Prostate Carcinosarcoma Developing After Combined Pelvic External Beam Radiation Therapy and Androgen Deprivation Therapy

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Carcinosarcoma of the prostate is a very rare disease, which consists of carcinomatous and sarcomatous components. The prognosis of patients with prostatic carcinosarcoma is poor. An 80-year-old man who had been suffering from urinary retention and constipation with rectal pain visited a hospital. A patient with a history of combined pelvic external beam radiation therapy (EBRT) and androgen deprivation therapy (ADT) for prostate adenocarcinoma 7 years ago was diagnosed with secondary malignancy such as prostate carcinosarcoma by prostate biopsy. This is also a rare case occurring after combined EBRT and ADT for adenocarcinoma in a short interval. Then, he underwent chemotherapy for one cycle. Chemotherapy was stopped because of rapid clinical aggravation, and the patient died 5 months later. It is important to keep in mind the possibility of carcinosarcoma in the case that prostate-specific antigen maintains stable level but extent of tumor is gradually increased after EBRT or ADT. (Korean J Urol Oncol 2019;17:195-198)

Key Words: Prostate • Carcinosarcoma • Prognosis

Carcinosarcoma of prostate is extremely rare cancer developing after external beam radiation therapy (EBRT) or androgen deprivation therapy (ADT). Carcinosarcoma is difficult to diagnose and treat owing to lack of experience.¹ Tumors consist of complex with malignant gland and spindle cell components. Sarcomatous portion of carcinosarcoma had diversities from 5% to 99%.² Serum prostate-specific antigen (PSA) levels are low in comparison with extent of tumor size. Presenting symptoms of patients are com-

monly urinary obstruction. Therapeutic modalities including radiation therapy (RT), ADT, chemotherapy (CTX) and surgery for carcinosarcoma of prostate had shown disappointing outcomes. It is hard to distinguish clearly between carcinosarcoma and other tumors in many cases, thus a diagnosis will be confirmed after biopsy. In this case, early biopsy is to help planning this rare case. We need to take into account carcinosarcoma which presented with low levels of serum PSA compared with aggravating cancer, in spite of the form of therapy.

CASE REPORT

An 80-year-old patient was diagnosed with prostate cancer 7 years ago. The PSA was 43.8 ng/mL. Prostate biopsy was performed by guided transrectal ultrasonography. Histopathological examination of the specimen showed an

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adenocarcinoma (Gleason score 3+3). We performed magnetic resonance imaging, computed tomography (CT), whole-body bone scan, and chest X-ray (CXR). No metastatic lesions except bladder neck invasion were found (Fig.

1A). The patient underwent EBRT for prostate adenocarcinoma. At 1 year after EBRT, the level of PSA had risen gradually despite the fact that characters of prostate showed no changing on CT (Fig. 1B). Additional ADT had

Fig. 1. (A) Magnetic resonance sagittal image shows that bladder neck invasion of prostatic adenocarcinoma on T2-weighted image. (B) Follow-up computed tomography shows a decreased prostate size at nadir state. Abdominal pelvic computed tomography anterior-posterior image (C) and transverse image (D) show huge ill-defined enhancing prostate.

Fig. 2. Immunohistochemical stain (×200): (A) spindle cells with marked atypical cells which are diffusely positive for cytokeratin, (B) spindle cells and polygonal large cells which are negative for p63, (C) spindle cells expressing vimentin, and (D) several spindle giant cells positively stained Desmin.

been followed up 3 years. The serum PSA maintained level of the nadir was 0.002 ng/mL. But, the patient did not visit hospital with a private matter during 3 years.

After 3 years, the patient visited Urology Department a complaining with urinary retention and rectal pain with constipation. On the physical examination, huge and hard rectal mass was palpable. The serum PSA was 3.51 ng/mL. CXR showed multiple wide-spread variable-sized nodules in the entire both lung fields. Chest, abdomen and pelvis CT showed an 8-cm-sized rectal mass with poor enhancement and multiple lymph nodes metastasis (Fig. 1C, D). Colonoscopy guided biopsy was done to distinguish recurred prostate cancer and gastrointestinal stromal tumor. The current biopsy contains a minor component of high-grade prostatic acinar adenocarcinoma (10%) and a major component of high-grade sarcoma (90%). The high-grade sarcoma components show spindle cells with marked atypia and frequent mitoses and scattered bizarre polygonal large cells are positive for cytokeratin (Fig. 2A). Occasional spindle cells are negative for p63 represented for basal cell marker (Fig. 2B). They are diffusely positive for vimentin (Fig. 2C). The spindle cells and polygonal large cells are focally positive for desmin, smooth muscle actin and myoD1 but negative for ALK-1, CD34, CD117, PSA, and cytokeratin AE1/3 (Fig. 2D). The high-grade sarcomatous components show heterogeneous sarcomatous elements consisting of predominantly rhabdomyosarcoma (60%) and leiomyosarcoma (30%). The high-grade acinar adenocarcinoma component is positive for cytokeratin AE1/3 and PSA (immunohistochemical stain, $\times 200$). This patient exhibited the short duration between initial presentation with adenocarcinoma and emergence of carcinosarcoma. The patient was scheduled for CTX as long as possible. Then, he was treated with docetaxel for one cycle. CTX was stopped because of rapid getting worse, and the patient died 5 months later.

DISCUSSION

The pathogenesis of prostatic carcinosarcoma is not clear and diverse analysis has been proposed for the various elements of carcinosarcoma. The prostatic carcinosarcomas interpreted the heterologous mix of carcinomatous (epithelial) and sarcomatous (mesenchymal) elements, and it could be related to previous RT or to ADT.³ In our case, sarcomatous

component was not found at the first biopsy. Carcinosarcoma was diagnosed with the second biopsy after 3 years of ADT with RT. Some reports content that RT and ADT may lead to transformation of carcinosarcoma.⁴ About half of carcinosarcoma cases, the first biopsies are proven acinar-typed adenocarcinoma. It was proposed the period for carcinosarcoma transformation from adenocarcinoma is averagely 3 years as seen in our case.⁵ Carcinosarcomas of prostate often are presented with low levels of serum PSA compared with adenocarcinoma, therefore serum PSA has low effects for the assessment of the sarcomatous element in carcinosarcoma, whereas it may be useful in assessing the progress of the adenocarcinoma component of the tumor. The epithelial component of carcinosarcoma of prostate stains shows positivity for cytokeratin and prostatic acid phosphatase. The sarcoma component of carcinosarcoma stains show negativity for PSA, epithelial membrane antigen, and keratin.⁶ It is hard to distinguish clearly between carcinosarcoma and other tumors in many diagnostic methods, thus a diagnosis will be confirmed after biopsy. The serum PSA remained low level after RT or ADT, nevertheless, the aggravating disease such as increasing tumor size or spreading metastasis was progress. In that case, it is good to planning for additional biopsy of the prostate. Early diagnosis and treatment may give a chance of improved prognosis in these patients. There is no standard option of treatment. There are various treatment modalities such as aggressive surgical treatments (radical prostatectomy or total pelvic exenteration) or EBRT or ADT or CTX. ADT would be preferred to treat the adenocarcinoma component of the prostatic cancer but would be useless to control the sarcomatoid component of the tumor. Aggressive surgery remains the recommendable therapy method. Early diagnosis and treatment may give a chance of improved prognosis in these patients. The most often use therapeutic modality has been an RT (43%). Other modalities such as surgery (40%), ADT (38%), and CTX (14%) have been used for the patients with prostatic carcinosarcoma in order of precedence.⁷ The sites of metastases were the lung, bone, lymph node, liver, brain, and peritoneum and so on. Most common site is lung.⁷ In cases of advanced disease supportive therapy would be required. Patients with severe obstruction of the rectum would require colostomy as seen in our case. The survival period was extremely disappoint-

ting. The mean period was 7 months.⁸ Our patient was treated with CTX, but CTX was stopped because of rapid clinical aggravation, and the patient died 5 months later. Early rebiopsy of prostate in case of progressed disease despite of PSA maintenance after RT or ADT may help diagnose various carcinoma, and early aggressive treatment may help to improve prognosis.

CONFLICT OF INTEREST

The author claims no conflicts of interest.

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