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Case Report

Adenocarcinoma of renal pelvis along with precancerous bladder lesions: A case report

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Summary

Primary adenocarcinoma of the renal pelvis, particularly when accompanied by precancerous lesions in other organs of the urinary tract such as the bladder or ureter, is a rare finding. This type of malignancy is usually associated with inflammation, long-term urinary obstruction, and renal calculi. In this report, we present a new case of intestinal-type adenocarcinoma of the renal pelvis with precancerous bladder lesions. Initially, the diagnosis was polypoid cystitis based on a small bladder biopsy. However, subsequent transurethral resection of the bladder one month later revealed intestinal-type cystitis glandularis with mucin extravasation. The exacerbation of clinical symptoms led to right nephroureterectomy two years later, which revealed adenocarcinoma of the renal pelvis. The patient underwent chemotherapy and is now disease-free six months later. The most significant challenge in managing adenocarcinoma of the renal pelvis is ruling out distant metastasis or direct invasion of the tumor from adjacent organs, as well as the possibility of multifocality in other foci of the urinary tract.

Keywords: Adenocarcinoma, Bladder lesions, Tumor, Renal pelvis

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Introduction

Primary adenocarcinoma of the renal pelvis is a rare finding, representing up to 2% of all renal tumors.[1] It is often associated with inflammation, long-term urinary obstruction, and renal calculi.[2] The main subtypes of this tumor include tubulovillous, mucinous, and papillary non-intestinal categories, with the first two types being intestinal-type adenocarcinoma and accounting for over 90% of all cases.[3] In rare cases, adenocarcinoma of the renal pelvis may be accompanied by adenocarcinoma or premalignant lesions in the bladder or ureter.[4] The most significant challenge in diagnosing and managing this tumor is first to rule out distant metastasis or direct invasion from adjacent organs, and second, to detect other concurrent precancerous or malignant lesions in other urinary tract organs.[5] Herein, we describe a patient with precancerous lesions of the bladder, followed by the tubulovillous variant of intestinal adenocarcinoma of the renal pelvis two years later.

Case Presentation

A 32-year-old man presented to our hospital with symptoms of dysuria and frequency. He had no hematuria, flank pain, or weight loss. He was a current smoker with no other abnormal clinical findings in his history. Initial physical examination did not reveal any specific findings. His laboratory tests were mostly within normal ranges, with serum creatinine level at 1.5 mg/dL and serum hemoglobin level at 14.6 g/dL. However, he had a positive urine culture for *Klebsiella pneumoniae*. Initial ultrasonic assessment showed that the left kidney appeared normal, but the right kidney was atrophic, measuring 7.5×3.5 cm with a simple cyst and gas bubble in the parenchyma. Additionally, a cystic solid mass measuring 3.2×2 cm was found on the right side of the bladder.

In the CT scan study, an atrophic kidney on the right side and a 7-millimeter stone were the only evident findings. The patient was then scheduled for cystoscopy, which revealed a 0.4×0.3×0.2 cm papillary-like mass around the right ureter in the trigone and right orifice. The initial pathology report of the cold cup biopsy of the bladder mucosa indicated moderate chronic cystitis with polypoid formation (polypoid cystitis) (Figure 1). During the next cystoscopic exam, which took place one month later, a

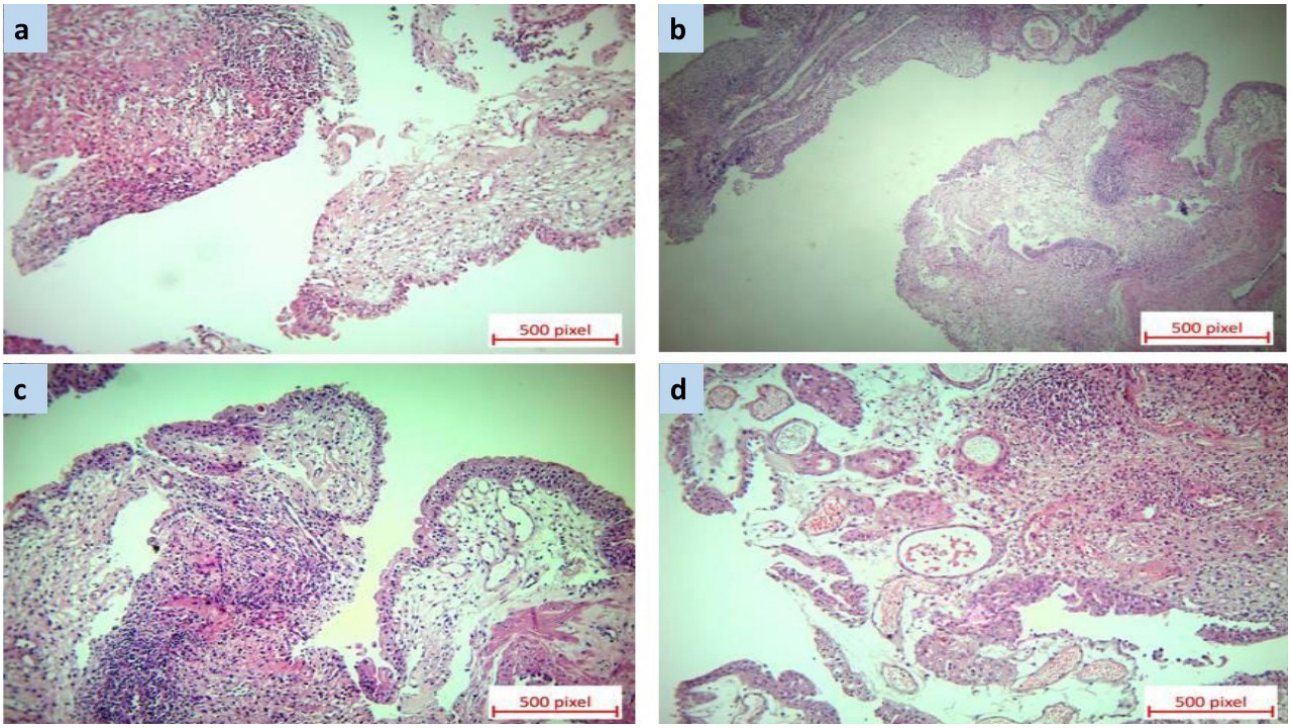

Figure 1. Moderate infiltration of mixed inflammatory cells in bladder biopsy with foci of edema of lamina propria and polypoid formation. **a.** Shows moderate infiltration of mixed inflammatory cells in the bladder tissue. **b.** Demonstrates edema of the lamina propria, where the tissue appears swollen and less dense due to fluid accumulation. **c.** Exhibits polypoid formation. The tissue shows raised, finger-like extensions with inflammatory infiltration. **d.** Displays a mixed inflammatory cell infiltration along with structural changes including both edematous areas and polypoid formations in the bladder biopsy tissue

polypoid mass in the trigone of the bladder was found. Microscopic examination of the transurethral resection of the bladder tumor showed cystitis glandularis, intestinal type with mucin extravasation (Figure 2).

The specimen was negative for carcinoma *in situ* (CIS) or malignancy. However, due to the presence of premalignant lesions in the bladder biopsy, patient follow-up was highly recommended. Two years later, due to the persistence of patient complaints and intensification of clinical manifestations, especially severe flank pain, a CT imaging study was performed, revealing right hydroureteronephrosis and decreased parenchymal thickness. Cystourethroscopic examination also showed right ureterovesical junction (UVJ) stenosis and multiple small lesions in the right ureter. Biopsy of the right ureter lesions showed severe acute on chronic polypoid inflammation with ulceration (Figure 3).

Right radical nephroureterectomy was performed as the next step, which showed adhesion to the duodenum during surgery. Macroscopic evaluation of the specimen showed a small kidney measuring $7 \times 4.5 \times 4.5$ cm along with a $3 \times 2 \times 1$ cm tumoral mass in the lower pole. Histological assessment of the mass confirmed the definitive diagnosis of intestinal-type and tubulovillous variant adenocarcinoma of the renal pelvis (Figure 3). The tumor was well-differentiated and involved the lamina propria, renal parenchyma, and muscular layer (pT3), but did not involve peripelvic fat, Gerota's fascia, or the renal vein. Vascular or lymphatic invasion was also not identified.

European Association of Urology (EAU) guideline is the current standard for the management of localized renal pelvis adenocarcinoma, since no organ-sparing approaches have been validated for this rare pathology. This extensive resection is critical due to the high risk of multifocal disease and the difficulty in obtaining negative margins in a field of chronic inflammation and metaplasia.[6] The only separated lymph node was free from tumor. The renal pelvic mucosa adjacent to the tumor showed precancerous lesions, such as tubulovillous adenoma and mucin-producing glands. During follow-up, positron emission tomography-computed tomography (PET/CT) scanning, endoscopy, and colonoscopy were performed, which were normal and ruled out metastasis or invasion of the tumor from adjacent organs, especially the gastrointestinal tract. The patient underwent chemotherapy with 5-fluorouracil plus oxaliplatin based on the standard protocol and was followed up. After six months, the patient was disease-free. This period is a positive but short-term outcome. Therefore, a long-term surveillance plan is essential and has been implemented. This includes regular CT scans for up to five years and frequent bladder monitoring via cystoscopy.

Discussion

The predominant type of tumors related to the renal pelvis is urothelial carcinoma, accounting for about 90% of all tumors originating from the renal pelvis or ureter.[3]

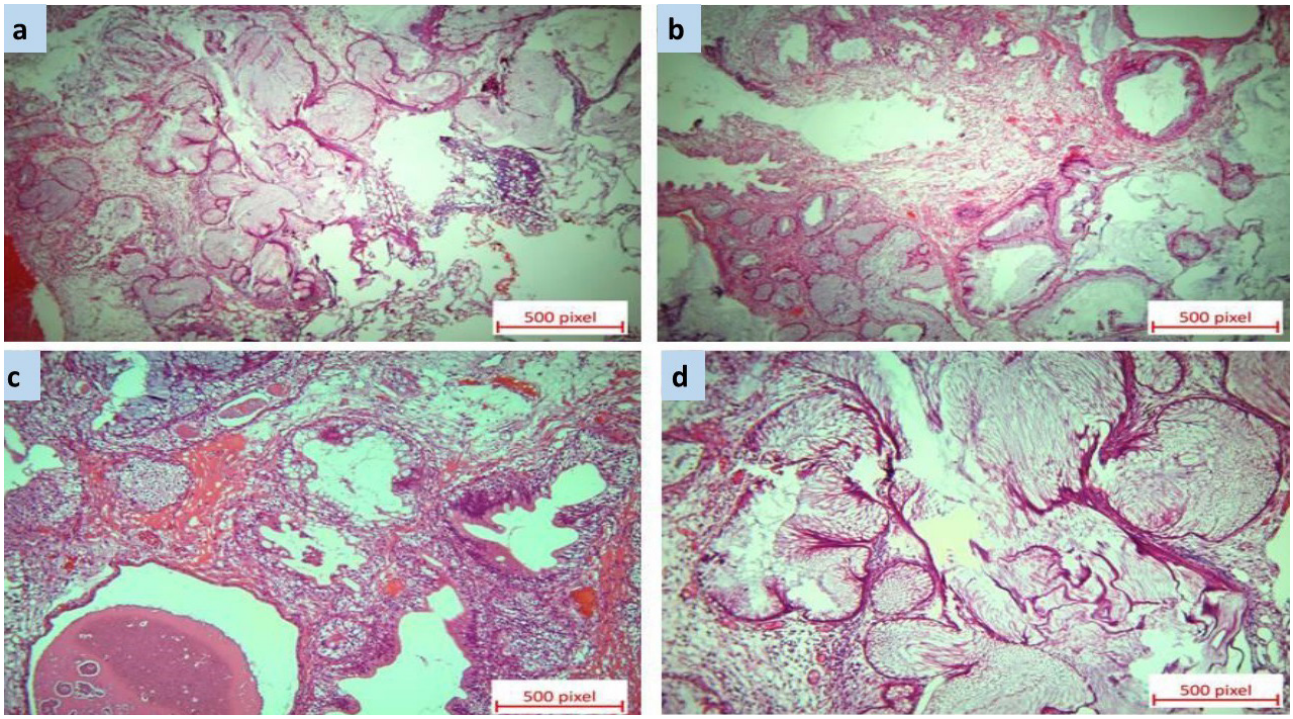

Figure 2. Intestinal metaplasia of cystic Von Brunn nests and mucin extravasation in transurethral resection of bladder. **a.** Shows tissue with irregular, dilated spaces or cavities surrounded by fibrous connective tissue. The architecture appears disrupted with cystic-like formations**. b.** Displays similar pathological changes with enlarged spaces and thickened connective tissue walls. **c.** Demonstrates more extensive tissue changes with larger cavities and increased fibrous tissue proliferation. **d.** Shows advanced pathological changes with complex branching patterns and extensive fibrosis

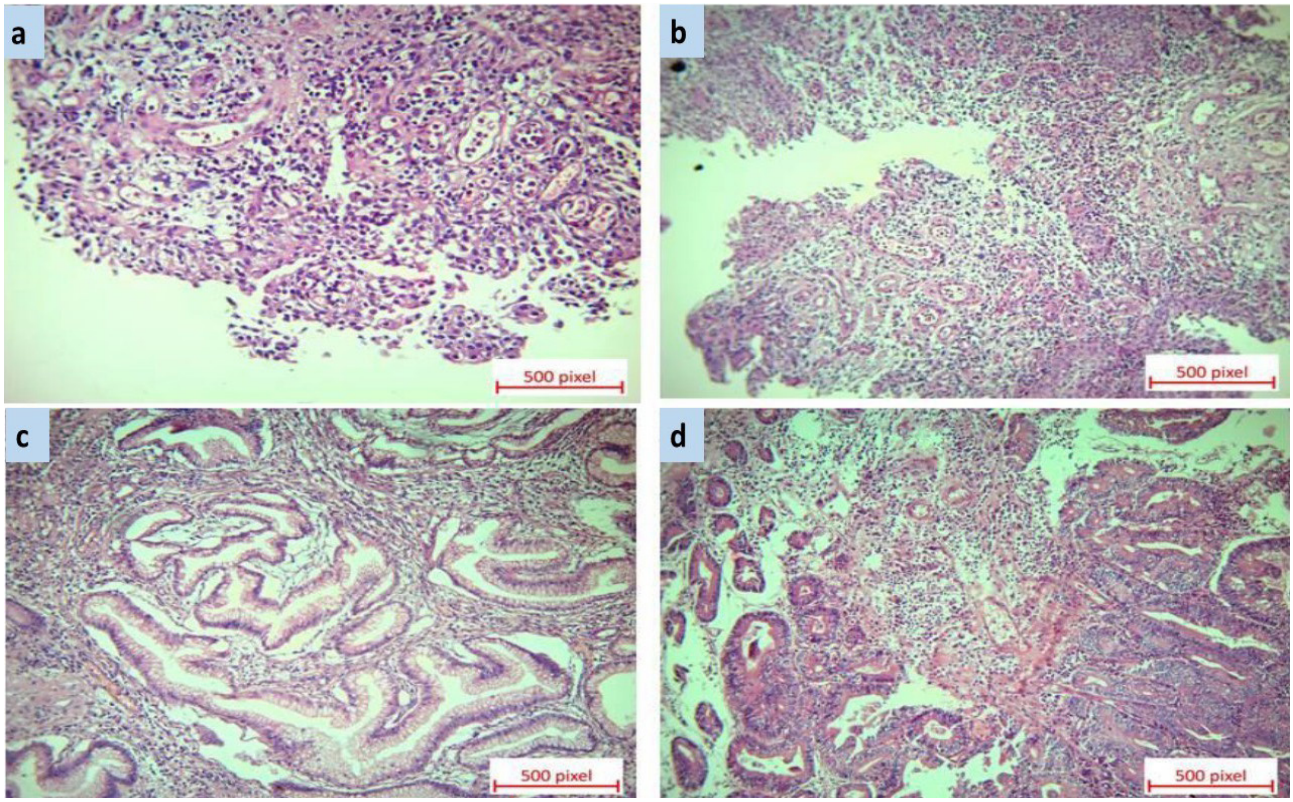

Figure 3. a-b. Display severe polypoid inflammation and ulceration of ureter. **c.** represents precancerous lesions as mucin producing glands in adjacent renal pelvic mucosa. **d.** shows intestinal type adenocarcinoma of renal pelvis

Other types of tumors, such as squamous cell carcinoma, leiomyosarcoma, or adenocarcinoma, are rare in this area. Adenocarcinoma can be found in less than 1% of all renal pelvis and ureter malignancies. Renal pelvis

adenocarcinoma often has an inflammatory basis, which can result from infection, calculi, or hydronephrosis.[7] The exact pathogenesis of these tumors remains uncertain; however, there is a close association with infection, activation of the inflammation cascade, trauma, and even chronic irritation.[8] This chronic inflammatory background is a key etiological factor, often leading to metaplastic changes in the urothelium, such as to intestinal-type cystitis glandularis, which is a recognized precancerous condition.

The occurrence of renal pelvis adenocarcinoma is noted equally in men and women, with a higher likelihood seen with advancing age.[9] Adenocarcinoma of the renal pelvis is initially manifested by hematuria, which may also be accompanied by a palpable abdominal mass and severe loin pain in later stages. In about two-thirds of affected patients, hydronephrosis or renal calculi may also be present, but some cases have been described as asymptomatic during disease progression.[10] The main challenges in diagnosing renal pelvis adenocarcinoma include differentiating it from benign lesions, as well as distinguishing it from more frequent metastatic adenocarcinomas or direct invasion, especially from the gastrointestinal tract. Differential diagnosis is particularly challenging on small biopsies that contain poorly differentiated tumors.

Although various imaging modalities can help physicians differentiate renal pelvis adenocarcinoma from other lesions in this region, in some cases, due to a mismatch between imaging findings and the absence of specific malignant markers in the early stages, these types of tumors can be misdiagnosed at an early stage. It should be noted that intravenous urogram (IVU) assessment may reveal a filling defect in the renal pelvis and ureter, along with hydronephrosis and hydroureter due to obstruction.[11] Ultrasonography may show an iso- or hypo-echoic soft tissue extending into the upper ureter with or without hydronephrotic changes.[12]

CT scanning can also provide information on the size, location, and extension of the suspected mass. Ultimately, the tumor can be definitively diagnosed based on histological assessment. The final therapeutic approach for renal pelvis adenocarcinoma includes nephrectomy and/or ureterectomy, which usually results in a favorable mid-term outcome without recurrence.[8] The prognosis is generally favorable when the disease is localized and completely resected; however, it can be poor in cases with advanced local invasion or metastatic disease at presentation. As described in the present report, during the first two years of follow-up in our case, the diagnostic approach was based on precancerous lesions of the bladder due to the lack of initial evidence for a diagnosis of a malignant mass in imaging studies. However, due to the exacerbation of clinical symptoms, subsequent evaluations revealed a mass in kidney imaging that was confirmed to be adenocarcinoma on microscopic examination, and the patient was successfully managed. In a similar case presented by Hudson et al. in 2013,[13] an 81-year-old female presented with difficulty voiding and mucosuria.

An intestinal-type villous adenoma of the renal pelvis with high-grade dysplasia and focal areas suspicious for invasive adenocarcinoma was finally diagnosed in histological evaluation. In another case presented by Renaud et al. in 2010,[14] a 57-year-old woman was described with the chief complaint of renal colic due to pyelolithiasis, which was ultimately diagnosed as intestinal-type adenocarcinoma of the renal pelvis on histological examination. These cases, similar to ours, emphasize the diagnostic challenge and the strong association with chronic irritation and metaplasia.

The uniqueness of our case lies in the diagnosis of concomitant intestinal-type adenocarcinoma of the renal pelvis with precancerous lesions of adenocarcinoma in the bladder. Such cases have been rarely reported before. In a case reported by Xiong et al in 2016,[15] a large cystic calculus with multiple tumors in the renal pelvis and ureter, along with multifocal tumors and a large calculus in the bladder, were identified. The pathology examination revealed a moderately differentiated tubular adenocarcinoma. The presence of concomitant precancerous lesions in the bladder signals a "field effect" of instability and metaplastic change throughout the urinary tract mucosa. Therefore, a diagnosis of intestinal-type adenocarcinoma in the upper tract should prompt a thorough and ongoing examination of the entire urothelium, especially the bladder. We recommend that such patients undergo intensified, long-term cystoscopic surveillance beyond standard protocols to monitor for the development of metachronous bladder adenocarcinoma, ensuring early detection and intervention if a second primary tumor arises.

Conclusion

In conclusion, simultaneous evaluation of other organs of the urinary tract, including the bladder and ureter, should also be considered in the management of renal pelvis adenocarcinoma. Our case describes a very rare occurrence of intestinal-type adenocarcinoma of the renal pelvis along with intestinal-type cystitis glandularis with mucin extravasation in the bladder, which is a precancerous lesion of adenocarcinoma. The patient was successfully managed despite the lack of a definitive diagnosis in the early years of clinical presentation. This case highlights the importance of considering a field effect of chronic inflammation throughout the urinary tract and maintaining a high index of suspicion for synchronous lesions in patients with long-standing irritative risk factors.

Authors' Contribution

Conceptualization: Maryam Abolhasani.
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Project administration: Maryam Abolhasani.
Supervision: Maryam Abolhasani.
Validation: Maryam Abolhasani.
Writing—original draft: Maryam Abolhasani, Nikoo Emtiazi.
Writing—review & editing: Nikoo Emtiazi.

Competing Interests

The authors declare that there are no competing interests.

Ethical Approval

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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This article has not utilized artificial intelligence (AI) tools for research and manuscript development, as per the GAMER reporting guideline.

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