



Nephrogenic Adenoma of Bladder—An Unusual Mimicker of Malignancy

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Abstract

Keywords

- nephrogenic adenoma
- metaplasia
- adenocarcinoma
- mimicker

Nephrogenic adenoma also referred to as nephrogenic metaplasia is a rare benign condition occurring most frequently in the urinary bladder. It is most commonly associated with chronic inflammation and genitourinary trauma and can present with a broad spectrum of histological features. It must be differentiated from malignant lesions, which can mimic both at cystoscopy and microscopically. Here, we report a case of nephrogenic adenoma in a middle-aged male with predisposing factors.

Introduction

Nephrogenic metaplasia, also known as nephrogenic adenoma (NA), is a rare condition affecting the bladder in response to chronic irritation. Earlier considered a tumor, it is now known to be a metaplastic response of the urothelium to infection, calculi or chronic catheterization. The reactive nature of this condition is supported by the fact that it occasionally coexists with cystitis glandularis.¹ We report a case of nephrogenic metaplasia in an adult male with a prolonged history of hematuria and dysuria.

Case Report

A 50-year-old male patient presented to the urology department with a 6-month-old history of recurrent dysuria and hematuria. He had a prior history of ureteroscopy with the placement of a double-J stent 2 years back in the left ureter. Computerized tomography abdomen showed bilateral renal calculi and mild hydronephrosis. Bladder showed diffuse thickening of the urinary bladder with papillary projections (►Fig. 1 with an arrow showing papillary projections).

Cystoscopy was done, which showed multiple superficial papillary lesions in the urinary bladder's left lateral and anterior walls. Transurethral resection of the bladder tumor was done, and the specimen was sent for histopathological examination. The gross sample consisted of multiple pale white friable tissue bits altogether measuring 0.6 × 0.5 × 0.3 cm. Microscopic examination showed cuboidal cells in a tubular and papillary pattern with clear cytoplasm, uniform nuclei and focal areas of hobnail arrangement (►Fig. 2A and B). The surrounding stroma was edematous, resembling granulation tissue with acute and chronic inflammatory cells (►Fig. 2C). Also seen were areas of cystitis glandularis (►Fig. 2D). A diagnosis of nephrogenic metaplasia was made. He has been started on pentosan polysulfate and advised close follow-up.

Discussion

The nephrogenic metaplasia was first described in 1949 by Davis TA as hamartoma of the bladder.² The term NA was coined by Friedman and Kuhlenbeck based on the morphologic similarity of the lesion to renal tubules.³ It is a condition

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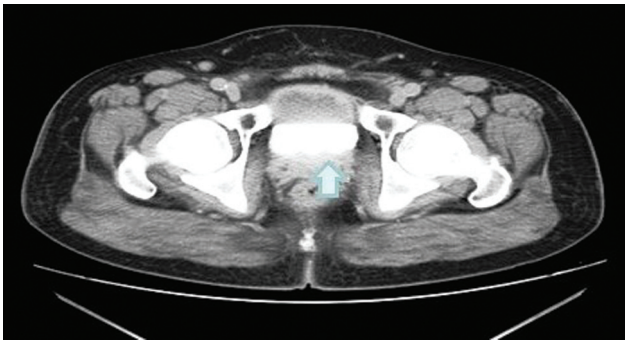


Fig. 1 Computed tomography bladder showing diffuse thickening of the urinary bladder with papillary projections (arrow is showing papillary projections).

showing a male preponderance and a wide age range, with 10% of cases occurring under 10 years of age.⁴ The most common site reported is the urinary bladder, followed by the

urethra and ureter.⁴ It has also been seen in the renal pelvis and rarely in the prostate.³ It is associated with genitourinary trauma, calculi, chronic inflammation, past surgery, repeated instrumentation, intravesical bacillus Calmette-Guerin therapy, and bladder diverticula.^{3,4} Our patient was a middle-aged man with a long-standing history of urinary complaints, history of surgical intervention, and radiological imaging showed bilateral renal calculi.

Various theories have been put forward regarding the pathogenesis of NA. Given its association with conditions with chronic irritation, it is thought to be a metaplastic response of the urothelium. Its origin has also been proposed to be from embryogenic mesonephric tissue. Recently, it has been suggested that it may arise from the seeding of exfoliated renal tubular cells in the urinary tract. The NAs occurring in renal transplant patients had the same sex chromosome status as the donor if the donor was of a different gender.^{3,5}

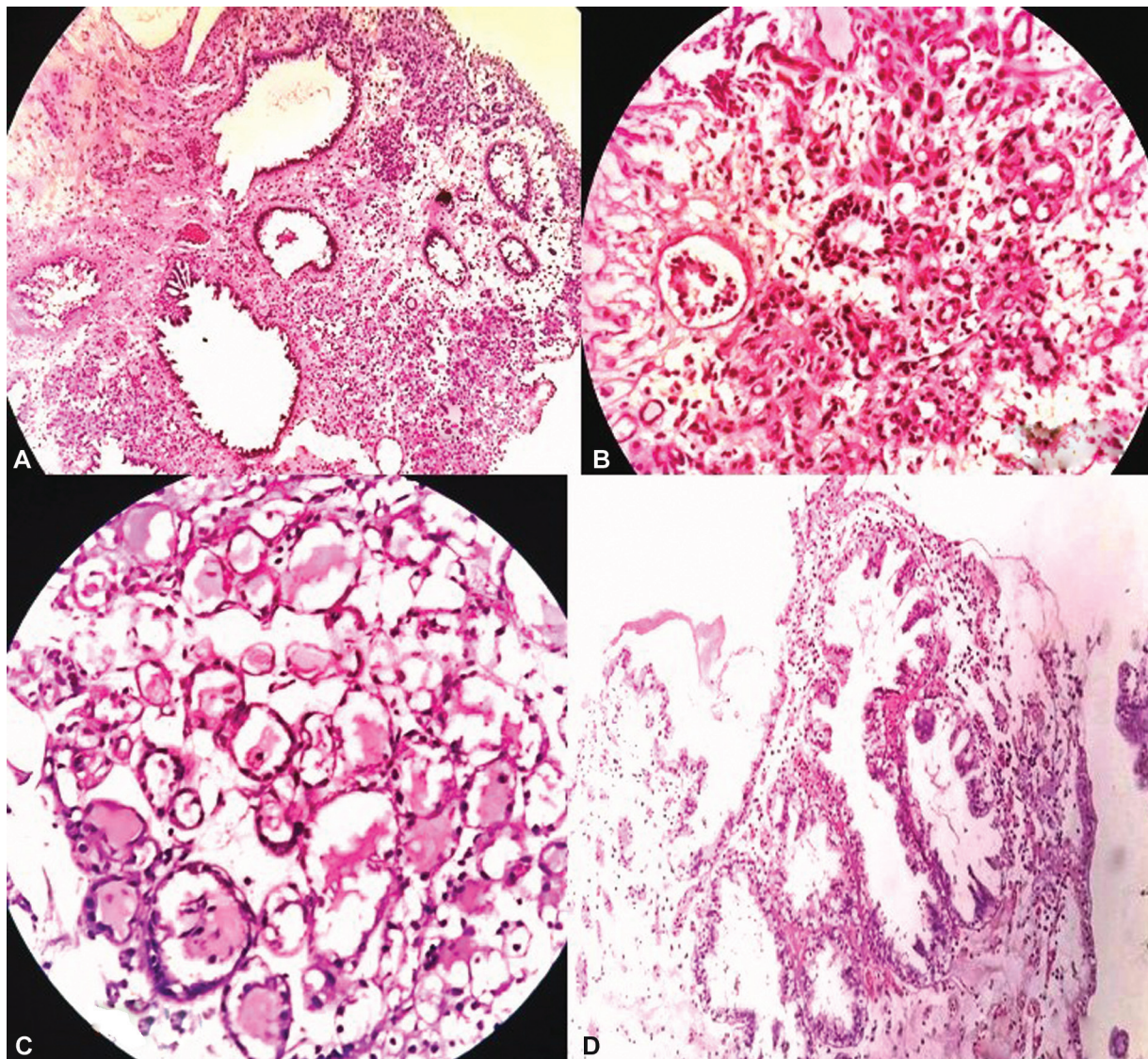


Fig. 2 (A and B) Histopathology showing cuboidal cells in a tubular and papillary pattern with clear cytoplasm, uniform nuclei, and focal areas of hobnail arrangement (hematoxylin and eosin [H&E], X100). (C) Histopathology showing edematous stroma with granulation tissue with acute and chronic inflammatory cells (H&E, X100). (D) Histopathology showing areas of cystitis glandularis (H&E, X100).

The clinical and cystoscopic findings are not diagnostic in NA, and the papillary, friable, velvety mucosa at cystoscopy can mimic urothelial carcinoma.⁶ The histological examination usually reveals the benign nature of the lesion. It consists of tubules, cysts, and papillae lined by cuboidal to low columnar cells with clear or pale eosinophilic cytoplasm and resting on a prominent basement membrane. The stroma is edematous and shows acute or chronic inflammatory cells.⁷ The immunohistochemical (IHC) profile of NA includes expression of renal tubule markers CK7, CD10, AMACR, PAX2, and PAX8, and the absence of urothelial markers (thrombomodulin and p63).⁷

The differential diagnosis includes urothelial papilloma, papillary urothelial neoplasm with low malignant potential, and low-grade papillary urothelial carcinomas when the lesion is predominantly papillary.⁴ These lesions are lined by stratified urothelium, unlike NA, where a single layer of cells lines tubules.

When there is a more significant lesion involving the lamina propria and muscular layer, differentials include prostatic adenocarcinoma, urothelial carcinoma with bland histology, and clear cell adenocarcinoma (CCA).^{4,8} Prostatic adenocarcinomas can be challenging to distinguish from NA, primarily when the latter occurs in the prostatic urethra. Positive staining for alpha-methyl acylCoA racemase (AMACR), lack of basal cell markers, and in a few cases prostate-specific antigen positivity in both conditions can add to the dilemma.⁴ The lack of significant atypia in NA with positive staining for PAX 2 and PAX 8 in NA helps distinguish the two conditions.^{4,5,8} The presence of multiple architectural patterns like nested, tubular, papillary, cystic, and solid within the same lesion is characteristic of NA. It helps distinguish it from the nested pattern of urothelial carcinoma with bland histology, urothelial carcinoma with tiny tubules, and microcystic urothelial carcinoma.^{4,5} Greater degree of atypia and irregular infiltrative growth pattern in the malignant lesions with positive staining for PAX2 and PAX 8 in NA are helpful in the diagnosis. Another close mimicker of NA is CCA. A large tumor with solid growth, more significant atypia, necrosis, and increased mitosis with an infiltrative growth pattern favors a CCA. IHC in CCA shows intense staining for Ki-67 and p53.⁵ A few studies have reported the progression of NA to adenocarcinoma.⁹⁻¹¹ However, vast majority of recent literature suggests that NA is a benign reactive lesion with no increased risk of bladder carcinoma.² Due to its symptomatic nature and tendency to recur, it has been recommended that these

patients are followed up with cystoscopy within 6 to 12 months and again later if symptoms recur.²⁻⁵

Conclusion

A NA is a rare benign metaplastic condition that can mimic malignancy in cystoscopy and histological examination. Hence, pathologists should be aware of its various histomorphological spectrum and should distinguish it from its mimickers. In complex cases, IHC markers may be required.

Source of Support

Nil.

Conflict of Interest

None declared.

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