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RARE CLEAR-CELL ADENOCARCINOMA ARISING IN THE MALE BULBOMEMBRANOUS URETHRA: SURGICAL RESECTION AND CHEMOTHERAPY OUTCOME

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Abstract

Background: Primary urethral adenocarcinoma in males is exceedingly rare; the clear-cell variant is especially uncommon and poses diagnostic and therapeutic challenges. We report a case of primary clear-cell adenocarcinoma of the bulbomembranous urethra (pT1, G2) with perineural invasion and early pulmonary metastases, managed by wide local excision with partial urethrectomy followed by systemic chemotherapy with documented radiologic response.

Case presentation: A 53-year-old man presented with progressive difficulty in passing urine and a perineal swelling. MRI pelvis (20/03/2025) identified an enhancing peri-urethral mass involving the ventral surface of the posterior penis and bulbomembranous urethra. He underwent wide excision of the tumour with part of the urethra and urethroplasty on 25/03/2025. Histopathology (25/03/2025) revealed an invasive adenocarcinoma with clear-cell features involving the bulbomembranous urethra (tumour size ~4.5 × 4.5 × 4.2 cm). Immunohistochemistry showed strong CK7 positivity, focal CK20 positivity, AMACR positivity, focal PAX8 and Napsin positivity; Ki-67 ~70%. Pathologic stage was reported as pT1, grade G2 (moderately differentiated) with perineural invasion. A whole-body 18F-FDG PET-CT (07/05/2025) demonstrated FDG-avid pulmonary nodules consistent with metastatic disease. The patient received systemic chemotherapy (cisplatin + gemcitabine) from June 2025 (6-cycle plan). A follow-up contrast CT thorax-abdomen-pelvis on 02/09/2025 documented “no obvious residual or metastatic lesions in the present study”. The patient remains under oncologic surveillance.

Conclusion: Clear-cell adenocarcinoma of the male urethra is rare and may present with obstructive urinary symptoms. Diagnosis rests on histopathology and immunoprofile. Multimodal management — surgical resection of the primary combined with systemic chemotherapy for metastatic disease — can produce meaningful radiologic response and disease control in selected patients. Awareness of this entity and close multidisciplinary coordination are essential for optimal outcomes.

Keywords: urethral adenocarcinoma; clear-cell adenocarcinoma; bulbomembranous urethra; partial urethrectomy; cisplatin-gemcitabine; perineural invasion

Introduction

Primary urethral carcinoma is rare in males, accounting for less than 1% of genitourinary malignancies.[1] The most common histologic types are urothelial carcinoma, followed by squamous carcinoma; adenocarcinoma is much less frequent.[2] The clear-cell subtype of urethral adenocarcinoma

(CCA) is exceptionally uncommon, with only a few dozen cases reported in the English literature.[3–5] Because of this extreme rarity, there is no widely accepted standard of care; diagnosis is often delayed, and therapeutic options vary widely. We present a case of clear-cell adenocarcinoma arising in the bulbomembranous urethra of a male patient, with early pulmonary metastases, treated with partial urethrectomy and systemic chemotherapy resulting in radiologic response.

Case presentation

A 53-year-old male (hospital number R-00068866) presented to Travancore Medical College & Hospital, Kollam on 24/03/2025 with a 4-week history of progressive difficulty in initiating and passing urine and a palpable swelling in the perineo-scrotal region. He had no prior urethral instrumentation except for a flexible cystoscopy on 18/03/2025 that showed a very narrow urethral lumen; the scope could not be introduced beyond the bulbar urethra.

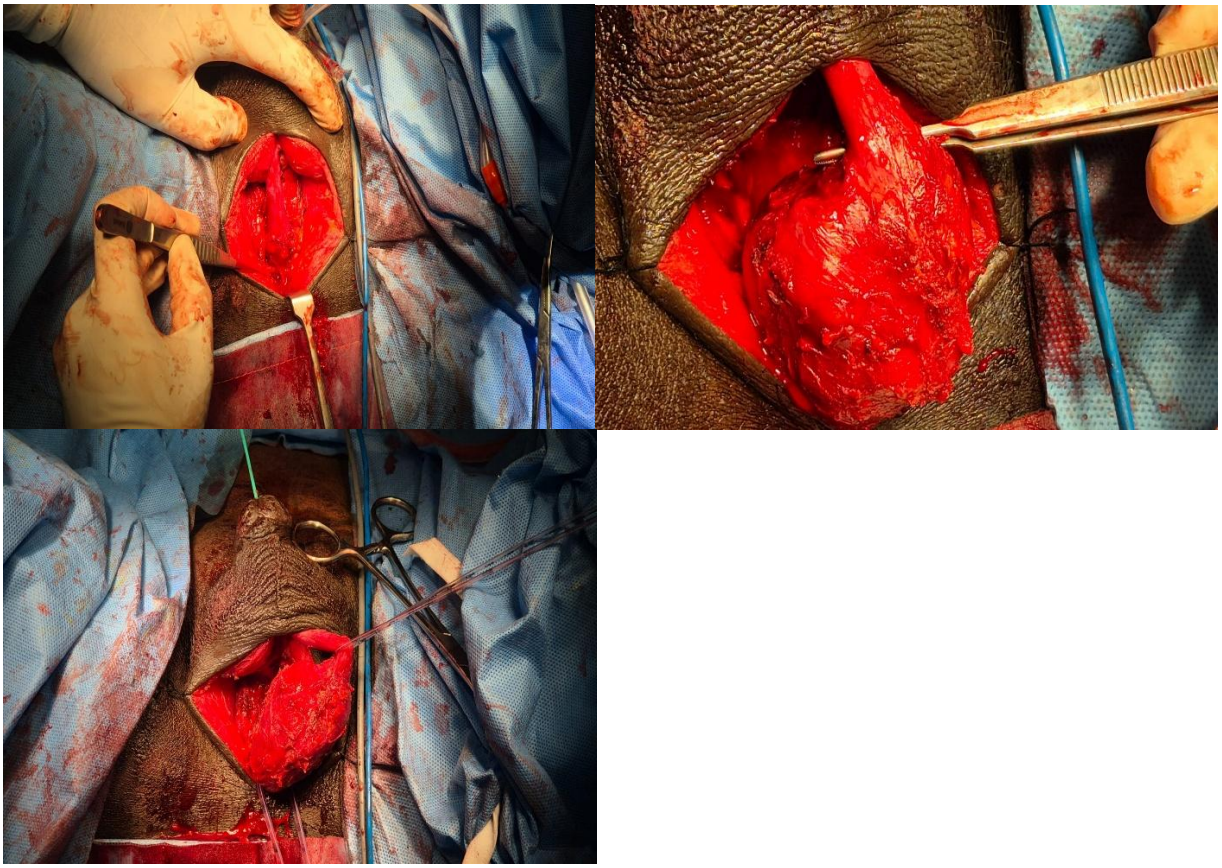
Clinical examination revealed a firm midline perineal swelling, and the urethral meatus was normal, but catheterisation attempts failed due to narrowing. Pre-operative investigations: PSA 4.21 ng/mL, HbA1c 6.52%, renal and liver function within normal limits. MRI pelvis (20/03/2025) showed an enhancing mass along the ventral surface of the posterior penis and adjacent anterior perineum, inseparable from corpus spongiosum and posterior urethra, with luminal extension into the bulbar urethra; size consistent with operative findings.

On 25/03/2025 the patient underwent perineal midline incision, wide excision of the tumour with part of the urethra and immediate mucosa-to-mucosa urethroplasty with spongiosal plication and drain insertion. The tumour was removed en bloc; proximal and distal urethral margins and mucosa submitted for histopathology. Post-operative recovery was uneventful; the drain was removed on 27/03/2025 and patient discharged on 29/03/2025 stable and afebrile, with catheter in situ.

Histopathologic examination (report dated 25/03/2025) described a soft tissue mass of ~4.5 × 4.5 × 4.2 cm arising in peri-urethral tissue, with grey-white granular neoplasm circumferentially involving and obstructing the urethral lumen. Microscopically, fragments showed invasive neoplasm arising from dysplastic urethral mucosa, composed of glands and tubulocystic spaces containing mucin, solid nests and papillary architecture; cells with abundant clear to eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli. Perineural invasion was identified focally, and proximal urethral margin showed tumour involvement; distal margin free. No lymphovascular invasion identified. Immunohistochemistry: CK7 strong diffuse positive, CK20 focal positive, AMACR diffuse cytoplasmic positive, PAX8 focal nuclear positive, Napsin focal cytoplasmic positive, Ki-67 ~70%. The report concluded: “Morphologic and immunohistochemical features compatible with adenocarcinoma of the urethra; clear-cell adenocarcinoma may be considered.” Pathologic staging (CAP protocol): tumour site bulbomembranous urethra; tumour size 4.5 × 4.5 × 4.2 cm; histologic type adenocarcinoma of urethra (clear-cell features); grade G2 moderately differentiated; tumour invades sub-epithelial connective tissue; margins: proximal margin involved; perineural invasion present; lymphatic/vascular invasion not identified.

Systemic staging included a whole-body 18F-FDG PET-CT on 07/05/2025 which showed metabolically active soft tissue thickening in the line of the anterior penile urethra (size ~12 × 10 mm, SUVmax 30.24) and the postoperative bed at bulbomembranous junction (8 × 8 mm, SUVmax 42.62). Multiple random small non-calcified solid nodules were identified in bilateral lungs (largest in left upper lobe measuring 7 mm, SUVmax 18.47). No metabolically active lymph nodes in bilateral inguino-femoral regions. The multidisciplinary tumour board recommended systemic chemotherapy. The patient was referred to the Regional Cancer Centre (RCC), Thiruvananthapuram, and chemotherapy was initiated in late June 2025 with cisplatin plus gemcitabine per plan (six-cycle schedule) as documented in the chemotherapy prescription dated 27/06/2025. Cycle and dose administration records show cisplatin 75 mg/m² and gemcitabine 1 g/m² given on day 1 and day 8 every 3 weeks; antiemetic and hydration protocol followed. After three cycles, a follow-up contrast CT thorax-abdomen-pelvis on 02/09/2025 reported “No obvious residual or metastatic lesions in the

present study". The patient is clinically stable and remains on oncology surveillance; further adjuvant or maintenance therapy is under consideration.



Discussion

Clear-cell adenocarcinoma of the male urethra is extraordinarily rare, with fewer than 20 well-documented cases in the English literature.[4,6] Most urethral cancers in men are urothelial or squamous in origin, whereas adenocarcinoma accounts for only ~6% of male urethral malignancies.[2] The pathogenesis of clear-cell adenocarcinoma remains poorly understood; proposed origins include Müllerian, mesonephric and nephrogenic metaplasia.[3] The clinical presentation often mimics urethral stricture disease: obstructive LUTS, hematuria, urinary retention, or catheterisation failure.[3] In our patient, the initial presentation of urinary obstruction and narrow urethral lumen did not immediately suggest malignancy.

Radiologic imaging (MRI and PET-CT) plays an important role in defining local extent and systemic staging. Clear-cell histology demonstrates tubulocystic, papillary or solid architecture, with clear cytoplasm and hobnail cells; immunophenotyping often shows CK7 positivity, PAX8/AMACR positivity and high Ki-67.[5] Our case demonstrated a consistent IHC profile (CK7 strong, CK20 focal, AMACR positive, PAX8 focal, Napsin positive, Ki-67 ~70%). Margin involvement and perineural invasion are adverse prognostic features.

Given the rarity there are no randomized trials guiding therapy. Surgical resection with negative margins remains the preferred approach for localized disease.[1–3] In metastatic presentations, platinum-based chemotherapy (cisplatin + gemcitabine) is commonly utilized by analogy to urothelial carcinoma regimens; case reports suggest potential benefit.[3,7] In our case the patient presented with early pulmonary metastases but demonstrated radiologic complete response after three cycles of chemotherapy — a favourable outcome in a historically poor prognosis setting.

This case highlights: (1) the need for high index of suspicion for atypical urethral narrowing and perineal swelling; (2) the utility of MRI and PET-CT in staging; (3) importance of histopathology with expanded IHC panel for accurate diagnosis; (4) requirement for multidisciplinary management;

and (5) the potential role of systemic chemotherapy even in metastatic clear-cell urethral adenocarcinoma. Long-term follow-up is mandatory.

Conclusion

Primary clear-cell adenocarcinoma of the male bulbomembranous urethra is exceptionally rare and aggressive. Accurate diagnosis requires histopathologic and immunohistochemical confirmation. Multimodal treatment — surgical excision and systemic chemotherapy — can achieve substantial response even in metastatic disease. Early recognition and coordinated care are key to improving outcomes.

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