

Diagnosis of Female Urethral Cancer Based on Multimodal Ultrasound: A Case Report

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Abstract: While histopathology remains the diagnostic gold standard for urothelial carcinoma, this case highlights the emerging role of advanced ultrasonographic techniques in characterizing urethral malignancies. We present a 51-year-old female with a one-month history of refractory lower urinary tract symptoms (urinary frequency, urgency, dysuria, and nocturia) unresponsive to conventional anti-inflammatory therapy. Multimodal ultrasonographic evaluation, incorporating conventional sonography, transrectal ultrasound, elastography, and contrast-enhanced ultrasonography (CEUS), revealed a complex proximal urethral mass with malignant features. Subsequent cystoscopic and histopathological examinations confirmed the diagnosis of primary urethral adenocarcinoma. This case underscores the diagnostic value of comprehensive ultrasound protocols in evaluating female urethral neoplasms.

Keywords: multimodal ultrasound, transrectal biplane ultrasound, shear wave elasticity, contrast-enhanced ultrasonography, female urethral adenocarcinoma

Introduction

Female urethral cancer is an exceedingly rare malignancy, constituting approximately 0.02% of all female malignant tumors and 0.003% of malignant tumors in the female genitourinary system.^{1,2} The histological types include urothelial carcinoma, squamous cell carcinoma, and adenocarcinoma. Primary urethral adenocarcinoma presents with non-specific clinical symptoms, often leading to advanced-stage diagnosis and a relatively poor prognosis compared to other histological types. Therefore, timely detection and accurate diagnosis are crucial for the treatment and prognosis of this disease.³

Previous studies have indicated that the evaluation of suspected female urethral cancer requires a comprehensive approach, including physical examination, urethroscopy, computed tomography (CT), and magnetic resonance imaging (MRI).⁴ Conventional ultrasound techniques, such as transabdominal, transperineal, and transvaginal ultrasound, have been utilized to evaluate female urethral carcinoma;⁵ however, these modalities typically provide only diagnostic clues, serve as adjunctive investigations, or are retrospectively identified after pathological confirmation.⁴

Multimodal ultrasound technology integrates multiple ultrasound imaging techniques, including two-dimensional ultrasound, three-dimensional ultrasound, shear wave elastography, and contrast-enhanced ultrasound. Due to its advantages of multidimensional real-time observation, quantitative analysis, high reproducibility, and absence of radiation exposure, this approach has been widely implemented in diagnostic evaluation and interventional procedures across various anatomical regions, including thyroid, breast, pelvic structures, and anal canal.⁶⁻⁸ In this case report, we employed a biplanar probe to minimize abdominal interference, optimize scanning angles, enhance image resolution, and facilitate multi-angle visualization. We conducted a comprehensive assessment of a female patient with primary urethral adenocarcinoma by integrating data from Doppler ultrasound, elastography measurements, and contrast enhancement curves. This approach aims to increase awareness of the sonographic features of this rare condition among ultrasound specialists and support clinicians in achieving prompt diagnosis and treatment implementation.

Case Presentation

A 51-year-old female patient presented with a one-month history of frequent urination, dysuria, dyspareunia, and increased nocturia, with pain relief after urination. Physical examination revealed a normal urethral orifice, but a vaginal examination detected a mass on the anterior vaginal wall, measuring 3.5 cm×3 cm, which was hard, fixed, and poorly mobile. No enlarged lymph nodes were palpable in the inguinal area, and the external genitalia appeared normal. Laboratory tests, including urinalysis and tumor markers, were within normal limits. Cystoscopy revealed an elevated vesicourethral junction with coarse, non-glossy urethral mucosa prone to bleeding, suggesting urethral stenosis originating from the posterior urethral orifice. Enhanced pelvic MRI demonstrated a 2.8×3.3×3.3 cm lesion in the bladder-urethral region with slightly hypointense T1 and heterogeneous T2 signal characteristics. The mass contained internal septations, exhibited hyperintense signal on diffusion-weighted imaging (DWI), and showed heterogeneous enhancement following contrast administration. While no enlarged lymph nodes were identified within the pelvis, bilateral pelvic sidewall lymphadenopathy was noted, with the largest node on the left side measuring approximately 1.3×1.8 cm. Ultrasound examination revealed approximately 200 mL of urinary retention and a hypoechoic mass in the proximal urethra, suspicious for malignancy, without evidence of enlarged lymph nodes in the pelvis or inguinal regions. The patient underwent neoadjuvant chemoradiotherapy for two months, during which PET-CT demonstrated a soft tissue nodule between the bladder and urethra with increased FDG uptake, suggesting persistent tumor activity despite treatment. Metastatic lymphadenopathy was identified adjacent to the left external iliac vessels and right internal and external iliac vessels, along with urinary retention and minimal pelvic fluid collection. Due to hematological complications including bone marrow suppression, the patient subsequently underwent surgical resection of the lesion with partial cystectomy and corresponding lymphadenectomy, followed by postoperative bladder catheterization and six cycles of adjuvant chemotherapy. Throughout a 22-month follow-up period, no evidence of lymphatic or distant metastases was observed. The patient remains in stable condition and continues with regular follow-up evaluations every three months.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of The Affiliated People's Hospital of Ningbo University (NO: 2024-N-013) and informed consent was provided by the participant. Institutional approval was obtained to publish the case details.

Imaging Equipment

Myriad R9s ultrasound system with a rectal dual-plane probe (convex array probe 3–9MHz, linear array probe 4–13MHz) and a vaginal probe (3–9MHz). Esaote ultrasound system with a rectal dual-plane probe (convex array probe 3–9MHz, linear array probe 4–13MHz).

Ultrasound Findings

Transperineal Ultrasound (Convex Array Probe): The proximal urethra exhibited an abnormal shape with a moderately echogenic solid mass measuring 28 mm (upper-lower diameter), 21 mm (anterior-posterior diameter), and 25 mm (left-right diameter). The proximal edge of the mass was approximately 9 mm from the urethral orifice, and the distal edge was about 14 mm from the external urethral orifice. The mass had clear boundaries, protruded towards the bladder, and showed abundant blood flow signals on color Doppler (Figure 1A).

Transrectal Ultrasound (Convex Array Probe): The mass appeared chestnut-shaped with clear borders and a more detailed internal structure compared to transperineal ultrasound. Blood flow signals were rich and disorganized. Transrectal ultrasound (linear probe) revealed the mass measuring 34 mm (upper-lower diameter), 32 mm (anterior-posterior diameter), and 42 mm (left-right diameter), with a slightly lobulated shape. Multiple punctate strong echoes with posterior acoustic shadows were observed within the mass, the largest measuring 5 mm (Figure 1B and C). The mass's proximity to the urethra and vagina was clearly distinguishable, with no involvement of the anterior vaginal wall but poor demarcation from the adjacent bladder wall on grayscale imaging.

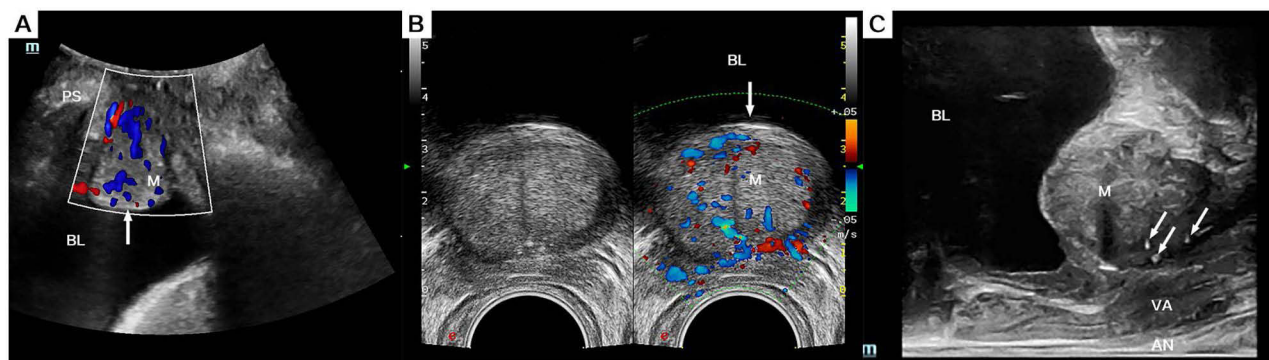


Figure 1 Transperineal (convex probe) ultrasound (A) a moderately echogenic solid mass is seen in the proximal urethra, with clear borders, convexity to the bladder, and abundant blood flow signal. Transrectal (convex array probe) ultrasound (B) the shape of the mass is like a chestnut, similar to the male “prostate”, with disturbed vascularization. Transrectal (linear probe) ultrasound (C) the mass is slightly lobulated, which can clearly show multiple punctate echoes (white arrows) within the mass and distinguish the mass from the urethra and vagina.

Transrectal Ultrasound (Linear Array Probe): The mass demonstrated rapid enhancement and washout, with high enhancement and a slight increase in volume in contrast mode compared to grayscale. Contrast perfusion was observed in the lower bladder wall, suggesting infiltration (Figure 2A and B).

Ultrasound Elastography: Shear-wave elastography revealed a maximum value of 62.92 kPa and a mean value of 43.83 kPa, with the elastic image slightly larger than the 2D image. Strain-based elasticity scoring was 5 (Figure 3A and B).

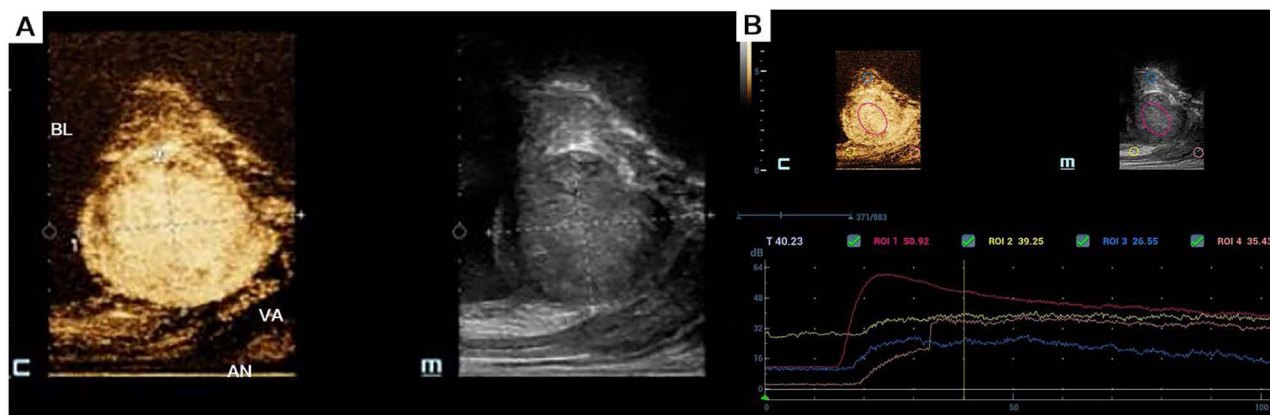


Figure 2 Transrectal (wire-array probe) ultrasonography: slight increase in volume in contrast mode compared to gray scale, see that the lower wall of the bladder is also infiltrated with contrast, consider infiltration (A), the mass is fast-entering and fast-exiting with high enhancement (B).

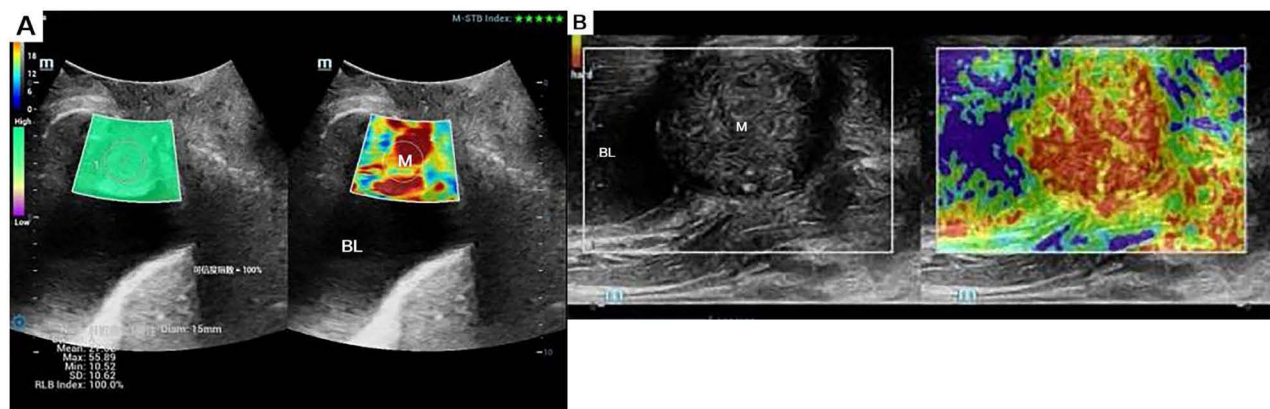


Figure 3 Ultrasonic acoustic touch shear wave elasticity (A) max:62.92kpa, mean:43.83kpa; strain-based elasticity score (B) 5 points.

Ultrasound Diagnosis

The mass's location in the proximal urethra, convex towards the bladder, and its close relationship with the urethra suggested a possible urethral origin. The proximal urethra's normal structure was lost, and the mass's growth pattern encircling the urethral lumen indicated urethral pressure causing urination difficulties. The vagina's structure was clear and well-delineated from the mass, excluding a vaginal origin and confirming a urethral source. The mass's sonographic features included a solid, lobulated mass with multiple small calcifications and abundant, disorganized peripheral and internal blood flow signals. Ultrasound contrast imaging showed rapid enhancement and washout with high enhancement, suggesting possible infiltration of the lower bladder wall. Elastography assessment indicated a hard mass texture. All ultrasound features pointed towards a malignant tumor, leading to an initial diagnosis of urethral malignancy.

Post-resection pathological diagnosis confirmed female urethral adenocarcinoma, consistent with the multimodal ultrasound diagnosis.

Discussion

Primary female urethral adenocarcinoma is extremely rare, with low incidence, high malignancy, and atypical clinical symptoms, often leading to misdiagnosis and advanced-stage detection.⁹ Early diagnosis is crucial for prognosis.^{10,11}

Urethral carcinoma typically presents as a solid, moderately echogenic or mixed echogenic mass on ultrasound, often compressing the urethra with rich blood flow signals.¹² Differentiating it from benign urethral tumors and periurethral structures like vaginal adenocarcinoma is crucial. Benign urethral tumors present as well-defined, solid masses with abundant blood flow and softer textures. Vaginal adenocarcinoma, with a younger age of onset and symptoms of vaginal bleeding, can be differentiated based on symptoms and relationship with the urethra.

In diagnostic evaluation, pathological examination undoubtedly represents the gold standard; however, it is not applicable for early assessment and diagnosis prior to treatment initiation. Alternative imaging modalities, such as urethral contrast studies implemented over two decades ago, can only evaluate urethral stenosis.¹³ Computed tomography can demonstrate urethral masses with soft tissue density,^{4,13} while MRI facilitates assessment of tumor invasion depth and pelvic lymph node status, contributing to clinical staging.⁹ However, due to radiation exposure concerns and prohibitive costs, these modalities are generally not considered first-line screening approaches.

Conventional ultrasound is essential for diagnosing and monitoring female urethral diseases but has limitations due to the urethra's short length and low position, which can be obscured by the pubic symphysis and intestinal gas.¹⁴ Transvaginal and transperineal ultrasound effectively identify urethral mass location and morphological characteristics,^{5,15} but may fail to visualize the entire urethra, potentially missing small or distal lesions. Three-dimensional reconstruction provides intuitive visualization of the urethral mass position and its anatomical relationship with adjacent structures, making it suitable for preoperative planning,⁵ though it offers limited advantage in differentiating between benign and malignant masses.

Prithal Gangadhader reported a case of female urethral adenocarcinoma presenting as a hypoechoic mass with poorly defined margins and minimal blood flow signals on color Doppler flow imaging (CDFI).¹⁶ In another case documented by Mei Le, urethral carcinoma with metastases to external iliac and inguinal lymph nodes, as well as pubic and ischial bone, demonstrated additional sonographic details on transrectal ultrasound, including a heterogeneous mixed echo mass with ill-defined boundaries resembling a "male prostate", containing coarse hyperechoic foci and abundant CDFI blood flow signals.¹⁷ These findings are consistent with our case and confirm that transrectal examination can reveal more detailed malignant features, including calcification points and rich, well-defined vascular patterns. The linear array transrectal probe maintains close contact with the urethra, with the ultrasound beam perpendicular to the urethral axis, enabling unobstructed imaging of the entire urethra and adjacent structures while optimizing hemodynamic characterization of the region.^{5,15}

Furthermore, multiple studies have confirmed that tissue stiffness positively correlates with malignancy risk using elastography techniques.^{18–20} Quantitative assessment of tissue hardness provides crucial evidence for differentiating benign from malignant lesions; in our case, the quantified high stiffness of the lesion closely corresponded with the texture on physical palpation and the fibrotic characteristics of the gross specimen after surgery. Finally, contrast-enhanced ultrasonography (CEUS) further characterized the microcirculation perfusion patterns of the lesion, aiding in

differentiating malignant from benign pathology.²¹ Our case exhibited the typical malignant perfusion pattern of “rapid enhancement-high enhancement-early clearance”, providing crucial imaging evidence for differential diagnosis. This multimodal diagnostic approach, integrating anatomical morphology, tissue biomechanical properties, and blood perfusion information, significantly enhances the sensitivity and specificity of urethral tumor diagnosis, providing reliable imaging evidence for clinical decision-making.

In conclusion, the unique anatomical location and atypical clinical presentation of female urethral adenocarcinoma contribute to frequent misdiagnosis, despite its high malignancy and poor prognosis. Multimodal ultrasound examination provides valuable assessment of lesion boundaries, internal architecture, vascular distribution, and depth of invasion into adjacent organs, offering intuitive and precise diagnostic information for pre-therapeutic clinical staging, surgical planning, and post-treatment surveillance.

Nevertheless, several limitations were evident in our ultrasound evaluation: 1) The two-dimensional grayscale examination was restricted by scanning range limitations and abdominal intestinal gas interference, preventing detection of pelvic sidewall lymphadenopathy and comprehensive assessment of distant metastases; 2) During contrast-enhanced ultrasound, the examining physician subjectively overlooked multidimensional evaluation of surrounding lymph nodes, aspects requiring enhancement in future diagnostic protocols; 3) As this represents a single case report of a rare entity, while elastography scores and values indicated significant lesion stiffness, the study lacks quantitative analysis across multiple cases necessary for determining definitive threshold values.

Ethics Approval and Consent to Participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of The Affiliated People’s Hospital of Ningbo University (NO: 2024-N-013) and informed consent was provided by the participant.

Consent for Publication

Written informed consent was obtained from the patient for publication of her case as well as the accompanying images.

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Disclosure

The authors have no conflicts of interest to declare for this work.

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