

## Advanced Bladder Cancer in a Young Female: A case report

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We present a rare case of advanced bladder cancer in a young female. A 27-year-old woman had the chief complaint of proteinuria. A clinical examination revealed a papillary, broad-based bladder tumor with a clinical stage of T3, N3, M0. Preoperatively, 3 courses of neoadjuvant chemotherapy with methotrexate, adriamycin, and cisplatin were performed, and proved to be effective. Radical cystectomy was done and the histopathologically it was diagnosis as Grade 2 transitional cell carcinoma, which did not show any p53 gene mutation. The patient's postoperative clinical course was uneventful, and she remained disease free for 27 months.

Bladder carcinoma in patients under 30 years of age tends to have a early stage and a low grade. However, the above described 27-year-old female patient demonstrated the advanced stage bladder tumor. Therefore, it should be kept in mind to accurately evaluate young patients with transitional cell carcinoma of the bladder and not to rule out the possibility of advanced disease even though a patient is young.

**Key words :** Bladder cancer, Young female, Transitional cell carcinoma

### INTRODUCTION

Few reports have been made on bladder tumors in young patients, and the prognosis in such cases is considered to be favorable. In the present case report, we describe a case of invasive transitional cell carcinoma of the bladder in a young female, who underwent total cystectomy.

### CASE REPORT

The patient was a 27-year-old female whose profession was an insurance saleswoman. Her chief complaint was proteinuria. Neither her family history nor the past history was remarkable. She has smoked 10 cigarettes a day for 10 years.

Since around April 1997, the patient had noticed macroscopic hematuria, but she had not consulted any doctor. She was subsequently found to have proteinuria on regular health check-up, and visited a physician at the Department of Internal Medicine in our hospital. Abdominal echography at that

time suggested left hydronephrosis and bladder tumor, resulting in hospitalization on February 3, 1998 with suspected bladder tumor.

**Physical findings on admission:** The patient was of average built and her nutritional status was moderate. Her height was 167 cm, weight 61 kg, blood pressure 110/68 mmHg, pulse 66 beats/min and regular. No sign of anemia was observed in the conjunctiva, and she did not have an icteric conjunctiva. No abnormality was seen in the thoracoabdominal region. She did not complain of CVA (costovertebral angle) tenderness. Superficial lymph nodes were not palpable.

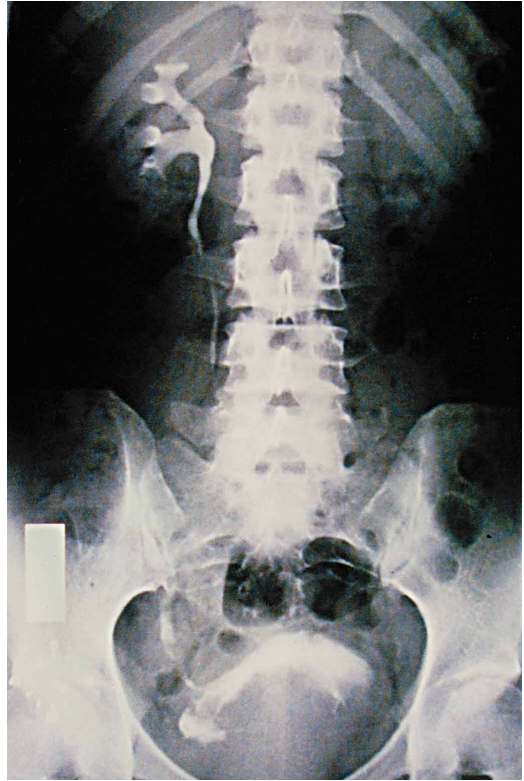
**Laboratory tests on admission:** Urinalysis showed 51 to 100 red blood cells and 10 to 29 white blood cells per high power field. Urinary cytology was class V. Her white blood cell count was 10,400/mm<sup>3</sup>.

**Results of imaging:** IVP (intravenous pyelography) revealed the left kidney to be unfunctional and an extensive filling defect

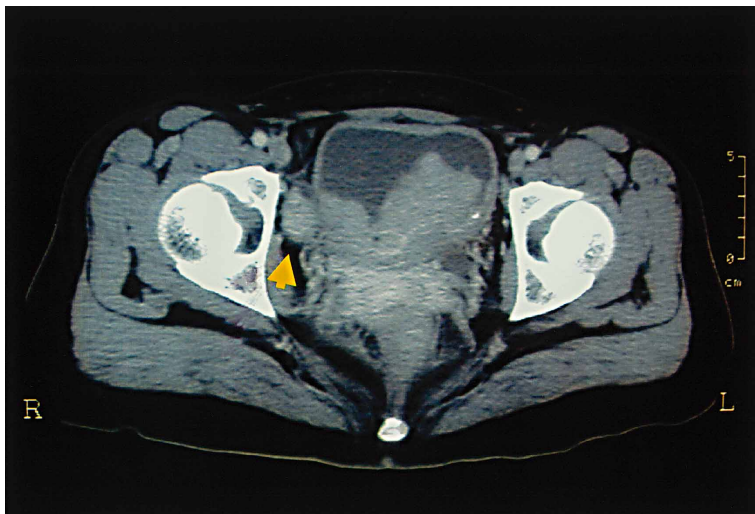
in the bladder (Fig. 1). Pelvic CT (computed tomography) showed extensive tumor invasion in the bladder and pelvic lymphnode swelling (Fig. 2).

**Cystoscopic findings:** Cystoscopy revealed papillary tumors without a stalk extensively invading from the bladder neck, to the posterior wall, the right lateral wall, and the apex of the bladder. The tumor was diagnosed to be Grade II transitional cell carcinoma (TCC) by biopsy and from the above findings, it was thought diagnosed as invasive bladder tumor with a clinical stage of T2, N3, M0. Three cycles of M-VAC chemotherapy (with methotrexate, vinblastine, adriamycin and cisplatin) were administered preoperatively, and the subsidence of pelvic lymph node swelling was confirmed on CT (Fig. 3). Thereafter, total cystectomy and construction of an ileal conduit were performed on the patient.

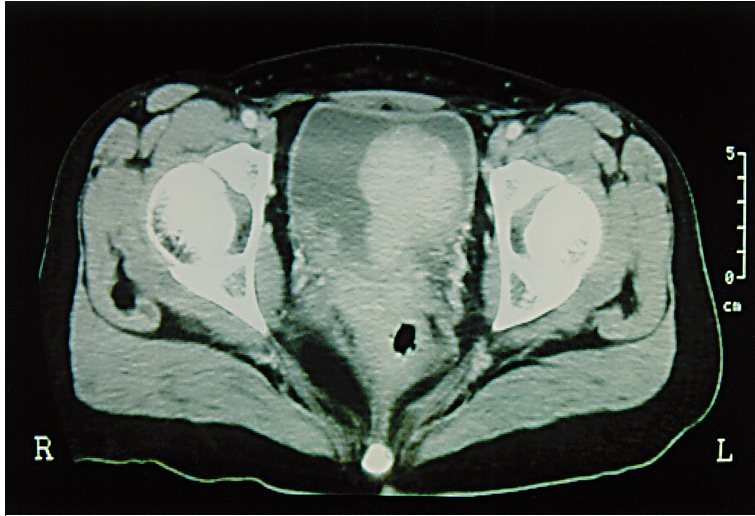
**Histopathological findings:** Bladder tumor tissue obtained through total cystectomy showed papillary hyperplasia and the formation of 10 or more layers of transitional epithelium. The tumor cells exhibited a moderate degree of mitosis and had invaded deeply into the muscle layer (Fig. 4). It was concerned about metastases to the pelvic lymph nodes but none was observed. Based on these findings, the patient's bladder tumor was judged to be Grade 2 TCC with a clinical stage of pT2, pN0.



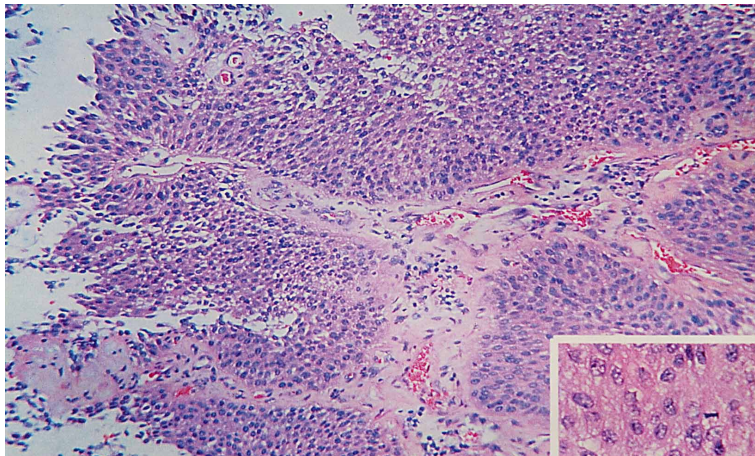
**Fig. 1** Intravenous pyelography shows the left kidney to be unfunctional and an extensive filling defect in the bladder.



**Fig. 2** CT reveals extensive tumor invasion in the bladder and pelvic lymphnode swelling (yellow arrow-head).



**Fig. 3** CT reveals the subsidence of pelvic lymphnode swelling.



**Fig. 4** Histopathological examination reveal transitional cell carcinoma with the formation of 10 or more layers of transitional epithelium. Tumor cells exhibited a moderate degree of mitosis.

**Postoperative course:** The patient was discharged without any additional postoperative therapy. Her postoperative course has been followed up at 3 month intervals at the outpatient department of our hospital, and no recurrent carcinoma has been observed.

#### DISCUSSION

Among various tumors in the urinary system, bladder tumors develop with a comparatively high frequency and are considered to be one of the most significant tumors in clinical practice. Bladder tumors are frequently detected in individuals aged around 65 years, but are rarely found in younger

individuals aged under 40 years. In Europe and North America, the incidence of bladder tumors is estimated to be 1% in individuals aged 40 years or under [1] and 0.8% in individuals aged 30 years or under [2]. In Japan, its incidence is estimated to be less than 1% in individuals aged 30 years or under [3].

When referring to case reports on bladder tumors in younger Japanese patients, such patients are found to have the most frequent chief complaint (before diagnosis of bladder tumor) of macroscopic hematuria, just like older patients with bladder tumors, but the duration from the initial symptom to the

definitive diagnosis is found to be longer in younger patients as compared with older patients [4]. This difference is considered to be caused by delayed confirmation of diagnosis in younger patients due to the fact that, because younger patients tend to be reluctant to undergo cystoscopy, bladder tumors are often diagnosed as nephritis, etc. without sufficient examination. Concerning the patient described in this case report, the duration from awareness of the blood in her urine to definitive diagnosis was approximately 10 months, however, this delay was due to the longer duration from the complaint of her subjective symptom to the first medical examination. The duration from the first medical examination to the diagnosis of her extensive invasive bladder tumor was relatively short.

Recently, considerably small tumors can be non-invasively detected as a result of advance in diagnostic echography. Furthermore, in the patient described in this case report, bladder tumors were diagnosed based on the abnormal findings in an echography conducted at another department. Therefore, echography, instead of cystoscopy, is considered to be essential particularly in the screening examination of bladder tumors in younger individuals.

Younger patients, like older patients, frequently develop bladder tumors which are histopathologically classified as transitional cell carcinoma [5]. However, it has been reported that bladder tumors in younger patients are characterized by their low histopathological malignancy grades as well as by their early stage of penetration depth [6]. Therefore, bladder tumors in younger patients are mainly treated with bladder preservation therapies including transurethral resection (TUR) of bladder tumors. However, although rare, some cases were reported that, like the patient described in this case report, total cystectomy was applied as the optimal indication or it was necessitated to perform total cystectomy after repeated partial cystectomy by recurrence [7, 8]. Among such patients, there was a report that extensively invading bladder tumors, to which application of total cystectomy would have been considered if the patient had been older, were undergone with TUR [9]. Regarding the patient described in this case report, the patient was a young female and

therefore we attempted to select a therapeutic method that would enable us to preserve the patient's bladder as far as possible but finally we had to give up. As this case was, in the case of younger patients who have bladder tumor, which will be treated by total cystectomy without hesitation if the patient has been older, bladder preservation therapies also tend to be considered. However, bladder preservation therapies are selected in patients with relatively long life expectancy taking their quality of life into account. Treatment methods for bladder tumor should be decided based on the depth of tumor penetration and grade of tumor malignancy, regardless of patient age, because the extent of tumor invasion in younger patients, like that in older patients, greatly depends on the grade of tumor malignancy.

It has been pointed out that, in DNA histogram analysis, aneuploidy patterns that are considered to be associated with poor prognosis were observed in some younger patients with bladder tumors [3], and their prognosis cannot necessarily be said to be favorable. On the other hand, Melicow [10] reported that, in the examination of bladder tumor tissues obtained from 2,500 or more patients, the incidence of low grade tumors was high in patients under 40, in contrast to the higher frequency of high grade tumors in patients aged 40 years or over. The reason why the malignancy grades of bladder tumors in younger patients are not generally high, may be that the possibility of mutation in the undetermined gene regions that are responsible for tumor malignancy grades is smaller in younger patients, because the amount of exposure to bladder carcinogens including contact with those substances is smaller in younger patients than in older patients. For example, it has been suggested that structural aberrations of chromosome 9 are related to bladder carcinogenesis [11] and to the multicentric growth [12] of bladder tumors, and that mutation in the p53 tumor suppressor gene is related to the malignant potential of bladder tumors [13]. In the patient described in this case report, mutation in the p53 tumor suppressor gene, which has been reported to be detected in many types of bladder tumors, was explored but not detected [14]. In future, it will become possible to explain the differences in

the mechanisms of carcinogenesis as well as of malignant alteration between bladder tumors in younger patients and those in older patients, in terms of gene mutation, which, in turn, will lead to the selection of a more specific treatment method.

#### REFERENCES

- 1) Javadpour N., Mostofi F. K.: Primary epithelial tumors of the bladder in the first two decades of life. *J Urol* 101: 706–710, 1969.
- 2) McCarthy P. J., Gavrell G. J., Leblanc G. A.: Transitional cell carcinoma of bladder in patients under thirty years of age. *Urology* 13: 487–489, 1979.
- 3) Asakura H., Tachibana M., Baba S., Deguchi N., Jitsukawa S., Hata M., Tazaki H.: Studies on biological characteristics of transitional cell carcinoma of the bladder in patients under 30 years of age. *Jpn J Urol* 80: 1218–1223, 1989.
- 4) Yasunaga Y., Yoshioka T., Sonoda T., Miyagawa M.: Transitional cell Carcinoma of the bladder in a Juvenile Patient: A case report. *Nishinohon J Urol* 51: 1217–1220, 1988.
- 5) Sakashita S., Takahashi K., Maru A., Koyanagi T.: Bladder tumors in patients less than 40 years old. *Nishinohon J Urol* 50: 1193–1196, 1988.
- 6) Franzblau A.H.: Bladder carcinoma in young. *Rocky Mt Med J* 65: 54, 1968.
- 7) Ishizuka O., Ogawa A., Okaneyama T., Kitami Y., Wajiki M., Ikado S.: Radical cystectomy and ileocystectomy preserving urinary continence and erection in a young man with bladder cancer. *Jpn J Clin Urol* 45: 235–237, 1991.
- 8) Ouchi H., Noguchi S., Masuda M., Yao M., Kubota Y., Hosaka M.: Recurrent and up-grading bladder cancer in a young female: A case report. *Acta Urol Jpn* 42: 311–313, 1996.
- 9) Kuromitsu K., Tasaki Y., Nomura Y., Seto H.: Transitional cell Carcinoma of the bladder in a young patient: A case report. *Nishinohon J Urol* 59: 849–852, 1997.
- 10) Melicow M. M.: Tumors of the urinary bladder: A clinicopathological analysis of over 2,500 specimens and biopsies. *J. Urol* 75: 480, 1956.
- 11) Kinzler K.W., Vogelstein B.: Lessons from hereditary colorectal cancer. *Cell* 87: 159–170, 1996.
- 12) Habuchi T., Kato T., Takahashi T., Ogawa O.: Significance of chromosome 9 alterations as an initial step in urothelial carcinogenesis. 46: 749–755, 2000.
- 13) Uchida T., Wada C., Ishida H., Wang C., Egawa S., Yokoyama E., Kameya T., Koshiha K.: p53 mutations and prognosis in bladder tumor. *J Urol* 153: 1097–1104, 1995.
- 14) Masuda A., Kikuchi Y. Y., Kawamura N.: Mutation analysis of the p53 tumor suppressor gene using paraffin-embedded specimens of human transitional cell carcinomas by the direct sequencing method. *Tokai J Exp Clin Med* 25: 69–77, 2000.