

## Small Cell Carcinoma of the Prostate : A Case Report of Long-Term Survival

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**ABSTRACT.** A 62-year-old man, who was initially thought to be suffering from prostate adenocarcinoma with normal prostate-specific antigen, underwent hormonal therapy and external beam radiotherapy in September 1997. Although the treatment was successful and the patient went into a complete remission, computed tomography performed six months after the initial workup revealed multiple metastases (paraortic lymph nodes (LNs), liver, and mediastinal LN). Because of the unexpected clinical course, a diagnostic reevaluation was performed and a diagnosis of small cell carcinoma of the prostate was made.

Two courses of intraarterial chemotherapy combined with radiotherapy achieved a second complete remission. The patient maintained a relatively good clinical condition with oral etoposides until March 2000, when multiple right lung and neck LN metastases followed by multiple liver, bone, and intracranial metastases were detected. Three courses of systemic chemotherapy combined with focal radiotherapy decreased the symptoms.

In April 2001, massive macrohematuria, which was certified as radiation cystitis by cystoscopy, occurred. Despite control of the hemorrhage with embolization via the bilateral internal iliac arteries, his general condition did not recover and he died in July 2001.

**Key words**    ① small cell carcinoma of the prostate    ② long-term survival  
                  ③ intraarterial chemotherapy combined with radiotherapy  
                  ④ radiation cystitis            ⑤ transarterial embolization







carcinoembryonic antigen (CEA), and PSA levels were 50ng/ml, 7.8ng/ml, and 0.1ng/ml, respectively. Figure 6 indicates the transition of the serum levels of those tumor markers with time. Involved field EBRT of 50Gy in 25 fractions in 37 days and 50.4Gy in 28 fractions in 38 days were delivered to the mediastinal and paraaortic LNs (Fig. 7a, b). Together with the EBRT, two courses of intraarterial chemotherapy consisting of carboplatin (200mg/body) and doxorubicin (50mg/body) to the mediastinal LN and the liver metastasis were performed by bolus injection via the right bronchial and right hepatic arteries, respectively, (Fig. 8a, b). These treatments achieved a second complete remission in May 1998 with normalization of the serum NSE level from 50 to 4.6ng/ml (the PSA remained at a normal level throughout the treatment; fig. 4c, d and fig. 5). He was discharged and remained clinically free of the disease for 15 months afterward on oral etoposides (100mg/day for two weeks, repeated every five weeks). In August 1999, a solitary pulmonary metastasis

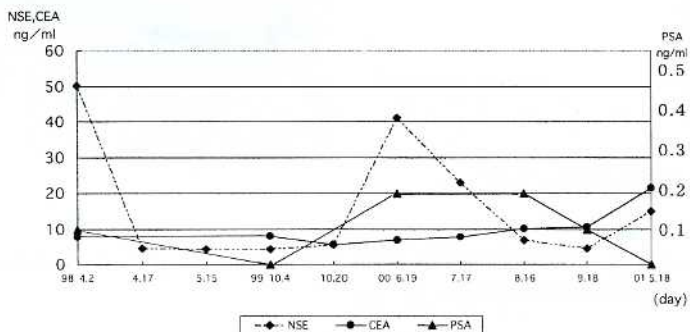
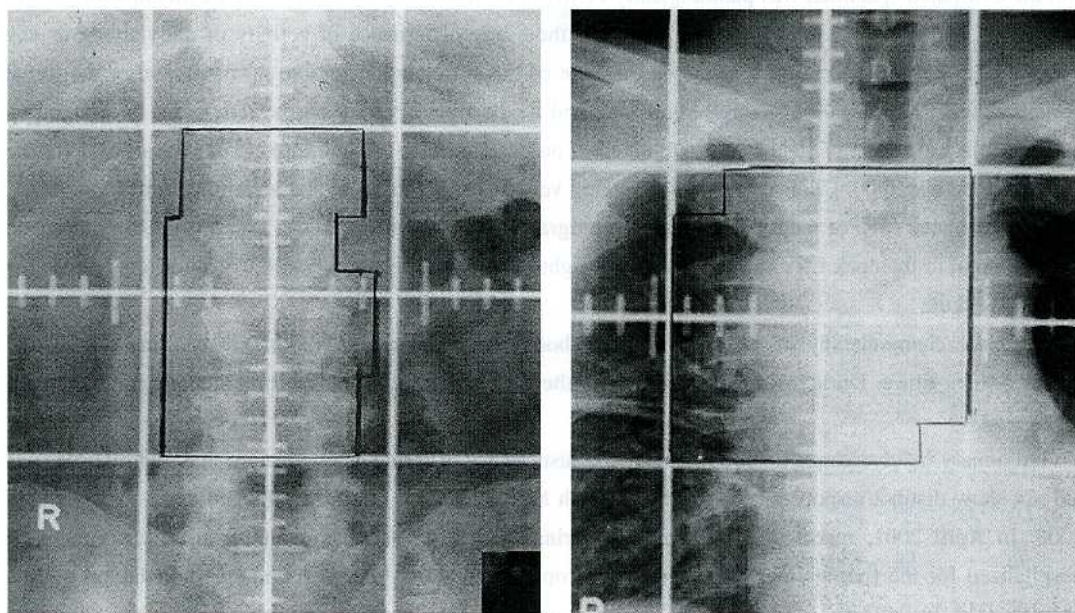


Fig. 6. Figure 6 indicates the transition of the serum levels of the tumor markers with time.



**a**

**b**

Fig. 7. a : Paraaortic field. EBRT of 50.4 Gy in 28 fractions in 38 days.

b : Mediastinal field. External beam radiotherapy (EBRT) of 50 Gy in 25 fractions in 37 days.



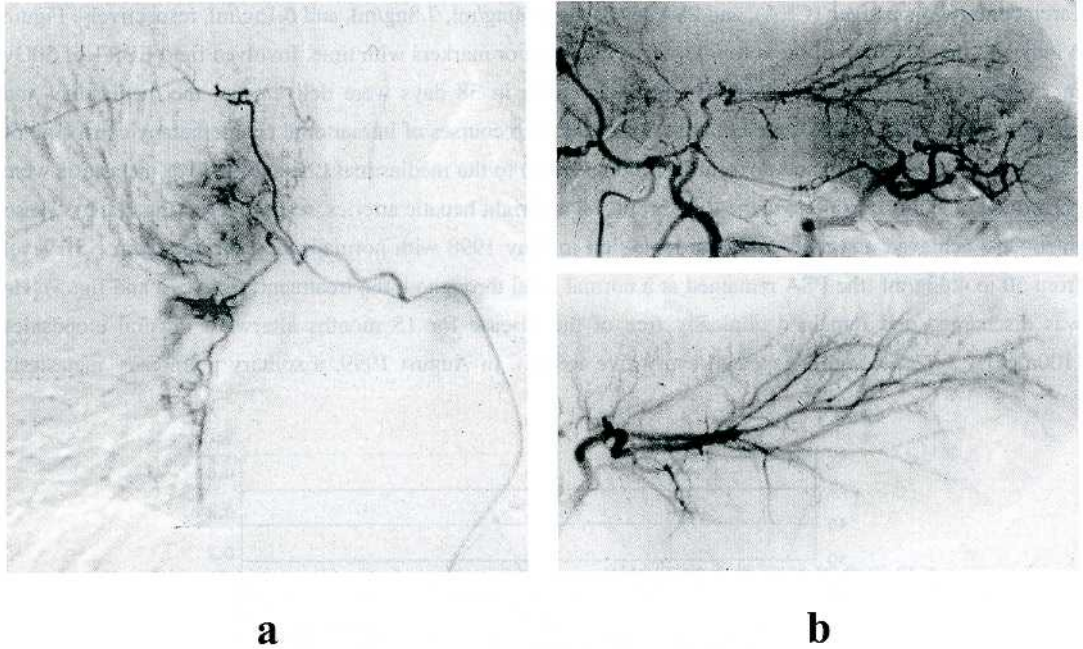
**a****b**

Fig. 8. Intraarterial chemotherapy of the mediastinal LN and the liver metastasis was performed by bolus injection via the right bronchial and right hepatic arteries (figure 8a, b).

appeared in his right lower lung. This was treated by video-assisted thoracoscopic surgery in October 1999, and the extirpated specimen was pathologically certified as small cell carcinoma. The treatment successfully maintained his health for another seven months without any disturbance of activity of daily living or any significant treatment-associated sequelae at the time of the systemic evaluation, 30 months after the initial presentation. In March 2000, multiple right lung and mediastinal LN metastases were noted on pulmonary CT, and bilateral neck LN metastases were detected on palpation. He was admitted to our department for the third time in June 2000. Clinical workups including vertebral MRI, cervical and abdominal ultrasonography, contrast enhanced MRI of the brain, and bone scintigraphy revealed metastases to bones (vertebrae, ribs, and the left tibia), to the neck LNs, to the liver, to the right intra-orbital, which impaired visual acuity, and to the base of the skull.

Systemic chemotherapy of paclitaxel (300mg/body) with carboplatin (380mg/body) was started and repeated three times. During the course, EBRT to the metastases of the right orbita and left tibia was also performed.

Pulmonary involvements, tibial bony pain, and disturbance of visual acuity disappeared, but other lesions did not show distinct responses. After a three-month hospitalization, he was discharged again in September 2000. In April 2001, repeated macrohematuria, urinary retention and bladder tamponade led him to be hospitalized for the fourth time. An urgent cystoscopic examination revealed findings of radiation cystitis characterized by diffuse erosion of the bladder mucosa with oozing hemorrhage (Fig. 9a). Because transurethral coagulation followed by continuous aluminum bladder irrigation did not bring about effective hemostasis, percutaneous transarterial embolization via the bilateral internal iliac arteries was carried out (Fig. 10a). After the procedure, the macrohematuria disappeared and a cystoscopic examination revealed recovery

**a** ant. TAE

**b** post. TAE

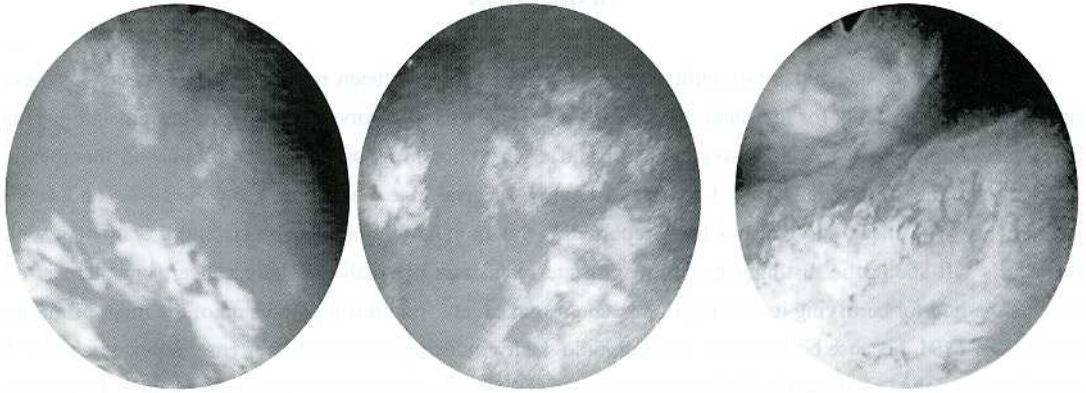


Fig. 9. Cystoscope findings of radiation cystitis on admission and the twelfth day after transarterial embolization (TAE). In Figure 9a, bladder epithelial diffuse loss and apoplexy are shown. Apoplexy almost disappears after TAE, and organization is shown (figure 9b).

**a** ant. TAE

**b** post. TAE



Fig. 10. Angiographic images on the twelfth day before treatment and after transarterial embolization (TAE). Gross bloody urine disappeared just after this treatment.

from the mucosal erosion and oozing bleeding (Figs. 9b, 10b). Despite the resolution of this urgent problem, the patient's general condition gradually became worse with bilateral paralysis of the lower extremities, a neurogenic bladder, and impairment of consciousness. During this terminal period, metastases to the bilateral lungs, spinal cord, right frontal lobe and cerebellum, which were responsible for his symptoms, as well as to the subcutaneous skin and the neck and axillary LNs were noticed. Those lesions showed a rapid progression and we no longer had any way to treat them properly. He died in July 2001. He was hospitalized for a total of nine months, and the time from his first consultation to death was 46 months. During his life under medical treatment, he was able to work for more than a year with minimum restrictions.



## DISCUSSION

SCCP can be considered a rare entity, since only 55 cases have been reported to date in the Japanese literature and it accounts for less than one percent of all malignant tumors originating in the prostate<sup>1)</sup>. This disease is characterized by aggressive behavior and a very poor prognosis with no established therapeutic regimen<sup>2),3)</sup>. The reported 2-year, 3-year, and 5-year survival rates have been 3.6%, 1.8%, and 0.9% respectively. The mean survival has been reported as 9.8 months without metastasis and 7.3 months with metastasis<sup>4)</sup>. It should be distinguished from prostate metastasis of small cell lung cancer, but there is no reliable method for certifying it as being of prostate origin except for clinical preclusion of the lung, primarily with CT or MRI, because both tumors are morphologically indistinguishable. In our case, repeated chest CT examinations failed to show the findings of a primary small cell lung cancer. Thus we consider the case as SCCP. There are two histological subtypes related to SCCP: pure small cell carcinoma (SCC) and SCC with adenocarcinoma. In addition to these, there is one possible subtype that can be transformed from an adenocarcinoma to a malignant neuroendocrine tumor in the clinical course<sup>5)</sup>. Basically we consider these tumors should be treated in the same way as SCC arising from the lung. In this regard, microscopic examination of the initial biopsy specimen seems crucial. The greater part of the tumor in our case showed typical features of SCC, but a poorly differentiated acinar adenocarcinoma of conventional type was also discovered in very limited areas. This may explain the normal level of serum PSA. Since typical acinar adenocarcinomas can be positive for neuroendocrine markers, immunoreactivity for these markers per se does not support the diagnosis of neuroendocrine carcinoma. From this standpoint, the histological diagnosis of SCC should be carefully determined from both neuroendocrine markers and morphologic features. Although combination chemotherapy is recommended and SCCP often reacts to such treatment, it is likely to rapidly recur. Treatment of recurrent SCCP has focused on systemic chemotherapy and/or radiotherapy, but the prognosis is distressing once there is recurrence<sup>4),6)</sup>. Therefore, we treated the recurrence in the liver, which would have become acutely lethal if left untreated, with intraarterial chemotherapy since liver metastasis is not suitable for radiotherapy, and the result was satisfactory. There have been no reports in the English literature concerning intraarterial chemotherapy for metastatic SCCP. Our approaches produced a favorable clinical course with a survival period of about 36 months longer than the median<sup>4)</sup>. Although the efficacy of our surgical approach for the lung metastasis is controversial due to the early appearance of multiple lung metastases after surgery, intensive local treatment with possible combined modalities suggests some role for these modalities in prolonging the survival of even patients with multifocal recurrence. Regarding the patient's macrohematuria caused by radiation cystitis, after failure with conservative therapy (transurethral coagulation and continuous aluminum bladder irrigation), as a last resort we turned to percutaneous transarterial embolization and successfully achieved hemostasis. We hope that our experience may prove beneficial in treating patients with this rapidly developing and lethal disease.

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