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case report

Nephrogenic adenoma of the urinary bladder: A Histopathological case report

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ABSTRACT:

We report the case of a 31-year-old man presenting with painless macroscopic hematuria, a rare symptom in young adults that often requires a thorough evaluation to exclude an underlying malignancy. Initial uroimaging and cystoscopic examination revealed a papillary lesion originating from the bladder neck and extending to the prostatic urethra, strongly suggesting a neoplastic process. The patient underwent transurethral resection of the bladder tumor (TURBT), and histopathological analysis of the resected tissue revealed architectural and cytological features characteristic of a nephrogenic adenoma, a rare benign metaplastic lesion of the urothelium. Microscopic examination revealed tubular and papillary structures lined with cuboidal to nail-shaped epithelial cells, embedded in an edematous stroma. No cytological atypia, mitotic activity, or signs of urothelial carcinoma or other malignant transformation were identified. Nephrogenic adenoma is often misdiagnosed as carcinoma due to its histological resemblance to malignant entities, including adenocarcinoma and nested variants of urothelial carcinoma. This case highlights the critical importance of accurate histopathological interpretation to avoid overtreatment, particularly in young patients, for whom the psychosocial and physical consequences of a cancer diagnosis can be profound. This report aims to raise awareness among clinicians about this rare entity, highlight the diagnostic challenges it poses, and emphasize the need for clinicopathological correlation to ensure appropriate patient management. The patient's postoperative course was uneventful, and no recurrence was observed during short-term follow-up.

Keywords: Urinary bladder, benign lesions, pathology of urinary bladder, nephrogenic adenoma

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INTRODUCTION:

Nephrogenic adenoma (NA), also known as nephrogenic metaplasia, is a rare, benign epithelial lesion of the urinary tract, most commonly affecting the bladder but also occurring in the urethra, ureters, and renal pelvis [1-2]. It is considered a reactive metaplastic process of the urothelium in response to chronic mucosal injury rather than a true tumor [3]. First described by Davis in 1949, NA is thought to arise from the implantation of renal tubular epithelial cells or the transformation of urothelial progenitor cells under the influence of local inflammatory or irritating stimuli [1]. The development of a nephrogenic adenoma is strongly associated with a history of chronic inflammation, recurrent urinary tract infections, urolithiasis, and previous surgical procedures such as transurethral resection, pelvic radiation therapy, indwelling catheters, or intravesical therapy. In many cases, including the one presented here, no clear triggering event is identified, suggesting that subtle or subclinical urothelial trauma may be sufficient to trigger metaplastic transformation [3-4]. Clinically, NA may present with hematuria, dysuria, urinary frequency, urinary urgency, or lower urinary tract irritation symptoms, although some cases are discovered incidentally during cystoscopic evaluation for other indications [3,5]. Despite its benignity, the lesion can present with an alarming endoscopic appearance, often manifesting as a papillary, polypoid, or sessile mass mimicking a malignant tumor [3]. Furthermore, its histopathological features, including small tubular structures, papillary fronds, and nail-like epithelial cells, can closely resemble invasive adenocarcinoma, clear cell carcinoma, or the nested variant of urothelial carcinoma [6-7].This histologic overlap poses a significant diagnostic challenge, particularly in young patients, for whom clinical suspicion of bladder cancer is generally low. In such a setting, misdiagnosis can lead to unnecessary radical interventions, such as aggressive surgical resection, systemic therapy, or even cystectomy, exposing the patient to avoidable physical and psychological burden [5,8].We report the case of a previously healthy 31-year-old man who presented with painless macroscopic hematuria. This diagnosis required cystoscopy and identification of a lesion of the bladder neck and prostatic urethra. The appearance of the lesion raised suspicion of malignancy, but histological examination of the transurethral resected tissue ultimately confirmed the diagnosis of nephrogenic adenoma. This case highlights the importance of recognizing nephrogenic adenoma in the differential diagnosis of bladder masses, particularly in young adults without traditional risk factors for bladder cancer, and reinforces the need for rigorous clinicopathologic correlation to avoid overtreatment.Given its rarity and the potential for diagnostic error, nephrogenic adenoma remains a crucial entity that clinicians and pathologists must be aware of. Our goal in presenting this case is not only to contribute to the existing body of literature but also to improve clinical vigilance and diagnostic accuracy when encountering bladder lesions in atypical patient populations.

Case Presentation

A 31-year-old man presented to the urology outpatient department with intermittent, painless gross hematuria, noted approximately seven days prior to his consultation. The hematuria was described as bright red, occurring throughout the urinary stream, and not associated with clots. The patient denied any dysuria, urinary urgency, frequency, nocturia, hesitancy, or incomplete voiding. He had no suprapubic or low back pain, nor a history of fever, chills, weight loss, night sweats, or fatigue. He also denied any recent strenuous physical activity or trauma. His medical history was unremarkable. He had no history of urinary tract infection, renal lithiasis, previous urological procedures, or instrumentation. He had no known family history of genitourinary malignancies and no personal history of smoking, exposure to industrial chemicals, or occupational risk factors associated with urothelial carcinogenesis. The patient reported a healthy lifestyle and had not recently taken any medications, herbal supplements, or anticoagulants. The physical examination revealed the patient to be alert, oriented, and hemodynamically stable. The abdominal examination revealed no tenderness, palpable masses, or bladder distension. The external genitalia were normal, and a digital rectal examination (DRE) revealed a smooth, symmetrically enlarged prostate, without nodularity or firmness. There was no suprapubic or costovertebral angle pain.

Laboratory tests were ordered as part of the initial evaluation. The complete blood count (CBC) was within normal limits, with no evidence of anemia or leukocytosis. Renal function tests were normal, indicating preserved renal function. The coagulation profile (PT, APTT, INR) was within normal limits. Urinalysis confirmed significant macroscopic hematuria, with more than 100 red blood cells (RBCs) per high-power field, but without pyuria or bacteriuria. Cell culture revealed no growth after 48 hours of incubation. Urine cytology was negative for atypical or malignant

urothelial cells. KUB ultrasound revealed focal thickening at the bladder neck, with no evidence of hydronephrosis or upper urinary tract obstruction.

Given unexplained hematuria in a young adult male, a flexible cystourethroscopy was scheduled for the patient, performed under local anesthesia. Cystoscopy revealed a sessile papillary lesion arising from the bladder neck and protruding into the prostatic urethra. The lesion measured approximately 1.5 to 2 cm in diameter, was reddish in appearance, exhibited focal friability, and exhibited mild vascularity. The surrounding bladder mucosa was grossly normal, with no other visible lesions, ulcers, or diverticula.

Due to the suspicious appearance of the lesion, the patient was admitted for transurethral resection of a bladder tumor (TURBT) under spinal anesthesia. A 26 Fr resectoscope was inserted, and complete resection of the lesion was performed. The tumor was found to be superficial and did not infiltrate the deeper layers of the bladder or prostatic tissue. Hemostasis was achieved, and tissue fragments were sent for histopathological examination using 10% formalin. No intraoperative complications occurred. A three-way Foley catheter (22 Fr) was inserted postoperatively, and continuous bladder lavage with isotonic saline was initiated to prevent clot formation. The lavage was discontinued after 24 hours, and the lavage was removed after confirmation of urine clarity and adequate voiding. The patient was discharged on the second postoperative day in stable condition with instructions regarding hydration, activity restrictions, and outpatient follow-up.

Microscopically, nephrogenic adenomas typically exhibit tubular, papillary, and microcystic architecture, similar to that of developing renal tubules. The provided hematoxylin-eosin (H&E)-stained histological section shows numerous small to medium-sized tubules and cystic structures, embedded in a fibrous and mildly inflamed lamina propria. These structures are lined by a single layer of cuboidal to low columnar epithelial cells with uniform, uniform nuclei and discrete nucleoli, indicating the benign nature of the lesion. Intraluminal eosinophilic secretions or hyaline material are occasionally observed, as shown in the image. Mitotic figures are rare or absent, and no signs of stromal invasion or cytological atypia are usually present. A distinctive feature supporting the diagnosis is the absence of significant nuclear pleomorphism, high mitotic activity, or necrosis, which helps differentiate nephrogenic adenoma from urothelial carcinoma or prostatic adenocarcinoma extending to the bladder. Immunohistochemically, nephrogenic adenomas are generally positive for PAX8, CK7, and AMACR, and negative for markers such as GATA3 and p63, further distinguishing them from primary urothelial tumors.

Histopathological Features of Nephrogenic AdenomaThe histological examination of the urinary bladder biopsy reveals characteristic findings consistent with nephrogenic adenoma (Figures 1,2).

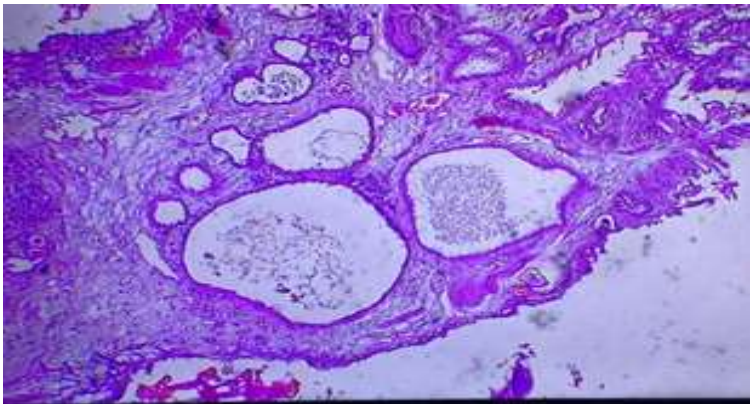

Figure 1. Multiple tubulocystic structures are lined by a single layer of cuboidal to flattened epithelial cells, resembling renal tubules. The stroma surrounding these tubules appears fibrotic and mildly inflamed.

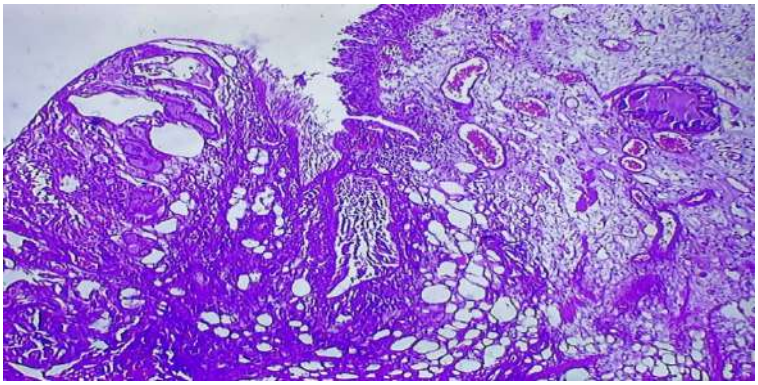

Figure 2. Architectural complexity of the lesion is seen, including back-to-back glands and papillary projections, without evidence of cytologic atypia or invasion into the muscularis propria.

DISCUSSION:

Nephrogenic adenoma (NA) is a rare, benign lesion of the urinary tract, most commonly located in the bladder. Although histologically nonmalignant, NA often presents significant diagnostic challenges due to its clinical and morphologic resemblance to urothelial carcinoma and other malignancies [1-3]. This condition is now widely considered to be a metaplastic response of the urothelium to chronic injury or irritation [3-4]. Although the exact origin of NA is still under investigation, proposed theories suggest that it may result either from the implantation of exfoliated renal tubular epithelial cells or from the metaplastic transformation of local urothelial stem cells [5,9]. Factors such as previous surgical procedures, chronic inflammation, radiation exposure, and prolonged catheterization have all been implicated in its development. Interestingly, in some cases, including the one we report, no identifiable triggering factor is present, highlighting the potential for spontaneous onset [3,5]. Clinically, nephrogenic adenoma typically presents with nonspecific lower urinary tract symptoms, such as urinary urgency, urinary frequency, dysuria, or hematuria [1,3]. Painless macroscopic hematuria, as in our patient, is a common initial sign and can be alarming, particularly in young adults in whom bladder tumors are relatively rare. In such cases, cystoscopic evaluation is crucial [3,10]. Nephrogenic adenoma can present as a papillary, sessile, or polypoid lesion, often suggesting a malignant bladder tumor [3,5]. In our patient, the lesion was discovered during cystoscopy as a papillary mass arising from the bladder neck and extending into the prostatic urethra—an unusual location that contributed to the clinical concern of urothelial carcinoma. Histopathological examination remains the cornerstone of the diagnosis of nephrogenic adenoma. Microscopically, nephrogenic adenoma is characterized by tubular and papillary structures lined with cuboidal or nail-shaped epithelial cells, often resembling renal tubular epithelium [1,9]. These features, although benign, can closely mimic invasive adenocarcinoma or clear cell carcinoma of the bladder, as well as nested variants of urothelial carcinoma [3,5]. Distinguishing between these entities is essential to avoid unnecessary aggressive treatment, such as radical cystectomy or systemic therapy, particularly in young and otherwise healthy patients [5,8]. Immunohistochemistry plays an important role in differentiating NA from a malignant tumor. Nephrogenic adenomas typically express markers such as PAX8, CK7, and AMACR, which support their renal tubular differentiation, and are generally negative for urothelial markers such as GATA3 and p63 [1,11,12].In our case, the final histological diagnosis of nephrogenic adenoma was made after transurethral resection of the bladder tumor (TURBT). The procedure was uneventful, and the patient recovered well postoperatively. Because nephrogenic adenomas are benign, complete surgical excision is generally curative. However, recurrence is not uncommon, with some studies reporting rates as high as 30–40%, particularly in patients with persistent irritating risk factors or incomplete resection [13]. Therefore, follow-up cystoscopy surveillance is generally recommended, although standardized surveillance guidelines remain to be established due to the rarity of this condition [3,14]. The significance of this case lies in several factors. First, the patient's young age and lack of predisposing risk factors make the presentation of NA rare and diagnostically complex. Second, the involvement of the prostatic urethra and bladder neck raised concerns about malignancy, highlighting the importance of a broad differential diagnosis. Finally, this case illustrates how histological expertise and judicious use of immunohistochemical staining can prevent

overtreatment and the resulting psychological and physical burden. Ultimately, this case highlights the importance of considering nephrogenic adenoma in the differential diagnosis of bladder tumors, particularly in young patients without classic risk factors for urothelial carcinoma. It also highlights the need for increased awareness of this benign entity among clinicians and pathologists to ensure accurate diagnosis, appropriate treatment, and to avoid excessive and unnecessary management [3-5].

CONCLUSION:

Nephrogenic adenoma is a rare but significant benign lesion of the urinary tract, which can pose a significant diagnostic challenge due to its clinical and histological resemblance to malignant tumors. Although it usually occurs in response to chronic irritation or previous urological procedures, it can also occur in patients without identifiable risk factors, as demonstrated in this case. Our 31-year-old patient presented with painless macroscopic hematuria and a suspicious lesion on cystoscopy involving the bladder neck and prostatic urethra, initially raising suspicion of malignancy. Histopathological examination after transurethral resection was crucial in establishing the correct diagnosis of nephrogenic adenoma, thus avoiding unnecessary radical treatment. This case highlights the critical importance of clinicopathologic correlation and the need to raise awareness of this rare entity among urologists and pathologists. An accurate diagnosis not only helps avoid overtreatment but also alleviates patient anxiety, particularly in young patients for whom the psychosocial impact of a cancer diagnosis can be significant. Although benign, nephrogenic adenomas can recur, warranting careful follow-up and monitoring. Documenting and sharing these cases allows clinicians to better recognize the various manifestations of nephrogenic adenomas and differentiate them from malignant pathologies, thus enabling more personalized and tailored patient care. This case is part of the growing literature supporting a conservative, evidence-based approach to the management of bladder lesions in patients with non-traditional risk profiles.

Disclosures

Conflict of Interest Statement: The authors declare that they have no actual or potential conflicts of interest, financial, personal, or otherwise, that could influence the work presented in this case report. They have no affiliation or involvement with any organization or entity with a financial or non-financial interest in the subject matter.

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Ethical Approval:

This case report was prepared in accordance with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments. As this was an individual case report with no experimental intervention, no formal ethical approval from our institution was required.

Informed Consent: Verbal informed consent was obtained from the patient for the publication of case details. The patient was fully informed of the purpose of the publication and agreed to the use of the medical data for academic and educational purposes. All identifiable information was removed to protect patient confidentiality, in accordance with applicable privacy laws and institutional policies.

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