Nephrogenic Adenoma: Clinical Features, Management, and Diagnostic Pitfalls

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OBJECTIVE To review the diagnosis and management of nephrogenic adenoma (NA), an uncommon benign lesion found in the urinary tract. This lesion arises from a proliferation of implanted renal tubular cells. Although more common in adults, it can occur in all ages. NAs can recur and cause significant morbidity in patients. NAs are also a potential diagnostic pitfall as they can clinically and histologically mimic malignancy in the urinary tract.

MATERIALS AND METHODS We performed an Institutional Board Review approved search of our surgical pathology database from 2005 to 2015 for cases of NA. A retrospective chart review was performed with a focus on the clinical, pathologic, and radiographic findings in these patients.

RESULTS We identified 32 cases of NA in 31 patients. Lesions were most common in Caucasian males (male-to-female ratio of 2:1) with an average age at diagnosis of 55 years (range 25-77). Bladder was the most common site of occurrence (81.2%), followed by ureter (9.4%), urethra (6.3%), and intrarenal collecting system (3.1%). Most patients (72%) were symptomatic and presented with hematuria (41%), lower urinary tract symptoms (28%), pelvic or flank pain (6%), hydronephrosis (19%), or urinary incontinence (13%). NA was asymptomatic and identified incidentally in 9 (28%) patients. One patient (3%) had a renal transplant and 8 (26%) patients had diabetes mellitus. Twenty-six (84%) patients were managed with endoscopic resection of their tumors.

CONCLUSION NAs are benign lesions that may cause significant morbidity and mimic malignant tumors. There should be increased suspicion in patients with predisposing factors. UROLOGY 95: 29–33, 2016.

Nephrogenic adenoma is an uncommon benign lesion that can be found anywhere in the urinary tract. This entity was first described in 1949 and originally referred to as a "hamartoma of the urinary bladder."[1,2] It subsequently came to be named nephrogenic adenoma due to its resemblance to renal tubules.[3-6] This entity was first recognized in adult patients who had chronic irritation of the urinary tract, such as urolithiasis, recurrent urinary tract infection, or previous genitourinary surgery. It was also recognized to have a high incidence in renal transplant patients.[7-9] Nephrogenic adenomas were initially thought to be a metaplastic process of the urothelium in response to injury or chronic inflammation.[4-6] It is now recognized that nephrogenic adenomas arise from a proliferation of implanted renal tubular cells and can occur in patients of all ages.[10] This benign lesion can both clinically and histologically mimic malignancy and presents a potential diagnostic pitfall.[11-14] Herein, we present our 10-year experience at the University of Alabama at Birmingham and review the current literature with regard to the diagnosis and clinical management of nephrogenic adenomas.

MATERIALS AND METHODS

We performed an Institutional Board Review approved search of our surgical pathology database from 2005 to 2015 for cases of tissue-proven nephrogenic adenoma. A retrospective chart review was performed with a focus on the clinical, pathologic, and radiographic findings in these patients. Descriptive statistics were derived with means and ranges for continuous variables and counts with percentages for categorical variables.

RESULTS

We identified 32 cases of nephrogenic adenoma in 31 patients (Table 1). Lesions were identified most commonly

Financial Disclosure: *The authors declare that they have no relevant financial interests.*

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Submitted: March 12, 2016, accepted (with revisions): April 26, 2016

Table 1. Patient demographics and tumor location

	n (%)
Average age (y; range)	55 (25-77)
Average follow-up (mo; range)	25 (0-110)
Race	
Caucasian	23 (74.2)
African American	6 (19.4)
Hispanic	1 (3.2)
Unknown	1 (3.2)
Gender	
Male	21 (68)
Female	10 (32)
Location	
Bladder	26 (81.2)
Ureter	3 (9.4)
Upper collecting system	1 (3.1)
Urethral diverticulum	2 (6.3)

in Caucasian males, with a male-to-female ratio of 2:1, and an average age at diagnosis of 55 years (range, 25-77). Bladder was the most common site of occurrence (81.2%), followed by ureter (9.4%). Two patients (6.3%), had urethral involvement, both associated with a urethral diverticulum, and in 1 patient (3.1%) the lesion was found in the intrarenal collecting system.

Most patients (72%) were symptomatic and presented with hematuria (41%), lower urinary tract symptoms (28%), pelvic or flank pain (6%), hydronephrosis (19%), or urinary incontinence (13%). Nephrogenic adenoma was asymptomatic and identified incidentally in 9 (28%) patients. Only 1 patient had no previous urologic history (Table 2).

We found that nephrogenic adenoma was commonly associated with a history of chronic irritation or inflammation to the urinary tract, such as urolithiasis, neurogenic bladder, chronic indwelling catheters, chronic urinary tract infections, urinary retention, pelvic organ prolapse, urethral or ureteral stricture, Bacillus Calmette–Guérin (BCG) treatment, and pelvic radiation (Table 2). One patient with a bladder lesion had previously undergone bladder augmentation. In our series, a history of urothelial carcinoma, prostatic adenocarcinoma, and cervical carcinoma was present in 12 (39%), 1 (3%), and 2 (6%) patients, respectively. One patient (3%) had a renal transplant and 8 (26%) patients had diabetes mellitus.

Common medications seen in our patient population included nonsteroidal anti-inflammatory drugs (45%), angiotensin-converting enzyme inhibitors/angiotensin II receptor antagonists (35%), and beta-blockers (32%).

On cystoscopic examination, 16 of 32 (50%) nephrogenic adenomas were papillary or polypoid, and 14 of 32 (44%) were flat. One patient (3%) had no visible lesion, and in 1 patient (3%) the nephrogenic adenoma was masked by a concurrent urothelial carcinoma. Flat lesions tended to appear as pale, white-tan, or yellow discolorations on the mucosal surface. Papillary or polypoid lesions were typically tan-pink and were clinically suspected to be urothelial carcinoma. Lesions were also associated with inflammatory-type changes such as erythema, scattered hemorrhages, mucosal edema, and thickening of the bladder wall. One lesion, identified in a urethral diverticulum, appeared cystic.

Table 2. Presentation and treatment of patients with nephrogenic adenoma

	n (%)
Clinical presentation	
Hematuria	13 (40.6)
Lower urinary tract symptoms	9 (28.1)
Pelvic or flank pain	2 (6.3)
Hydronephrosis	6 (18.8)
Urinary incontinence	4 (12.5)
Incidental finding/asymptomatic	9 (28.1)
Past medical history	
Urothelial carcinoma	12 (38.7)
Prostatic adenocarcinoma	1 (3.2)
Cervical squamous cell carcinoma	2 (6.5)
Urolithiasis	9 (29)
Neurogenic bladder	6 (19.4)
Chronic urinary tract infections	6 (19.4)
Benign prostatic hyperplasia and/or urinary retention	4 (12.9)
Chronic kidney disease	2 (6.5)
Pelvic organ prolapse	1 (3.2)
Urethral stricture	1 (3.2)
Overactive bladder	1 (3.2)
Pelvic radiation	2 (6.5)
Solid organ transplant	1 (3.2)
Previous BCG treatment	7 (22.6)
Diabetes mellitus	8 (25.8)
No urologic history	1 (3.2)
Medications	
NSAIDs	14 (45.2)
ACE inhibitor/ARB	11 (35.4)
Beta-blocker	10 (32.3)
Surgical treatment	
Endoscopic biopsy/resection	26 (83.9)
Urethral diverticulectomy	2 (6.5)
Ureteral reimplantation	1 (3.2)
Radical cystoprostatectomy (for UC)	1 (3.2)
Nephroureterectomy (for upper tract UC)	1 (3.2)

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor antagonist; BCG, Bacillus Calmette–Guérin; NSAID, nonsteroidal anti-inflammatory drugs; UC, urothelial carcinoma.

Twenty-six (84%) patients were managed with endoscopic resection of their tumors, 2 (7%) underwent urethral diverticulectomy, and 1 patient (3%) had a ureteral reimplantation. Two (7%) patients were treated with either radical cystoprostatectomy or nephroureterectomy for concurrent urothelial carcinoma. No patients were prescribed long-term antibiotic therapy. Only 1 patient had a recurrent nephrogenic adenoma, which presented in a patient with neurogenic bladder 30 months after his initial resection. No patient with a nephrogenic adenoma underwent malignant transformation on follow-up biopsy. Two of the 12 (17%) patients with concurrent urothelial carcinoma had recurrences of bladder cancer on follow-up cystoscopy. One patient had a history of multifocal, high-grade urothelial carcinoma involving the bladder, urethra, and upper tract. The other patient had recurrent