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A Rare Case Of Primary Urethral Carcinoma Treated With Radiation Therapy

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Abstract

Primary neoplasms of the female urethra are exceptionally rare, representing less than 0.02% of all malignancies affecting women. Due to their insidious onset and non- specific symptoms, these tumors are often diagnosed at advanced stages, which results in poor clinical outcomes. Early detection is crucial to reduce the risk of metastatic dissemination and prevent morbid complications such as chronic urinary catheter dependency. Tumors arising from the distal urethra tend to present at an earlier stage and are associated with better prognosis and higher potential for cure. However, when treated with single modality approaches, female urethral carcinoma has shown local recurrence rates between 36% and 60%, with three-year survival ranging from 0% to 29% (1). The concurrent use of radiation therapy and chemotherapy has improved local control, systemic control, and overall survival in this rare malignancy (2,3).

Nonetheless, limited data and clinician familiarity impede the establishment of standardized management protocols, as most evidence derives from isolated case reports.

Keywords: NIL

Introduction

A 45-year-old female presented with complaints of burning micturition for three months, accompanied by difficulty in passing urine and decreased urinary frequency for two months. She also experienced urinary urgency and mild lower abdominal pain, which was relieved by oral analgesics. On examination, a growth measuring approximately 4 x4 cm was seen araising from the urethra,encasing vulva.A prominent, fixed, and hard left inguinal lymph node measuring 2.5 x 2 cm was palpable. The cervix was visualized and appeared normal in shape and consistency, while the per rectum examination was unremarkable. A punch biopsy of the urethral mass was performed, and histopathological analysis revealed moderately differentiated infiltrating squamous cell carcinoma.

Subsequently, Magnetic Resonance Imaging of the abdomen and pelvis demonstrated a lesion measuring 57 x 28 x 44 mm in the urethra, extending to the base of the urinary bladder. Multiple enlarged lymph nodes were noted bilaterally in the inguinal, external iliac, internal iliac, common iliac, and para-aortic regions, with the largest node in the left inguinal region measuring 33 x 28 mm. Chest X-ray findings were normal. Based on clinical and radiological findings, the patient was diagnosed with carcinoma of the urethra, staged as T3N2M0, Stage IV.

Prior to treatment initiation, the patient underwent cystoscopy and suprapubic catheterization under general anesthesia due to obstructive urinary symptoms. As the disease was deemed inoperable, she was planned for concurrent chemoradiation therapy. The radiation therapy protocol involved delivering 46 Gray in 23 fractions to the whole pelvis, including para-aortic, common iliac, internal iliac, external iliac, and inguinal lymph nodes, followed by a boost of 14

Gray in 7 fractions using Intensity-Modulated Radiation Therapy (IMRT) to the gross disease and involved nodes. Weekly cisplatin chemotherapy was administered at a dose of 40 mg/m².

During the course of treatment, the patient developed repeated urinary tract infections and bowel disturbances, which were managed conservatively with oral medications

On the first follow-up three months post-treatment, MRI of the abdomen and pelvis revealed a mildly enhancing residual lesion measuring 10 x 14 x 13 mm in the urethra, extending up to the base of the urinary bladder, with features suggestive of chronic cystitis. Several lymph nodes in the bilateral inguinal, external iliac, internal iliac, common iliac, and para-aortic regions were noted to be enlarged but reduced in size compared to baseline, consistent with a partial response to treatment.

A Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography (FDG PET-CT) scan demonstrated a FDG-avid lesion measuring 11 x 8 mm in the proximal urethra near the bladder. A sub-centimetric left supraclavicular lymph node also showed FDG uptake (SUV max 2.1), suggesting metastasis. Additionally, pleural-based soft tissue thickening with increased FDG uptake was identified in the basal segment of the right lower lung lobe, measuring 7 x7 mm with an SUV max of 2.8. Ultrasound-guided Fine Needle Aspiration Cytology (FNAC) of the supraclavicular lymph node confirmed malignancy.

In view of disease progression, the patient was started on palliative chemotherapy with six cycles of Paclitaxel and Carboplatin administered every 21 days.

PET-CT scan performed three months after chemotherapy completion showed increased size and FDG uptake of the left supraclavicular node along with multiple new FDG-avid lymph nodes in the retroocular, retroperitoneal, right common iliac, bilateral external iliac regions. Multiple FDG-avid sclerotic lesions were also observed in the thoracic vertebrae and left scapula, indicative of disease progression. The patient subsequently refused further treatment and passed away in November 2024, and survived for 21 months after diagnosis.

Discussion

Female urethral carcinoma is an exceptionally rare malignancy, accounting for approximately 0.02% of all female cancers and about 1% of genitourinary tract tumors in women(4) . Due to its rarity, diagnosis and management are challenging, and there are no widely accepted standardized treatment guidelines. Histologically, urothelial carcinoma (transitional cell carcinoma) is the predominant subtype, reported in 54% to 65% of cases, followed by squamous cell carcinoma (16% to 22%) and adenocarcinoma (10% to 16%).Although these histologic types differ in origin and characteristics, current literature suggests that histological subtype alone has limited prognostic significance, with overall survival rates remaining relatively poor, ranging from 30% to 40% irrespective of cellular differentiation (5)5 year OS with patient of urethral carcinoma in Europe stands with 54%.according to RARECARE(6)

In this case, the patient presented with classic lower urinary tract symptoms, including difficulty in micturition, urgency, and reduced frequency, accompanied by discomfort. These symptoms are commonly reported, although other presentations include dysuria, dyspareunia, perineal pain, urinary retention, overflow incontinence, and palpable masses at the urethral meatus .The tumor often invades local structures such as periurethral tissues, vagina, and vulva and may extend proximally to involve the bladder neck(4,7,). Occasionally, the disease presents asymptomatically as firm nodular lesions in the labia, perineum, bladder neck, or vagina, reflecting metastatic spread(4)

Management strategies for female urethral carcinoma are not well defined due to its low incidence. Treatment usually involves surgical resection, including tumor excision, radical nephroureterectomy, or anterior pelvic exenteration, often supplemented by adjuvant radiotherapy or chemotherapy . Tumor size and location are important prognostic factors. Bracken et al. demonstrated significantly reduced five-year survival rates of 13% for tumors larger than 4 cm, compared to 60% for tumors smaller than 2 cm .Tumors located proximally, involving the entire urethra, tend to have worse outcomes than those located distally

Palpable lymphadenopathy is observed in approximately one-third of patients, with over 90% showing metastatic disease at diagnosis. In such

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advanced stages, 5- and 10 year median overall survival rates are approximately 44% and 29%, respectively, while disease-free survival for locally advanced tumors ranges between 33% and 45% . Patients undergoing anterior pelvic exenteration have demonstrated favorable five-year survival outcomes of up to 73%, and advances in surgical techniques have reduced surgical mortality from 23% to between 0-5.3% (8).

Radiation therapy plays a critical role, especially in pelvic urethral carcinoma at stages III and IV, where external beam radiation therapy combined with interstitial brachytherapy has shown substantial efficacy. For early-stage disease, surgery alone remains the treatment of choice (2).

In this case, the presence of pelvic lymphadenopathy and para-aortic node involvement warranted definitive chemoradiation. The patient received external beam radiation therapy to 46 Gray in 2 Gray fractions, followed by a 14 Gray boost to gross disease and involved nodes.

Despite partial response observed on imaging, post-treatment PET-CT revealed new supraclavicular nodal uptake, indicating disease progression. Palliative chemotherapy with Paclitaxel and Carboplatin was initiated, but the disease ultimately progressed to involve multiple osseous sites, reflecting the aggressive nature and poor prognosis of this malignancy.

This case highlights the importance of early recognition and comprehensive staging at diagnosis, as delayed detection significantly compromises prognosis. Multimodal treatment approaches including surgery, chemoradiation, and systemic therapy remain essential to improve outcomes, although novel therapeutic avenues are urgently needed for this aggressive disease.

Conclusion

Primary female urethral carcinoma is a rare and aggressive malignancy characterized by poor prognosis due to delayed diagnosis and limited standardized treatment protocols. Early detection and accurate staging are critical to optimize patient outcomes. Treatment must be individualized based on tumor size, location, and nodal involvement. Multimodal approaches including surgery, radiation, chemotherapy, or combinations improve locoregional control and survival. Further large-scale studies and clinical trials are needed to establish consensus guidelines and explore novel therapeutic options for this challenging malignancy.

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