2c). Pathology showed high grade urethral carcinoma (TCC) without metastases in other urogenital organs examined within the surgical specimen. After a

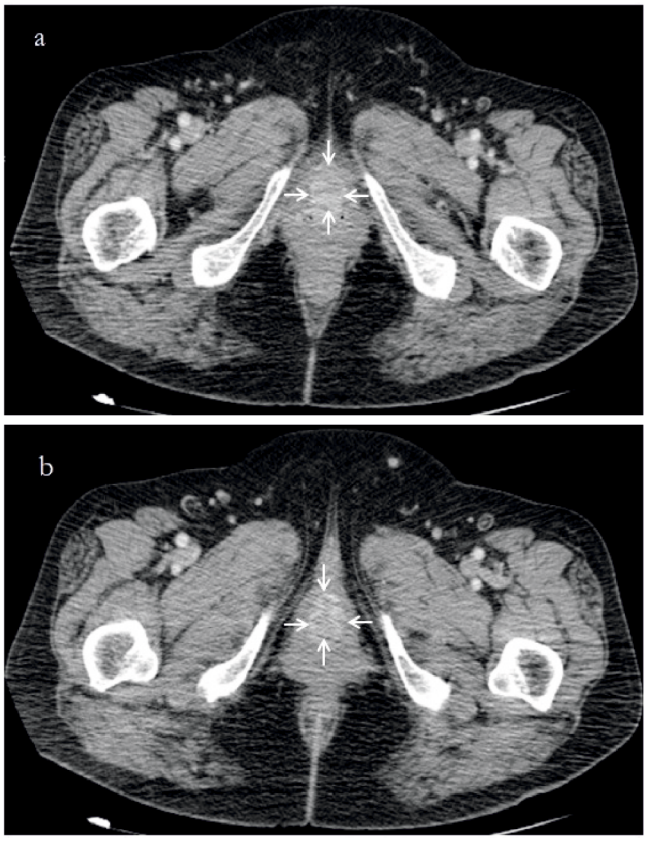

Figure 1a,b. The 2 cm size mass with predominantly peripheral contrast enhancement in the urethra in whole abdominal contrast-enhenced tomography.

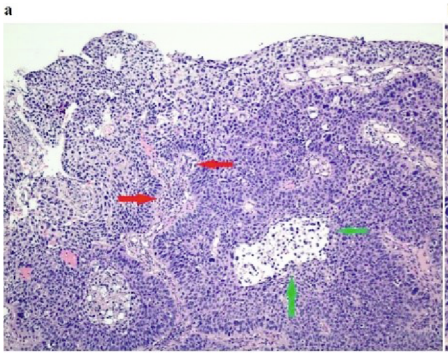

Figure 2a. Cold cup urethra biopsy material. Infiltration of malignant tumor which had invasion in large areas and developed as trabecular, insular and solid areas. Tumor areas include fibrovascular stromal proliferation (red arrows) and cystic necrotic areas (green arrows) (Magnification x 10).

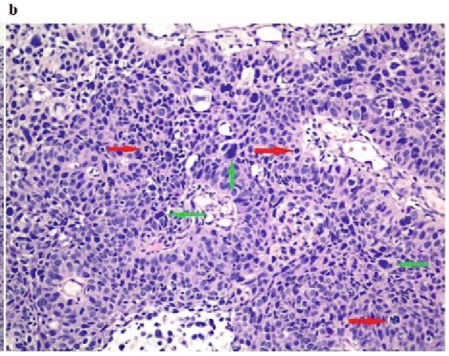

Figure 2b. Urethra biopsy material. Malignant cells with hyperchromatic and pleomorphic nucleus, unclear margins, narrow eosinophilic cytoplasm and high nucleus/cytoplasma ratio and with solid trabecular development forming focal follicle-like structures in some areas. Pleomorphism in cells is quite prominent and occasionally bizarre nuclear forms (green arrows) and frequent and atypical mitosis (red arrows) are observed (Magnification x 40).

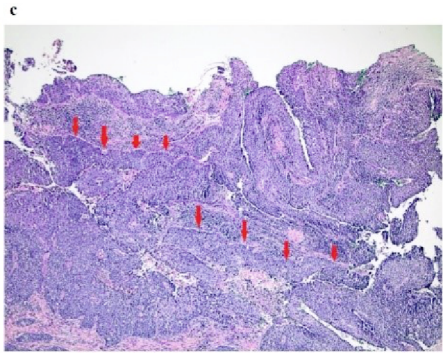

Figure 2c. Radical cystourethrectomy material. Tumor cells with coarse hyperchromatic and pleomorphic nuclei, whose borders are not clearly selected, are observed. Frequent and atypical mitosis are evident in tumor cells (red arrows) (Magnification x 40).

three-month postoperative follow-up, she was asymptomatic without any findings in the physical examination and in whole abdomen contrast-enhanced computed tomography. The patient was consulted to the medical oncology department, and after detailed evaluation, adjuvant chemotherapy was not suggested. The patient's follow-ups are still continuing in our clinic. Written consent was obtained from the patient.

Discussion

Urethral cancers account for only 0.003% of all urogenital malignancies in women. In broad-based epidemiological studies, on the other hand, this cancer was reported to have an annual incidence rate of 1.5 cases per million in the USA. The female urethral lumen is covered by transitional epithelial cells proximally and by a non-keratinized stratified squamous cell layer distally (1). Many factors such as recurrent urinary tract infections, urethral diverticulum and human papillomavirus are blamed for its etiology (3). Traditional imaging methods such as voiding cystourethrography and retrograde urethrography could help in diagnosis. Urethrography often shows focal, irregular narrowing of the urethra. However, extraluminal or periurethral spread cannot be characterized with these imaging methods. A high-resolution transvaginal, transperineal and transurethral ultrasonography performed by an experienced radiologist help in diagnosis, but time consuming and the operator-dependent nature of the examinations constitute some disadvantages in this approach. In computed tomography, urethral cancers are observed as a contrast-enhanced mass in soft tissue attenuation. In magnetic resonance imaging, squamous cell carcinomas or transitional cell carcinomas of urethra exhibit heterogeneous contrast enhancement with hypointense signal feature in T1A images and hypointense-intermediate signal feature in T2A images compared to normal corporal tissue whereas adenocarcinomas are relatively hyperintense in T2A images. On the other hand, both computed tomography and magnetic resonance imaging are very important for clinicians in assessing the local and systemic spread of the urethral tumors (4,5). Because distant staging should concentrate on chest and liver, with CT of the thorax and abdomen in all patients with invasive disease (6). As with urethral tumours in males, MRI has limited utility in depicting stage I disease. However, the target-like appearance of the normal urethra on axial T2-weighted images will be disrupted in stage II lesions. With stage III and IV disease, differentiation of primary urethral lesions from those of the vulva or vagina may be difficult (5). Nevertheless, the gold standard for the diagnosis of patients is cystourethroscopy with urethra biopsy. In terms of pathological evaluations, previous studies showed that about 45% of the cases had transitional epithelium cell carcinoma, 29% adenocarcinoma and 19% squamous cell carcinoma (3). Race, advanced age, lymph node positivity, non-squamous histology and advanced stage were found to be associated with poor prognosis in urethral tumors (6). On the other hand, it was revealed that survival is better in distal tumors compared to proximal tumors. However, it was mentioned that primary urethral carcinomas are a highly aggressive malignancies, and 5-year survival rate varies between 40 and 60%. There is no standardized treatment approach accepted worldwide (7). Treatment is planned according to the tumor localization, clinical stage and clinical condition of patient. Local mass excision and partial urethrectomy are often of limited use in distally located superficial urethral cancers not reaching large sizes. This approach has disadvantages such as high recurrence rates and vulnerability to complications such as urinary incontinence and urethral stenosis (8,9). Another surgical approach is anterior exenteration (total urethrectomy, pelvic lymphadenectomy with cystectomy, salpingectomy, hysterectomy and resection of the anterior wall of the vagina) and urinary diversion (2). It is observed that tumor load in particular is preferred by masses of excess proximal origin. Previous studies reported that disease free survival rate was over 70% when tumors of non-aggressive histological subgroups were treated with anterior exenteration alone (10). We think that major surgical approaches in the treatment of female urethral cancers are very important in order to keep tumoral survival at an ideal level, even if the patients' age and cobormid status elevated.

Another treatment protocol is radiotherapy. Milosevic et al. (11) applied radiotherapy for 34 patients with urethral tumors, observed tumor recurrence in 21 patients and reported a 45% seven-year survival rate for the disease. In the same study, 16% of patients were reported to have very serious complications related to the treatment (11). In a similar study, Garden et al. reported that five-year local control rates after radiotherapy was 64%, and 49% of these patients had local complications and 15% of them had serious complications (12). It is very difficult to fight with urethral tumors with only chemotherapy agents. In many studies, it was shown that the rates of recurrence were above 25% in treatment regimens using only this treatment approach (3). On the other hand, most author preferred adjuvant polychemotherapy for locally advanced female urethral cancers such as pT3-4 disease and for

selected high risk. To this end, gemcitabine, cisplatin, and ifosfamide, or cisplatin, 5-fluorouracil and gemcitabine are frequently used treatment strategies. These chemotherapy protocols could be combined with surgical approach or with radiotherapy, or all three approaches could be used together (1). For our case, combined treatment was not required due to the lack of remote organ dissemination and perfect removal of malignant formations.

Urethral cancers are rarely seen in women, and since this oncological pathology has nonspecific findings, delays are experienced in diagnosis and treatment protocols. Detailed gynecological examination and imaging methods such as magnetic resonance or computed tomography are very important in the diagnosis of female urethral cancer. On the other hand, biopsy taken under cystourethroscopy is essential for the diagnosis to be confirmed.

Yazarlık katkısı: Fikir/Hipotez: EK, DA, MB, FAD. Tasarım: EK, DA, MB, FAD. Veri toplama/Veri işleme: EK, DA. Veri analizi: EK. Makalenin hazırlanması: EK, DA, FAD. Makalenin kontrolü: EK, DA, FAD.

Etik Kurul Onayı: Gerekli değildir.

Hasta Onayı: Olgu sunumu için hastadan izin alınmıştır.

Hakem Değerlendirmesi: İlgili alan editörü tarafından atanan iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.

Çıkar Çatışması: Yazarlar tarafından çıkar çatışması bildirilmemiştir.

Finansal Destek: Yazarlar tarafından finansal destek almadıkları bildirilmiştir

References

1- Dell'Atti L, Galosi AB. Female Urethra Adenocarcinoma. Clin Genitourin Cancer 2018;16:263-267.

2- Yıldız B. Urethra Cancers. Turkiye Klinikleri J Med Oncol-Special Topics 2011;4:31-34.

3- Chen H, Zou LL, Dong CJ, Li T, Dong ZQ. Advanced primary urethral cancer: a case report. J Med Case Rep 2019;29:365.

4- Kawashima A, Sandler CM, Wasserman NF, LeRoy AJ, King BF Jr, Goldman SM. Imaging of urethral disease: a pictorial review. Radiographics 2004;24:195-216.

5- Del Gaizo A, Silva AC, Lam-Himlin DM, Allen BC, Leyendecker J, Kawashima A. Magnetic resonance imaging of solid urethral and peri-urethral lesions. Insights Imaging 2013;4:461-469.

6- Champ CE, Hegarty SE, Shen X et al. Prognostic factors and outcomes after definitive treatment of female urethral cancer: a population-based analysis. Urology 2012;80:374–382.

7- Peyton CC, Azizi M, Chipollini J et al. Survival Outcomes Associated with Female Primary Urethral Carcinoma: Review of a Single Institutional Experience. Clin Genitourin Cancer 2018; 16:1003-1013.

8- Dalbagni G, Zhang ZF, Lacombe L et al. Female urethral carcinoma: an analysis of treatment outcome and a plea for a standardized management strategy. Br J Urol 1998;82:835.

9- Charry GP, Cabello BR, Simón RC, Enguita CG. Primary female urethral carcinoma a case report: a review of the diagnosis and treatment. Urol Nephrol Open Access J 2015;2:80-83.

10- Weng WC, Wang CC, Ho CH et al.Clear cell carcinoma of female urethral diverticulum: a case report. J Formos Med Assoc 2013;112:489-491.

11- Milosevic MF, Warde PR, Banerjee D et al. Urethral carcinoma in women: results of treatment with primary radiotherapy. Radiother Oncol 2000;56:29-35.

12- Garden AS, Zagars GK, Delclos L. Primary carcinoma of the female urethra. Results of radiation therapy. Cancer 1993;15:3102-3108.