

NEPHROGENIC ADENOMA OF THE BLADDER : TWO CASE REPORTS AND LITERATURE REVIEW

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In the two cases we report here, tumors were diagnosed as nephrogenic adenoma by pathohistological examination. Case 1 was a 72-year-old female presenting with a bladder tumor 8 months after receiving ureteral tumor surgery. Transurethral resection of bladder tumor (TUR-Bt) was performed. Case 2 was a 57-year-old female who had received intravesical bacillus Calmette-Guérin (BCG) treatment 6 times after her fifth TUR-Bt. Two tumors were found by cystoscopy, and TUR-Bt was performed. There have been 39 cases of nephrogenic adenoma of the bladder reported in Japan; 21 were male and 18 female with a mean age of 56.5 years. The main complaint was hematuria, which was seen in 16 cases followed by pollakisuria in 6 cases. Nephrogenic adenoma occurred after surgery of the urinary tract in 16 cases, followed by urinary tract infection in 9 cases and intravesical BCG treatment in 6 cases. The ratio of cases occurring after intravesical BCG treatment has increased since BCG approval for bladder carcinoma treatment in December 1996 in Japan, and an increase in the number of cases is expected in the future.

(Acta Urol. Jpn. 48 : 463–466, 2002)

Key words: Nephrogenic adenoma, Bladder, Bacillus Calmette-Guérin

INTRODUCTION

Nephrogenic adenoma is a relatively rare benign tumor that occurs in the urinary tract. We treated two cases of nephrogenic adenoma of the bladder, one that occurred during follow-up after total nephroureterectomy and the other after intravesical bacillus Calmette-Guérin (BCG) treatment following transurethral resection of bladder tumor (TUR-Bt). In this report, we have also reviewed and discussed cases of nephrogenic adenoma of the bladder which previously have been reported in Japan.

CASE REPORT

Case 1 was a 72-year-old female who received right total nephroureterectomy for transitional cell carcinoma of the right ureter in March, 1997. Eight months after surgery, cystoscopic examination revealed a broad-based papillary tumor in the bladder dome. In January, 1998, TUR-Bt was performed. Pathohistological examination revealed that the bladder tumor was covered with a single layer of cylindric epithelium and had a tubular structure similar to renal tubules. There were no atypical nuclei, but some interstitial edema and infiltration of inflammatory cells were indicated, and the tumor was diagnosed as nephrogenic adenoma (Fig. 1).

Case 2 was a 57-year-old female whose main complaint was macroscopic hematuria. She had

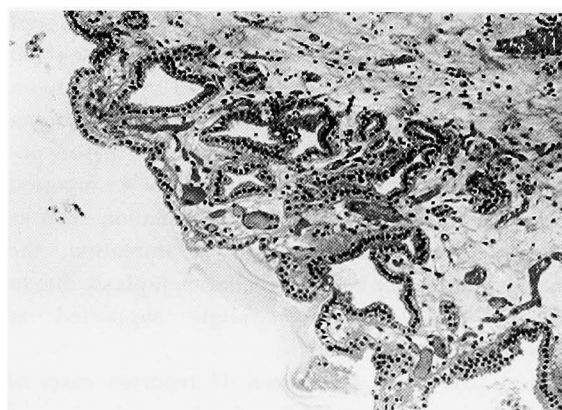


Fig. 1. Pathohistological observations (Case 1). A tubular structure similar to the renal tubules covered with a single layer of cylindric endothelium was indicated with some interstitial edema and infiltration of inflammatory cells (HE stain $\times 200$).

received TUR-Bt five times between 1993 and 1998 for transitional cell carcinoma of the bladder. After her fifth TUR-Bt in February, 1998, intravesical BCG treatment (Tokyo strain of BCG; 80 mg instilled with 40 ml of saline once a week) was performed 6 times, but since hematuria developed treatment was suspended. Two papillary tumors were discovered by cystoscopy, one approximately 2 cm in diameter in the left lateral wall and another approximately 1 cm in diameter in the dome. In April, 1999, TUR-Bt

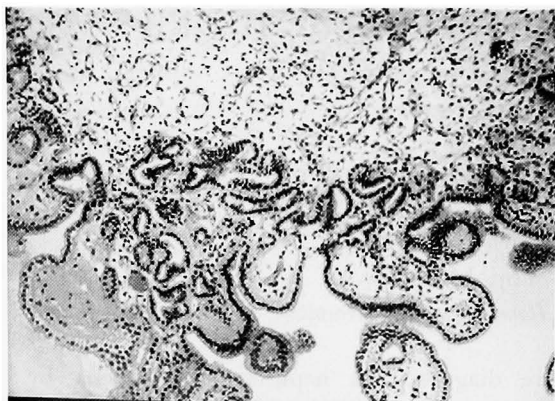


Fig. 2. Pathohistological observations (Case 2). The endothelium was cylindric to cuboidal with papillary proliferation, and adenoma was indicated (HE stain $\times 200$).

was performed. Pathohistological examination revealed that the tumors had both cylindric and partly cuboidal endothelium with papillary proliferation. Adenoma was indicated but without atypical nuclei, and the tumors were diagnosed as nephrogenic adenoma (Fig. 2).

DISCUSSION

Nephrogenic adenoma is a benign tumor first reported as a hamartoma in 1949 by Davis¹⁾, and tumors with a tubular structure similar to renal tubules histologically were so named by Friedmann and Kuhlenbeck²⁾ in 1950. Nephrogenic adenoma was initially thought to originate from the mesonephrogenic ductules²⁾. However, as most of the reported cases have a history of chronic stimulation such as calculi, invasive surgery and inflammation, the theory that it may be a urothelial metaplasia due to chronic stimulation is strongly supported at present^{3,4)}.

In Japan, there have been 37 reported cases of nephrogenic adenoma of the bladder, and our cases were the 38th and 39th (Table 1). There were 21 male cases and 18 female cases and the ages of the patients greatly varied, ranging from 3 to 81, with a mean age of 56.5. The main complaint was hematuria in 16 cases followed by pollakisuria in 6 cases. In 8 cases,

the adenoma was accidentally found by cystoscopy during follow-up for other diseases. Nephrogenic adenoma most frequently occurred after surgery of the urinary tract in 16 cases followed by urinary tract infection in 9 cases and intravesical BCG treatment in 6 cases.

In BCG treatment, an immune reaction mediated by macrophages and chronic granulomatous inflammation is thought to induce urothelial metaplasia, which may be the cause of nephrogenic adenoma^{5,6)}. It should be noted that after BCG was approved as an intravesical infusion treatment for bladder tumors in December 1996, the ratio of cases due to BCG treatment has increased. While only one out of 19 cases before 1996 had a history of intravesical BCG treatment (5.3%), 5 out of 20 cases did so after 1997 (20.0%). This suggests that the incidence of nephrogenic adenoma may continue to increase in the future. Urologists must be cognizant that the incidence of nephrogenic adenoma increases after surgery of the urinary tract and intravesical BCG treatment.

Two points should be noted with regard to nephrogenic adenoma of the bladder. The first is the high recurrence rate. Porcaro et al.⁷⁾ reported that it recurred in 63% of the cases within 24 months of TUR, and Heidenreich et al.⁴⁾ reported that in the long-term follow-up of 4 years, the recurrence rate was 80%. The second point is malignancy. Although nephrogenic adenoma itself is a benign tumor, studies have been made regarding its relationship with mesonephric carcinoma⁸⁾. Histologically, mesonephric carcinoma has a well differentiated tubular lesion as does nephrogenic adenoma, but it is a malignant tumor that invades the muscularis of the urinary bladder. As there have been few reports on this tumor, which is an extremely rare malignancy, it is unclear whether or not mesonephric carcinoma is a cancerous form of nephrogenic adenoma. However, the possibility of nephrogenic adenoma developing into a malignant tumor has not been completely ruled out⁹⁾, and further attention must be paid to this matter. We strongly advise careful follow-up be made for potential occurrence of nephrogenic adenoma of the bladder even though transurethral resection of nephrogenic adenoma may be successful.

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Table 1. Review of cases with nephrogenic adenoma of the bladder in Japan

Number of cases	39 (male: female=21: 18)
Mean age	56.5 (3-81)
Sign and/or symptoms	Hematuria: 16, Pollakisuria: 6, Miction pain: 2, Pyuria: 1, Dysuria: 1, Cystoscopically abnormal finding: 8, Abnormal urine cytology: 1, Unknown: 4
Predisposing factors	Surgery: 16, Infection: 9, Intravesical BCG treatment: 6, Intravesical pirarubicin treatment: 2, None: 2
Treatment	TUR-Bt: 30, Open surgery: 7, None: 2

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(Received on April 17, 2002)
(Accepted on June 1, 2002)

(迅速掲載)

和文抄録

膀胱 Nephrogenic adenoma の 2 例 (本邦報告例の文献的考察)

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症例 1 は 72 歳の女性で尿管腫瘍に対する腎尿管全摘術 8 カ月後の膀胱鏡時に膀胱腫瘍を認めた。症例 2 は 57 歳の女性で 5 回の TUR-Bt の後に計 6 回の BCG 膀胱内注入療法を行い, その後の膀胱鏡で 2 個の膀胱腫瘍を認めた。2 例とも TUR-Bt を施行した。組織学的診断では 2 例とも nephrogenic adenoma であった。

今回の 2 例を含めて, これまで計 39 例の本症がわが国で報告されている。男性 21 例, 女性 18 例で平均年齢

は 56.5 歳である。おもな症状は血尿が 16 例と最多で, ついで頻尿が 6 例である。本症の誘因としては尿路の外科的手術が 16 例で, 尿路感染症が 9 例, BCG 膀胱内注入療法が 6 例である。特に BCG が保険認可された 1996 年 12 月以降は BCG 膀胱内注入療法に引き続いて起こる症例の比率が高くなっており, 将来的な膀胱 nephrogenic adenoma の増加が予想される。

(泌尿紀要 48 : 463-466, 2002)