Female Prostate? - Clear Cell Adenocarcinoma of Female Urethra

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Clear cell adenocarcinoma of the female urethra is extremely rare. Because the primary urethral carcinomas are rare, standard diagnostic algorithm and management has not been established yet. We report a case of clear cell adenocarcinoma of the proximal urethra in a 76-year-old female. She was presented with voiding difficulty for several years after pubovaginal sling operation due to stress urinary incontinence twelve years ago. Before this period, she had managed with medication for detrusor hypocontractility. Recently she complained bloody vaginal discharge, and her vaginal examination revealed palpable mass on the anterior vaginal wall. Pelvic MRI showed a 5x4.5cm sized tumor surrounding the proximal urethra which was mimicking prostate with no lymphadenopathy. Biopsy of the mass confirmed it to be clear cell adenocarcinoma. She underwent anterior pelvic exenteration and ileal conduit with bilateral pelvic lymph node dissection. The patient received adjuvant radiotherapy and chemotherapy as treatment. We should carefully evaluate patients with voiding symptom after anti-incontinence surgery and multimodal treatment should be applied for locally advanced urethral carcinoma. (Korean J Urol Oncol 2016;14:93-96)

Key Words: Urethral carcinoma, Clear cell adenocarcinoma, Pubovaginal sling operation

Primary carcinomas of female urethra are rare, accounting for less than 1% of genitourinary malignancies. Among them, the clear cell carcinomas of female urethra are extremely rare, accounting for only 10% of urethral cancer. Primary urethral carcinomas may present with obstructive symptoms, dysuria, urethral bleeding, urinary frequency and palpable mass.

Obstructive voiding symptoms are not uncommon complications after the pubovaginal sling and midurethral sling (MUS) procedure. We report a case of a clear cell adenocarcinoma of female urethra in patient with obstructive voiding symptom after pubovaginal sling operation for stress urinary incontinence.

CASE REPORT

A 76-year-old female patient was presented with voiding difficulty for a long time after pubovaginal sling operation due to stress urinary incontinence twelve years ago. Before this period, she had managed with medication for detrusor hypocontractility. Recently her voiding symptoms had worsened with complained bloody vaginal discharge, and her vaginal examination revealed non-tender, fixed hard, egg sized palpable mass on the anterior vaginal wall. No palpable inguinal lymphadenopathy was identified while the urinalysis showed hemato-pyuria. Pelvic MRI with contrast revealed a 5x4.5cm sized tumor surrounding the proximal urethra with no lymphadenopathy (Fig. 1). On cystourethroscopy, the urethra and bladder seemed normal. Abdominal CT scan with contrast and chest X-ray was nonspecific findings. Needle biopsy of the mass revealed a clear cell adenocarcinoma of the urethra. The patient
Fig. 1. (A, B) MRI shows a 5x4.5cm sized tumor surrounding the proximal urethra on T2-weighted image.

underwent anterior pelvic exenteration to remove anterior vaginal wall, urethra, bladder, distal ureter and uterus under the supervision of the urology and gynecologic oncology team. Bilateral pelvic lymph node dissection and an ileal conduit urinary diversion were performed. Pathology reported clear cell adenocarcinoma with micropapillary pattern, with invasion to the bladder neck and vagina but with no pelvic lymph node metastasis (pT3N0M0) (Fig. 2A). Histology showed tumor cells with nuclear hobnailing, hyperchromatic nuclei and eosinophilic cytoplasm (Fig. 2B). Her postoperative course was uneventful as she was discharged home on day 10 after operation. In the outpatient clinic, she was supposed to go on the adjuvant radiotherapy on the pelvis however, she refused the treatment. A year after the surgery, she was presented with bilateral inguinal non-tender palpable mass. Puncture biopsy of the mass revealed metastatic clear cell adenocarcinoma yet on the FDG PET/CT, there were no other problems. She underwent salvage chemotherapy, regimen of gemcitabine plus cisplatin and after six months, her lymphadenopathy had reduced partially and other metastatic lesion had not been presented until now.

DISCUSSION

Primary urethral carcinoma of female is an extremely rare disease. The age-adjusted incidence rate of female primary urethral carcinoma was 1.5 per million in the United States and 0.6 per million in the European Union. A Surveillance Epidemiology and End Results (SEER) study reported that the
incidence of primary urethral carcinoma peaked the most in the age group of 75 years old.\textsuperscript{5}

In female, squamous cell carcinoma is the most common histologic type of urethral carcinoma, accounting for 70% of all cases. Urothelial cell carcinoma (20%), adenocarcinoma (8-10%) are the next most common cell types in urethral carcinoma.\textsuperscript{1} Clear cell adenocarcinoma is a histologic subtype of urethral adenocarcinoma. The urethral diverticulum, recurrent urinary tract infections, chronic irritation and viral infections are associated with female primary urethral carcinoma.\textsuperscript{6} Therefore, it clearly shows the association between the clear cell adenocarcinoma and urethral diverticulum.

About half of the patients with urethral carcinoma are presented with the following symptoms; urethral bleeding, hematuria, palpable mass, bladder outlet obstruction, dysuria and pelvic pain. Patients with these symptoms should have external genitalia and pelvic examined carefully. In addition, patients with urethral palpable mass should have the bilateral inguinal area examined thoroughly as well.\textsuperscript{7} Diagnostic cystourethroscopy and biopsy enable assessment of a urethral mass and confirmation of the pathology.\textsuperscript{3} Imaging studies of urethral carcinoma enable assessment of extent of the tumor, lymphadenopathy and distant metastasis. For assessment of local stage, pelvic magnetic resonance imaging (MRI) is superior to computed tomography (CT).\textsuperscript{8} For the distant staging, chest and abdomen CT is performed.\textsuperscript{9}

Voiding dysfunction after incontinence surgery is a potential complication of all stress incontinence procedures.\textsuperscript{10} Obstructive voiding dysfunction is recognized as the most common reported complication of TA sling placement, affecting 17-50% of patients.\textsuperscript{11} In this report, because she only complained about the obstructive voiding symptom after pubovaginal sling operation, we diagnosed the urethral cancer later in time.

Treatments of localized urethral carcinoma in female include urethrectomy, urethra-sparing surgery and radiotherapy.\textsuperscript{3} For advanced primary female urethral carcinoma, the combination of anterior pelvic exenteration, chemotherapy and radiotherapy has been preferred for local and distant cancer control. Because inguinal lymph node dissection have no clear evidence of improved survival rate and is associated with high morbidity, routine inguinal dissection is not preferred. But, patient with lymphadenopathy should be performed lymph node dissection. In addition, cisplatin-based chemotherapy is effective on the treatment of lymph node metastasis.\textsuperscript{3}

CONCLUSION

Although primary clear cell adenocarcinoma of female urethra is extremely rare, physicians should have suspicion of urethral carcinoma in patients with urinary symptom. Biopsy, optimal imaging studies should be performed for the accurate diagnosis. For locally advanced urethral carcinoma, patient should be managed by a multidisciplinary team of urologists, oncologists and radiation oncologists and the treatments include surgery, radiation therapy and chemotherapy.

REFERENCES