A urethral clear cell carcinoma case successfully treated with organ preservation surgery and adjuvant chemoradiation

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A B S T R A C T

Urethral clear cell carcinoma is an aggressive tumor rarely observed in the urinary tract. To date, the diagnostic workup of such cases has not yet been standardized, and there has been no established standard treatment approach. The present study reports a rare case of urethral clear cell carcinoma successfully treated with organ preservation strategies and adjuvant chemoradiation with the goal of organ preservation. This treatment approach could be used for patients who refuse radical surgery and patients with concerns about severe morbidity from radical surgery, even in advanced-stage urethral clear cell carcinoma.

1. Introduction

Urethral clear cell carcinoma (UCCC) is an aggressive tumor rarely observed in the urinary tract, accounting for less than 0.01% of genitourinary (GU) cancers in females.1 - 4 UCCC occurs in both sexes; however, it has been reported more frequently in the female urethra at a ratio of 1:4.5 - 7 To date, there has been no established diagnostic or standard treatment approach. Herein, we report a successful treatment of an advanced case of UCCC wherein organ preservation surgery was performed followed by chemoradiation therapy (CCRT) as a treatment scheme, with no evidence of disease at 10 years of follow-up.

2. Case presentation

A 58-year-old female presented with a 2-month history of urethral bleeding. She underwent GU examination with urinary bladder magnetic resonance imaging (MRI) and cystoscopy. The mass around the urethra was visualized during the GU examination. Cystoscopy revealed no abnormalities in the bladder. MRI of the pelvis demonstrated a 3.5-cm enhancing mass involving the posterior urethra and anterior wall of the vagina. Two enlarged masses were observed in the left internal iliac chain, which were suspected to be metastatic lymph nodes. A positron emission tomography/computed tomography (CT) image revealed increased fluorine-18 fluorodeoxyglucose uptake in the urethra and left iliac lymph node area (Fig. 1). The biopsy result was positive for UCCC. Under the impression of a clinical stage of T2N3M0, the surgeon recommended radical surgery, including pelvic lymph node dissection according to the standard treatment approach. However, she refused to undergo this treatment because urethral preservation was not possible with this surgery. Therefore, with the goal of organ preservation, urethral tumor resection followed by adjuvant CCRT was initially planned. The surgical procedure proceeded with the resection of the urethral tumor, using a vaginal approach. An anterior vaginal incision was made and the urethral mass was circumferentially excised in its entirety. During the urethral tumor resection, careful surgical technique was utilized to limit injury to the bordering urethra. The tumor mass had well defined edges and was easily removed surgically. Histological findings revealed tubulopapillary structures. The papillae were variably sized, and the tumor cells had a cuboidal to columnar appearance with clear cytoplasm (Fig. 2). Hobnail cells were also observed. The pathological diagnosis was clear cell carcinoma, with a 7.0 × 3.2-cm mass invading the urethral muscle. The bilateral resection margin was involved, and lymphovascular invasion was noted.

Approximately a month after surgery, radiation therapy (RT) with the simultaneous boost technique using volumetric modulated RT (VMAT) was introduced for this case (Fig. 3). Chemotherapy was administered simultaneously during RT. A total dose of 55.8 Gy using 1.8 Gy daily fractions was delivered with a fractionated dose for planning target volume. The total dose for clinical target volume for the primary and left lymph node area was 77.5 Gy using 2.5–3 Gy daily
fractions. The patient received four monthly cycles of intravenous 1000 mg/m² 5-fluorouracil and 10 mg/m² mitomycin during RT. During CCRT, there were no other side effects except for grade 1–2 periurethral skin reactions. Approximately 30 months after completing RT, follow-up abdominopelvic CT revealed no definite visible mass around the urethra and no evidence of local tumor recurrence in the pelvic cavity. Follow-up was conducted every 3 months with urine cytology and alternating pelvic MRI and/or CT scans. The patient was well at the 10-year follow-up, without recurrence or metastases.

3. Discussion

UCCC of the female urethra is extremely rare. Clinically, a definitive diagnosis of UCCC is challenging with no specific signs or symptoms and should be differentiated from tumors of the vagina. The management of UCCC is not well established. There is a report that cystourethrectomy with pelvic lymph node dissection is recommended as a standard treatment, and adjuvant RT was used in cases with pelvic lymph node involvement. Other studies have shown that urethrectomy in conjunction with cystoprostatectomy or urethrectomy in combination with anterior exenteration could be considered a good treatment option for UCCC, and a small UCCC tumor may be effectively treated by urethrectomy alone. However, urethrectomy can cause many side effects,
which has an incidence rate of >20%. Although the prognosis of UCCC is known to be good in the early stages, the prognosis in advanced stages is generally poor. In our case, as an organ preservation surgery for our patient, urethral tumor resection was performed because the patient refused to undergo radical surgery and wanted to undergo the less invasive surgery as much as possible, as she had concerns regarding the loss of urethral function and surgery-related morbidities. Subsequently, as adjuvant therapy, CCRT was performed after organ preservation surgery. There is a report supporting the use of chemotherapy for treating UCCC. For RT, VMAT was employed, which is one of the most developed radiotherapy techniques, and which, in our case, helped spare normal tissue with local control. Using VMAT, concomitant boost radiation therapy to this lesion could be used for the control of metastatic lymph nodes (Fig. 3). As a result, we found that these lesions were controlled on the CT performed 2 years after the completion of RT. This organ preservation surgery and adjuvant chemoradiation approach should be considered, given the opportunity to preserve the urethra with a local control effect. As mentioned earlier, UCCC appears to be aggressive, with lower survival outcomes and poor prognosis, especially with lymph node involvement. Although radical surgery was not performed in our patient with advanced-stage UCCC with pelvic lymph node involvement, urethral preservation, and treatment of UCCC could be achieved with organ preservation surgery and adjuvant CCRT. This treatment approach could be used for patients who refuse radical surgery and patients with concerns about severe morbidity from radical surgery, even in advanced-stage UCCC.

4. Conclusion

We report that a case of advanced-stage UCCC showed no evidence of recurrence 10 years after the patient underwent urethral tumor resection followed by CCRT with the goal of organ preservation. Although radical surgery was recommended for this patient with advanced-stage disease, organ preservation surgery and adjuvant CCRT could also be possible not only for organ preservation but also for achieving excellent treatment outcomes in UCCC.

Ethic statement and informed consent

This study was approved by the Ethics Committee of Gachon University Gil Medical Center (GDIRB2020-450). The requirement for patient consent was waived by our institutional legislation because the data were anonymized and retrospectively obtained.

Author contributions

SH Lee: Methodology, Conceptualization, Data curation, and Writing - Review & Editing SY Ha: Data curation SY Ha and SJ Sym: Writing - Original draft preparation. All authors discussed the results and commented on the manuscript. All authors approved the final manuscript.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Declaration of competing interest

The authors declare that there are no competing interests.

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