



Nephrogenic Adenoma In the Prostatic Urethra and In the Ureter: Urothelial Lesions Associated with Chronic Infections and Injuries In the Urinary Tract

Ricardo LR Felts de La Roca, Guilherme B Lamacchia, Luiz Fernando G da Silva, Emilio M Pereira

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ABSTRACT

Purpose: To report our findings on urothelial lesions diagnosed as nephrogenic adenomas and determine the importance of a correct clinical and anatomopathological interpretation.

Materials and Methods: We report the surgical and anatomopathological findings for 3 cases involving nephrogenic adenoma into the urothelium. One case was in the prostatic urethra of an 84-year-old male who underwent suprapubic prostatectomy due to benign prostatic hyperplasia. Another one was microscopic, and in the lumen of a 4 cm proximal ureteral stenosis of a 30-year-old man due to a ureteral perforation during an ultrasonic ureterolithotripsy 18 months prior. After repeated (6) transureteral endoscopic manipulations, always stented with a double-J ureteral catheter, we finally performed an excision of the ureteral stenotic segment and end-to-end ureteroureteral anastomosis. The final case was in a 5-year-old female, exhibiting recurrent urinary infections and renal lithiasis, who presented with a polypoid lesion in the proximal ureter that we detected and resected by ureteroscopy.

Results: In the older male patient, who underwent surgical manipulation with repeated vesical catheterizations and experienced recurrent urinary infections, the microscopic exam revealed benign prostatic hyperplasia and an incidental lesion 1 cm in diameter in the prostatic urethra with pathological characteristics of nephrogenic adenoma. In the younger male, the nephrogenic adenoma was incidentally found as a microscopic lesion in the ureteral fibrotic lumen. In the child's case, she underwent an ultrasonic percutaneous nephrolithotripsy due to a voluminous renal calculus, which later resulted in residual obstructive renal calculi at the pyeloureteral junction that necessitated ureteroscopy for nephrocutaneous fistula. It was then that a 0.8 cm polypoid lesion was observed in the proximal ureter during implantation of a double-J ureteral catheter, which was resected and diagnosed as nephrogenic adenoma.

Conclusion: In areas of the urinary tract that have experienced recurrent urinary infections or traumas, or have undergone surgical manipulation, polypoid lesions can develop or appear microscopically. These lesions do not promote such chronic alterations but could result from them, likely due to cellular implants of renal tubules in areas of the urothelium in which the implantation is suitable and are recognized by microscopy as benign urothelial processes. Although such findings are rare, they likely occur more frequently than believed.

INTRODUCTION

The anatomopathological finding of nephrogenic adenoma in the urothelium is rare. It is considered a benign lesion of the

urothelium that is attributed to chronic irritation of the mucosa due to permanent tissue damage, infections, lithiasis, exposure to radiation, or instrumentation on the urinary tract. They are generated by tubular renal cells that have been eliminated

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CORRESPONDENCE: Ricardo Leo Roberto Felts de la Roca, MD, Jardim Paulista, São Paulo, SP, 01424-000, Brazil (ricardo@delarocaurologia.com.br)

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in the urinary stream and implant themselves in an area of a previously wounded urothelial tract [1].

Recent evidence has shown that nephrogenic adenoma is not a metaplastic lesion but rather a proliferation of exfoliated and implanted renal epithelial cells in the urinary tract. Histologically, they appear singly or in a combination of tubules, small papillae, and microcystic structures lined by cells, with little cytological atypia and focal hobnail changes. Solid formations and compressed, spindled cells within a fibromyxoid background are rarely observed. A differential diagnosis includes, but is not limited to, malignant neoplasms occurring at the same sites—in particular, urothelial carcinoma with deceptively bland morphology (with small tubules, microcystic and nested variants), prostatic adenocarcinoma if it develops in the prostatic urethra, and metastasis of clear-cell renal carcinoma or urothelial carcinoma with microcysts when it exists in other sites of the urinary tract.

Based on the exceptional nature of these findings, we describe 3 cases in which this lesion was detected.

CASE REPORTS

First case: An 84-year-old Portuguese male was evaluated at another hospital 2 years prior, presenting with prostatism, whose transrectal ultrasonography (TRUS) revealed a prostate that weighed approximately 104 g (total PSA of 11.74 ng/ml and free PSA of 1.67 [ratio, 14%]). Transrectal prostatic biopsies revealed benign prostatic hyperplasia (BPH), and a transurethral endoscopic resection of the prostate was indicated.

Postoperative complications of acute renal failure and anemia occurred, lasting 30 days after surgery and requiring dialysis until recovery. The anatomopathological examination of the product of the prostatic tissue resection (20 g) revealed nodular hyperplasia of the prostate.

The patient was referred to our service, with complaints of recurrent urinary infections since the previous surgery, including episodes of hematuria, which abated temporarily with antibiotics; vesical irritative symptomatology; and moderate prostatism. TRUS showed a prostate of 194 g and a trabeculated bladder with no tumoral lesion in its walls. A suprapubic prostatectomy was performed, the vesical catheter was removed 7 days after surgery, and the continent patient was discharged from the hospital.

Three months after, the patient recorded improvements in urinary flush and previous irritative symptoms, with no macroscopic hematuria. Control examinations of the urine revealed decreased leukocyturia and hematuria, with negative cultures. The anatomopathological exam showed a prostate of 109 g, and a diagnosis of benign prostatic hyperplasia and a

focus on unspecific chronic prostatitis was made.

In the prostatic urethra, a nephrogenic adenoma was observed, without characteristics of malignancy, measuring 1 cm on its longest axis (Figure 1, Figure 2).

Second case: A 30-year-old male was submitted 18 months prior to a trans-ureteroscopic ureterolithotripsy due to a 10 mm ureteral stone that resulted in ureteral perforation and migration of the stone to the ureteral outer layer, and then stented with a double-J catheter. During the current treatment period, he was submitted to 6 endoscopic maneuvers to reach the stone, unsuccessfully, which resulted in a 4 cm fibrotic ureteral segment, with minimal lumen. An ureteroureteroanastomosis was done laparoscopically, and in the excised ureteral segment, anatomopathological fibrosis and a nephrogenic adenoma were found microscopically.

Third case: A 5-year-old Brazilian female presented with a neurogenic bladder, vesicostomy, and a staghorn calculus in the right kidney measuring 35 mm x 25 mm. She was born with myelomeningocele, and underwent an operation at age 2 to correct hydrocephaly by ventriculoperitoneal derivation catheter. The patient underwent percutaneous nephrolithotripsy wherein 80% of the renal calculi were removed by approaching the inferior calyx. On the second postoperative day, the patient presented with lumbar pain and high urinary leakage surrounding the nephrostomy catheter. A urotomography was done and revealed the displacement of residual fragments of the calculi to the renal pelvis and proximal ureter. Implantation of a double-J ureteral catheter by ureteroscopy was indicated for ureteral unblocking and posterior extracorporeal lithotripsy of these calculi by external shock waves.

During the procedure, as we inserted the ureteroscope to treat the ureteral stones in the proximal ureter, a slightly irregular area was observed 2 cm from the renal pelvis harboring diminutive polyps, one of which was 8 mm with a small base and without ulcerations. It was removed for biopsy, with no complications. The patient was discharged from the hospital the following day without a nephrostomy catheter or lumbar urinary leakage. The anatomopathological exam of this polyp presented an 8 mm nephrogenic adenoma, with no evidence of malignancy.

DISCUSSION

Transurethral endoscopic resection of the prostate is the standard treatment for urinary obstructions that are caused by the prostate, effecting high levels of success and low mortality and morbidity rates. It is indicated for the relief of prostatism symptoms that develop in more than 42% of patients with enlarged prostates, acute urinary retention, and chronic

Figure 1. Acinar proliferation with cystic areas in the submucosa of the prostatic urethra (hematoxylin-eosin, 10 x).

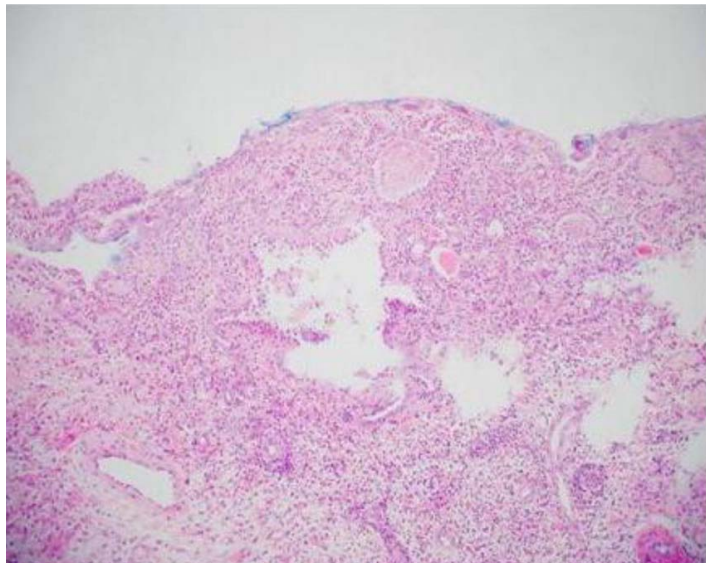
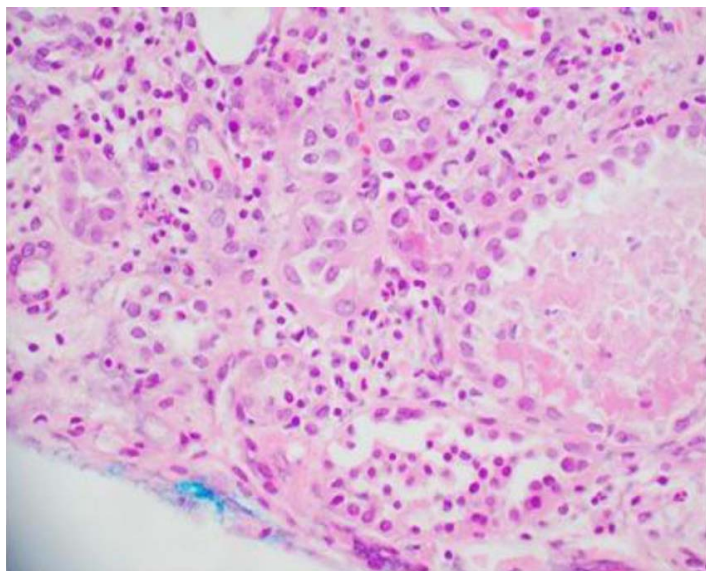


Figure 2. Tubules coated by cuboid cells with eosinophilic cytoplasm, at times with intraluminal secretion; nephrogenic adenoma (hematoxylin-eosin, 40 x).



complications of incomplete vesical emptying, which occur in approximately 27% of cases. Symptom complexes of recurrent urinary infections develop in 3.6% of cases after surgery,

2.9% experience bleeding that require transfusions, and 1.4% experience water reabsorption syndrome during resection [2,3].

In the postresection period, patients can expect to develop irritative symptomatology with alterations in micturition patterns, which tend to improve simultaneously over time, with cicatrization of the prostatic bed. This symptomatology can be associated with urinary infections, requiring urocultures before the empirical administration of antibiotics [4].

This irritative symptomatology is observed in 12 to 40% of patients in the first trimester postresection, and in cases in which recurrent urinary infection or obstruction of the urinary flow occurs, constant urological follow-up is needed to diagnose and treat the occasional anatomic alterations in the operated area and alterations in bladder function [5].

Complaints regarding the ability to hold urinary volume due to vesical instability should be examined by urodynamic evaluation [6].

Urinary infection can follow renal lithiasis, and in 15% of cases, the infection causes the formation of calculi. In both situations, it is recommended that the infectious symptoms be treated first and the lithiasis second to avoid causing sepsis with serious complications [7].

Rare ureteral polypoid lesions, diagnosed as fibroepithelial polyps of the ureter, have been reported and should be distinguished from malignant or benign lesions as papillomas and inflammatory pseudopolyps. In 58% of cases, a history of urological alterations that are associated with the detection of polyps is considered, such as urinary lithiasis (32%), recurrent urinary infection (5%), stenosis of the pyeloureteral junction (14%), or the presence of a double-J ureteral catheter (9%). These polyps can be removed by highly successful endoscopy, although stenosis can develop, which requires open surgical correction [8].

There are cases of the presence of polyps or vegetative lesions on the vesical cavity or in the urethra of children, diagnosed as nephrogenic adenomas by anatomopathological examination. Although they are rare, the presence of these adenomas in the bladder is linked to a previous urological history of surgical events, such as ureteral reimplantation and heminephroureterectomy. It is also associated with recurrent infections in female children. In contrast, nodular areas have developed in the bulbar urethra of boys who present with hematuria or dysuria and no previous urological history. These lesions can undergo open resection if they present as large, vegetative vesical masses, or they may undergo endoscopy if they are sufficiently small and in the bladder or urethra. Nevertheless, they can recur, especially with regard to vesical localization, if they are located in the urethra; such patients have complained of dysuria, suggesting

continuity of the lesions [9-11].

There are rare reports of nephrogenic adenoma in the prostatic urethra, as found in a patient who was treated for a lower ureteral calculus by extracorporeal lithotripsy [12].

In vesical form, most symptoms are related to urinary infection or hematuria, likely having several recurrences, after its resection. Although it is considered a benign process, it must be followed up with routine examinations due to its tendency to relapse and the possibility of malignization. It is more common in adults than in children, in which case it is described as a papillary lesion with regard to vesical topography [13], similar to a carcinoma of low-grade transitional cells, and noninvasive, ranging from small to large vegetative masses that can obstruct ureteric orifices [14]. It affects adult males 3.7:1 versus women, compared to 1 boy for every 3.5 girls. They recur and multiply frequently [15] and may present frequent recurrences, even 1 year after resection [10]. BCG instillation therapy is believed to be an initiation factor for nephrogenic adenoma [16,17] as well as complementary treatment for bladder cancer.

At the prostate location, nephrogenic adenoma can, histologically, be confused with prostate adenocarcinoma due to its cellularity, particularly when the adenoma extends itself in the form of small tubules to the prostatic fibromuscular stroma (77% of cases). It can present as morphological variants, which can be confused with mucinous adenocarcinoma, especially the fibromyxoid variant [18,19]. This variant consists of long fusiform cells with rare tubular or cordlike structures. Thus, nephrogenic adenoma of a prostatic urethra mimics prostate cancer due to the presence of tubules, cords and signet-ring cells, protrudent nucleolus, muscular involvement, mucinous secretions, and a positive test for PSA and PSAP (a partial negative test for 34bE12 by immunohistochemistry notwithstanding). To make a correct anatomopathological diagnosis, we can use methods to recognize typical nephrogenic characteristics in lesions, such as the presence of tubules (96% of cases), papillae (19%), and vessels (73%). We can also recognize the adjacent urothelium, thyroidization (38%), the absence of mitotic figures, the associated inflammation, and positivity for cytokeratin 7 (100%). We can also determine diffuse positivity (11%), focal positivity (44%), or negativity (44%) for 34bE12.

CONCLUSION

The presence of nephrogenic adenoma in the prostatic urethra can be found microscopically, as ureteral or as polyps lesions, and it can be considered an incidental finding due to persistent, local, chronic irritative, or inflammatory processes. Childhood nephrogenic adenoma in the proximal ureter is rare, considering that the most common location is in the bladder site. The correct anatomopathological diagnosis is fundamental in determining the benignity of such lesions, understanding its

likely etiopathogenesis, treating the causes, and scheduling the proper follow-ups.

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