Nephrogenic Adenoma of the Urinary Bladder: Clinical Experience and Review of the Literature

Chuan-Shu Chen, Chen-Li Cheng*

Division of Urology, Department of Surgery, Taichung Veterans General Hospital, Taichung, Taiwan, R.O.C.

Background: Nephrogenic adenoma (NA) is a rare disease of the urinary tract. We report our clinical experience with this disease in the urinary bladder and review the literature.

Methods: Between April 1994 and July 2004, 8 patients were diagnosed with NA of the urinary bladder: 3 men and 5 women, aged 23–77 years (mean 49.6). Multiple predisposing factors were analyzed. The mean follow-up time was 56 months.

Results: NA was not associated with transitional cell carcinoma in our series. All patients had recurrent urinary tract infection. Urinary tuberculosis was diagnosed in 2 patients. Two patients had undergone previous open urosurgery, and 4 patients had received previous endourologic management. A history of urolithiasis was found in 1 patient. Previous long-term urinary catheterization was noted in 3 patients. Two patients had received pelvic radiation therapy for cervical cancer. Urinary frequency and microscopic hematuria were found in all patients. All nephrogenic adenomas were treated with transurethral resection. Recurrent nephrogenic adenomas were diagnosed in 3 patients (median time to disease relapse, 7 months). Recurrent tumors were also treated with the endourologic method.

Conclusion: NA is an uncommon benign metaplastic lesion occurring in the urothelium. Transurethral resection of NA provides a definite diagnosis and relief of symptoms. The recurrence rate of NA is relatively high, so careful and long-term follow-up is necessary. [*J Chin Med Assoc* 2006;69(4):166–168]

Key Words: nephrogenic adenoma, urinary bladder, urothelium

Introduction

Nephrogenic adenoma (NA) is an uncommon lesion of the urinary tract that is considered to be induced by chronic irritative factors, such as infection, trauma, surgery, calculi, foreign bodies, and chemical agents.[1] The first report of a case was by Davis in 1949.[1] However, in 1950, the term "nephrogenic adenoma" was introduced by Friedman and Kuhlenbeck because the structure of NA resembled that of a renal tubule.[2] We report our clinical experience with NA of the urinary bladder and review the relevant literature.

Methods

Between April 1994 and July 2004, 8 patients (3 men and 5 women) diagnosed with NA were included, by a computer search, in the pathologic report database of our hospital. Age at diagnosis of NA ranged from 23 to 77 years (mean, 49.6 years). All patients underwent transurethral resection (TUR) for pathologic diagnosis and relief of urinary symptoms, and were followed up with urinary cytology and cystourethroscopy at our urologic outpatient clinic. The mean follow-up time was 56 months (range, 5–128 months). TUR was the treatment of choice for recurrent cases.

*Correspondence to: Dr. Chen-Li Cheng, Division of Urology, Department of Surgery, Taichung Veterans General Hospital, 160, Section 3, Chung-Kun Road, Taichung 407, Taiwan, R.O.C.
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Results

The history of predisposing factors showed that all patients had recurrent urinary tract infection. Urinary tuberculosis was diagnosed in 2 patients (1 prostatic tuberculosis and 1 renal tuberculosis). These 2 patients received complete anti-tuberculosis medical treatment. Nonendoscopic urinary tract surgery had previously been performed in 2 patients (ureteroneocystostomy for iatrogenic ureteral injury in 1, and multiple urethroplasty for traumatic urethral injury in the other). Endourologic management had previously been used in 4 patients (TUR of the prostate for benign prostatic enlargement in 3 patients; 1 of these 3 patients had ureteroscopic lithotripsy for ureteral stone, and another had optic urethrotomy for urethral stricture). Only 1 patient had a history of urolithiasis. Long-term urinary catheterization for urethral stricture was necessary in 3 patients (ureteral double-J stent in 2 patients and urethral catheter in the other). Two patients had pelvic radiation therapy for cervical cancer.

All patients complained of urinary frequency, so they were brought for urologic examinations. Their urinalyses revealed microscopic hematuria. All patients' urine cytology findings showed some polymorphic neutrophils, but no malignant cells. The appearance of NA under cystourethroscopy was mostly papillary, but 1 case showed polypoid tumor growth (Figure 1). No lesion was larger than 1 cm in diameter. All NAs were treated with TUR, and the microscopic findings showed tubular structures lined with a layer of cuboidal or hobnail epithelial cells with uniform nuclei (Figure 2). Under regular follow-up, NA recurred in 3 patients (once in 1 patient and twice in the other 2). The median time to disease relapse in these 3 patients was 7 months (range, 4–13 months). The recurrent NAs were also treated with TUR. In our series, no malignant change of NA was found.

Discussion

NA is an unusual lesion confined to the lamina propria of the lower urinary tract. In 1950, Friedman and Kuhlenbeck[2] used the term "nephrogenic adenoma" to describe a distinctive lesion of the urinary tract with characteristic epithelial tubules resembling renal collecting tubules. The epithelial cells are clear or vacuolated with uniform nuclei, but without mitosis. NA is not an extremely rare lesion, and many might have previously been misclassified as chronic cystitis. Clear cell adenocarcinoma also must be differentiated from NA, because they too have similar histologic features. The predominance of clear cells, presence of severe atypia, necrosis, high metabolic rate, and strong staining for P53 are factors that favor the diagnosis of clear cell adenocarcinoma.[3]

NA can occur anywhere in the urinary tract, from the renal pelvis[4] to the urethra, but is most common in the urinary bladder. In our series, all NAs were found in the urinary bladder. Olivia and Young[5] reviewed 80 cases of NA, and a male predominance of 2:1 was found. However, our case series showed a female predominance.

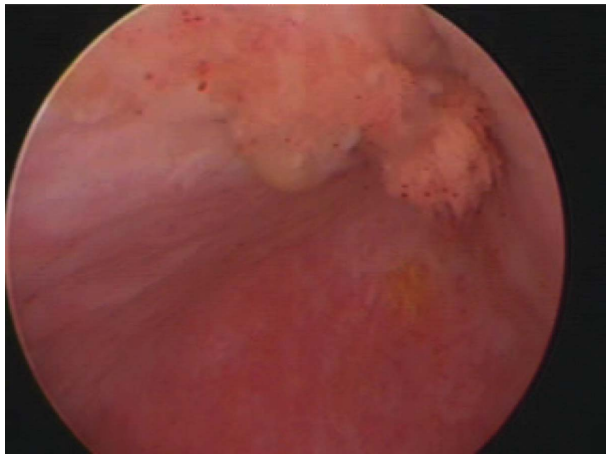

Figure 1. Cystoscopic findings of nephrogenic adenoma show a papillary tumor growth over the anterior wall of the urinary bladder, similar to the picture of low-grade transitional cell carcinoma.

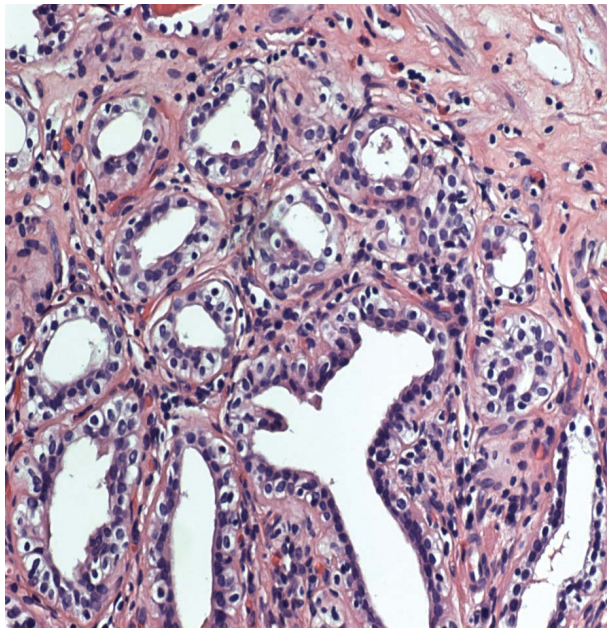

Figure 2. Microscopic findings of nephrogenic adenoma show tubular structures lined with a single layer of cuboidal epithelium (hematoxylin and eosin, × 360).

The etiology of NA has not been clearly defined. There is a history of chronic irritation or inflammation in almost all cases. However, chronic irritation and inflammation of the urinary tract are secondary to predisposing factors, such as trauma, chronic infection, previous surgery, urinary calculi, irradiation, and urinary catheterization. Most of our cases had these predisposing factors. NA might be associated with chronic inflammation induced by intravesical bacillus Calmette-Guérin treatment.[6] Some reports revealed that NA was usually found in immunosuppressed patients following renal transplantation, so immunosuppression may be a contributory factor.[7] In our series, 2 patients (25%) with urinary tuberculosis had received complete anti-tuberculosis medical treatment. These 2 patients might have been in an immunocompromised condition or had urothelium in a state of chronic inflammation. These factors could account for why these 2 patients had NA.

Porcaro et al[8] reported on cases with commonly presented irritative bladder symptoms, such as frequency, dysuria, and urgency. Hematuria was often observed. All of our cases presented with urinary frequency and microscopic hematuria.

NA may appear polypoid, papillary, or flat under cystoscopy, and most are localized and small, measuring less than 1 cm in diameter.[2,8] Some lesions appear similar to low-grade transitional cell carcinoma, so the definite diagnosis of NA is based on pathologic analysis. TUR of the lesions is the best choice for accurate diagnosis and symptom relief.[9] Total cystectomy and urinary diversion have rarely been performed, and only when the lesions were extensive or symptoms were too severe.[10] A high recurrence rate (38–75%) of NA has been found during long-term follow-up.[11] Our patients' recurrence rate (37.5%) was also high. Despite frequent recurrence, there have been no reports that NA transforms to a malignant or metastatic lesion.[2] All recurrent lesions should be treated with TUR.

Because of the high recurrence rate of NA, the approach to postoperative follow-up is important. Navarre et al[12] suggested that cystourethroscopy be given every 3 months for 2 years, every 6 months for 3 years, and then once a year in the absence of internal infection or voiding complaints. Therefore, we advised our patients to return for postoperative urine cytology and cystourethroscopy in our outpatient department, initially, every 3 months. However, because our patients did not believe that NA was a malignant disease and thought that cystourethroscopy was painful, compliance with postoperative follow-up was poor, in spite of our thorough explanation about the high recurrence rate of the disease. Consequently, all recurrent NAs were detected only when urinary frequency or hematuria recurred. Therefore, our current policy is that, if symptoms (either urinary frequency or hematuria) recur, cystourethroscopy will be strongly suggested.

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