

Primary Mucinous Bladder Adenocarcinoma

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Abstract: Mucinous adenocarcinoma, a rare subtype of primary bladder adenocarcinoma, accounts for approximately 20% of primary bladder adenocarcinomas and should be distinguished carefully from secondary adenocarcinomas of gastrointestinal origin. Herein, we report an unusual case of primary mucinous adenocarcinoma arising from a villous adenoma in a 52-year-old male presenting with urinary difficulties and recurrent bladder tumours. The patient had a significant medical history including right nephrectomy and left ureterolithotomy. Radiological and pathological evaluations revealed invasive mucinous adenocarcinoma. Surgical management included radical cystectomy, left nephroureterectomy, right ureterectomy, segmental rectal resection, and bilateral pelvic lymphadenectomy. This case emphasizes the complexity of diagnosis and management, highlighting the importance of distinguishing primary bladder mucinous adenocarcinoma from secondary gastrointestinal malignancies.

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Introduction

Bladder cancer is the 10th most common malignancy globally, with a significantly higher incidence in men than women. Urothelial carcinoma represents the majority of bladder cancers (90–95%), while adenocarcinomas constitute approximately 2%. Mucinous adenocarcinoma, a rare subtype of primary bladder adenocarcinoma (PBA), represents about 20% of adenocarcinomas (Tatli et al., 2012).

Adenocarcinomas of the bladder may be subclassified into three major categories: a) urachal adenocarcinoma, arising from the embryologic remnant at the bladder dome; b) non-urachal (pure) primary adenocarcinoma, which includes enteric, mucinous, signet-ring cell and mixed subtypes; and c) secondary adenocarcinoma, representing direct extension or metastasis from adjacent organs such as colon, prostate or gynecologic sites (Santos et al., 2015). The mucinous subtype is characterized by abundant extracellular mucin pools with clusters of neoplastic cells, often exhibiting columnar morphology and occasional signet-ring features.

Histologically, mucinous bladder adenocarcinoma demonstrates irregular glandular architecture floating in lakes of mucin, with tumour cells showing moderate-to-marked nuclear atypia and frequent mitoses. Immunohistochemically, primary mucinous adenocarcinoma typically co-expresses cytokeratin 7 (CK7) and cytokeratin 20 (CK20), with variable CDX2 positivity, whereas markers such as GATA3 and uroplakin are consistently negative, helping to exclude urothelial differentiation. By contrast, secondary colorectal adenocarcinomas invading the bladder often show strong CDX2 and nuclear

β -catenin expression but lack CK7. Tuna (2018) recommend a panel including CK7, CK20, CDX2, β -catenin, and GATA3 to reliably discriminate primary bladder adenocarcinomas from metastases – critical given the therapeutic and prognostic implications.

Due to its rarity and overlapping morphology with metastatic lesions, primary mucinous bladder adenocarcinoma poses significant diagnostic challenges. Moreover, its propensity for aggressive local invasion – often involving periurethral or prostatic tissue – and occasional fistula formation further complicates management. Herein, we present an unusual and aggressive case of primary mucinous adenocarcinoma arising in a background of villous adenoma, with involvement of the prostatic urethra and development of a rectovesical fistula.

Case report

A 52-year-old man who had undergone right nephrectomy in 1989 for a nonfunctioning kidney secondary to severe vesicoureteral reflux presented on July 20, 2024, with a three-week history of gross hematuria, dysuria, urinary frequency, and two episodes of acute urinary retention. He had been on thrice-weekly hemodialysis for five years, maintaining approximately 200 ml of residual urine output per day. His medical history also included chronic left hydronephrosis – attributable to recurrent obstructive episodes over the past decade – hypertension controlled with amlodipine 10 mg and losartan 50 mg daily, and hyperlipidemia managed with atorvastatin 20 mg nightly.

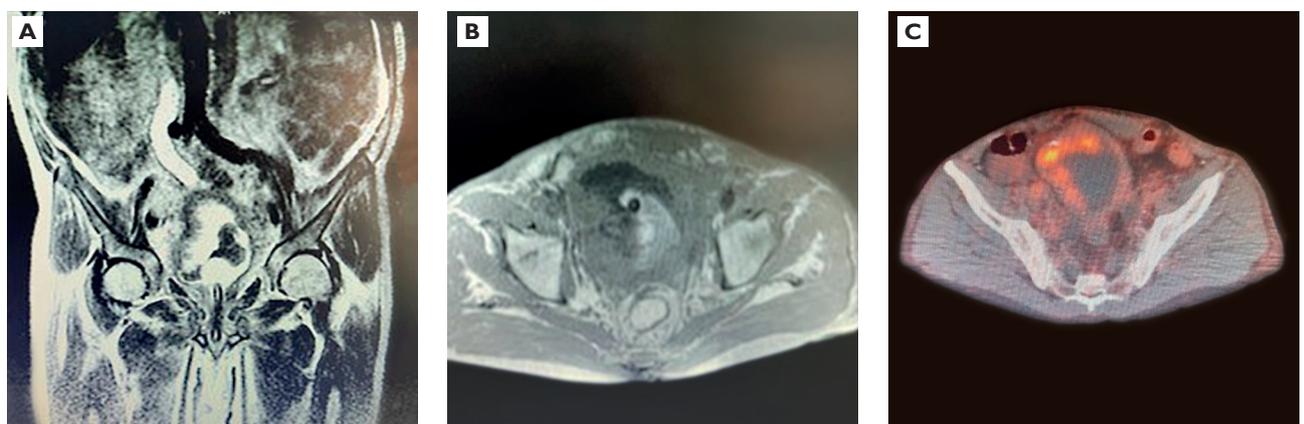


Figure 1(A and B): A mass configuration measuring approximately 4.2×1.6 cm, displaying a papillovillous appearance and disrupting the wall integrity, is observed in the right half of the bladder lumen. Amorphous signal void areas within the lumen are considered in favour of coagulum. Additionally, on the left side, starting from the 2 o'clock position to the 4 o'clock position, wall integrity is lost. An extravesical mass measuring approximately 5×3 cm, thought to be associated with the bladder wall, is detected in the left perivesical area. (C) A primary tumoral lesion with increased FDG-PET (fluorodeoxyglucose positron emission tomography) uptake and heterogeneous characteristics has been observed, appearing to invade the perivesical fatty plane, particularly on the left side, as well as the right and anterior walls of the bladder.

Four days after presentation, renal and bladder ultrasound demonstrated a large heterogeneous mass measuring 112×60×143 mm within the bladder and persistent grade 3 hydronephrosis of the left kidney. On August 2, 2024, pelvic magnetic resonance imaging (MRI) further characterized a 4.2×1.6 cm papillovillous lesion on the right bladder wall, accompanied by a separate 5×3 cm extravesical component extending from the 2 to 4 o'clock positions (Figure 1). The study revealed loss of bladder wall integrity, a fistulous tract toward the rectourethral space, and encasement of the left ureter as it traversed the mass.

For tissue diagnosis and partial debulking, the patient underwent transurethral resection of the bladder tumour (TURB) on October 18, 2024. Intraoperatively, gelatinous mucinous material and papillary foci were noted. Multiple biopsy samples were obtained from both the bladder mass and suspicious lesions in the prostatic urethra; two of these specimens lacked identifiable muscularis propria.

Staging investigations included an ¹⁸F-FDG PET-CT on November 10, 2024, which showed heterogeneous uptake within the bladder lesion (SUVmax 8.4) and two pelvic lymph nodes (SUVmax 4.6) but no distant metastases. A colonoscopic examination performed on November 12, 2024, revealed no evidence of primary colorectal pathology, reinforcing the suspicion of a primary bladder tumour.

Definitive surgical management took place on January 06, 2025. The patient underwent an open radical cystoprostatectomy combined with left nephroureterectomy – electively performed because of the left kidney's chronic nonfunction and infection risk – and a low anterior resection of the rectum to address the rectourethral fistula. Urinary diversion was constructed with an end ileal conduit (Bricker) and right lower-quadrant stoma. His postoperative course

was notable only for a mild paralytic ileus that resolved by postoperative day five, and he was discharged after a 14-day hospitalization.

Histopathologic examination of the en bloc specimen confirmed a moderately differentiated, intestinal-type mucinous adenocarcinoma infiltrating the bladder neck's muscularis propria and the prostatic urethra (pT4) (Figure 2). Two of twelve pelvic lymph nodes were positive (pN2). Immunohistochemistry showed strong CK20 and CK7 positivity, negative GATA3, and both nuclear and cytoplasmic β -catenin staining, supporting the diagnosis of primary mucinous adenocarcinoma of the bladder arising in a background of villous adenoma and effectively excluding colorectal or urachal origin. No adjuvant therapy was administered, and at six-month follow-up the patient remains free of recurrence.

Discussion

Primary adenocarcinomas of the bladder represent approximately 2% of all bladder malignancies. Mucinous adenocarcinoma is a histological subtype accounting for about 20% of primary bladder adenocarcinomas. Secondary adenocarcinomas, including metastases from colorectal and urachal adenocarcinomas, should be carefully excluded to ensure accurate diagnosis. Histologically, bladder adenocarcinomas are categorized into mucinous, enteric (colonic), signet-ring cell, and mixed types. Each subtype exhibits unique morphological and immunohistochemical features that can guide diagnosis and treatment decisions. It represents a relatively rare histopathological subtype of primary bladder cancer. Previous studies suggest a progression in the pathogenesis of primary mucinous adenocarcinoma, evolving sequentially from mucinous metaplasia

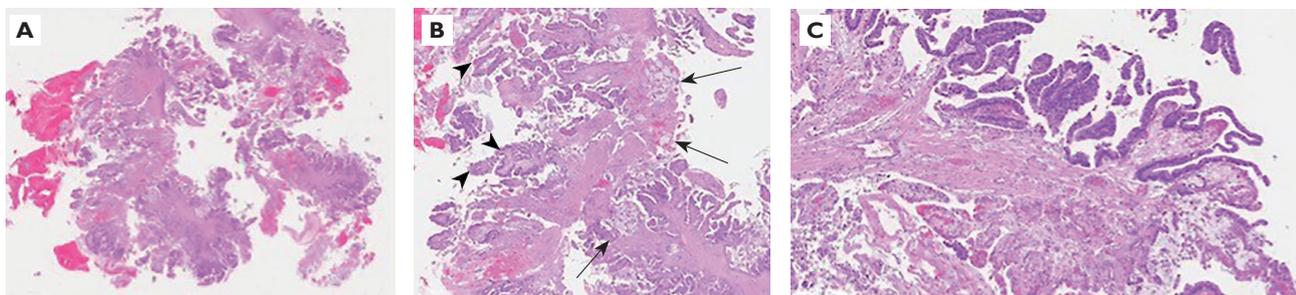


Figure 2(A): In the transurethral resection material, focal mucinous/colloid component containing intestinal-type well-differentiated adenocarcinoma and villous adenoma with high-grade dysplasia are observed together in the prostatic urethra. (B) The tumour infiltrates the muscularis propria bundles of the bladder neck. Intestinal-type well-differentiated adenocarcinoma (arrow) and villous adenoma with high-grade dysplasia (arrowhead). (C) An area of invasive mucinous adenocarcinoma showing continuity with the villous adenoma (upper part of the image) is observed together. (A) Haematoxylin and eosin staining, 40× magnification, (B) haematoxylin and eosin staining, 130× magnification, (C) haematoxylin and eosin staining, 400× magnification.

and mucinous adenoma into invasive mucinous adenocarcinoma (Di Lauro et al., 2013; Zhang et al., 2014).

Clinically, primary mucinous adenocarcinoma is characterized by aggressive behaviour and a high propensity for invasion and metastasis. At diagnosis, metastatic dissemination is reported in up to 40% of cases, primarily through lymphatic pathways, commonly involving iliac (internal, external, common) and obturator lymph nodes. Additionally, direct local invasion to adjacent structures such as the prostate and posterior urethra has been documented. More distant metastases, although less frequent, have also been reported in organs including the ovary, uterus, abdominal wall, colon, and penis (El-Ghobashy et al., 2009; Jo et al., 2011).

Our review of the literature highlights the exceptional rarity of urethral involvement by primary mucinous adenocarcinoma of the bladder, as illustrated by the current case. Clinical manifestations of primary mucinous adenocarcinoma are typically nonspecific and include suprapubic pain, hematuria, dysuria, and irritative voiding symptoms (Zaghloul et al., 2006).

The histogenesis of primary mucinous adenocarcinoma remains controversial, with two primary hypotheses proposed: origin from vestigial embryonic glandular remnants within the transitional epithelium, or glandular metaplasia arising from transitional epithelial cells.

Given the limited number of reported cases, well-established clinical and radiological characteristics remain undefined. Nevertheless, this case underscores the importance of meticulous ultrasonographic evaluation of the bladder and adjacent structures, particularly in patients presenting with atypical urinary symptoms, to facilitate timely diagnosis and treatment.

The mainstay of management for primary mucinous adenocarcinoma of the bladder involves surgical intervention, predominantly radical cystectomy with pelvic lymphadenectomy. Although the benefit of routine postoperative adjuvant therapy remains debatable, adherence to guideline-recommended chemotherapy protocols may offer therapeutic advantage. Moreover, diligent postoperative surveillance is imperative to detect early recurrence,

both local and distant, given the aggressive nature and metastatic potential of this malignancy.

Conclusion

This case highlights the importance of thorough histopathological and immunohistochemical evaluation in differentiating primary bladder mucinous adenocarcinoma from secondary gastrointestinal malignancies, especially in patients with complex urological histories and chronic renal disease. The presence of a rectovesical fistula and extensive local invasion underscores the tumour's aggressiveness. Comprehensive pathological and clinical assessment is crucial for accurate diagnosis and appropriate management.

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