Management of biochemical recurrence after radical prostatectomy for prostate cancer
A case report

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Abstract

Rationale: How to manage patients with prostate cancer (PCa) with biochemical recurrence (BCR) following primary curative treatment is a controversial issue. Multiple disciplinary team (MDT) mechanism may propose an appropriate treatment plan for patients and can effectively improve patient prognosis and survival, reduce patient diagnosis and treatment waiting time, and greatly improve patient satisfaction.

Patient concerns: Here, we presented a case of a 77-year-old man with a persistently elevated serum level of prostate-specific antigen (PSA), who had a history of radical prostatectomy (RP) and of 9 years endocrine therapy.

Diagnoses: Castration-resistant prostate cancer and locally recurrent prostate cancer.

Interventions: Androgen-deprivation therapy was first utilized 2 months after RP, due to the consideration of BCR on May 5, 2007. And during the next 9 years, he was treated with different endocrine agents but failed to maintain serum levels of PSA stable. Finally, the MDT suggested patient to perform salvage radiation therapy (SRT). Under MDT mechanism, we avoid secondary surgery, so as to reduce the patients’ mental suffering and cost of patient care.

Outcomes: EPIC26 scale assessment revealed leak-free urine, good urine control, no defecation abnormalities or blood in the stool, no breast tenderness and breast enlargement significantly improved. The patient now has no adjuvant therapy, including endocrine therapy. The patient achieved good prognosis through local RT.

Lessons: Pelvic SRT for patients with locally recurrent PCa may restore the same radical effect as RP. And more importantly, MDT mechanism plays an important role in making the most appropriate decisions for patients.

Abbreviations:
- ADT = androgen-deprivation therapy
- BCR = biochemical recurrence
- CRPC = castration-resistant prostate cancer
- MDT = multiple disciplinary team
- MRI = magnetic resonance imaging
- PCa = prostate cancer
- PSA = prostate-specific antigen
- RP = radical prostatectomy
- SRT = salvage radiation therapy

Keywords: biochemical recurrence (BCR), castration-resistant prostate cancer (CRPC), multiple disciplinary team (MDT), salvage radiation therapy (SRT)
1. Introduction
Currently, more prostate cancer (PCa) patients depend on multidisciplinary care in managing their disease, as treatment has evolved to become increasingly multidisciplinary, using combinations of surgery, radiation, and/or systemic therapy. The conception of multiple disciplinary team (MDT) was first proposed by the United States in 1990s. Patients and medical workers can choose the most suitable treatment through multidisciplinary cooperation, and to avoid unnecessary treatment, so as to reduce patients’ mental suffering and cost of patient care. In this study, we present a case report of a 77-year-old man who met the definition of biochemical recurrence (BCR), castration-resistant prostate cancer (CRPC) and local recurrence demonstrated by magnetic resonance imaging (MRI).

2. Case presentation
A 77-year-old man was seen in the radiation oncology center at our hospital because of a persistently elevated serum level of prostate-specific antigen (PSA) in March 7, 2016. Ten years earlier, he was found to have a PSA level of 52.736ng/ml at his annual physical examination. And pelvic MRI revealed an evidence of PCa. The reminder of the examination is unremarkable. Thus, a systematic transrectal ultrasound-guided biopsy in February 7, 2007 demonstrated bilateral focus of adenocarcinoma (Gleason score, 9 out of 10 [left side, grade 4 plus grade5]; 7 out of 10 [right side, grade 3 plus grade 4]). The patient was treated with radical prostatectomy (RP) because of the definite diagnosis on March 8, 2007. Surgical pathology showed no tumor invasion in the left and right seminal vesicles and deferens, and no metastasis was found in bilateral iliac lymph nodes, but with bladder neck invasion. So, the pretreatment clinical and postoperative pathologic features suggested that he fell into pT4N0M0 stage and the National Comprehensive Cancer Network high-risk group. Following surgery, the patient was regularly monitored serum level of PSA. And it decreased to 0.001ng/ml 25 days after RP. However, 2 consecutive follow-up PSA values higher than 0.2ng/ml approximately 2 months after RP. Casodex was then used as one of an adjuvant therapy at another institution at May 10, 2007, due to consideration of the BCR. During the next 9 years, he was treated with different endocrine agents because of unstable serum levels of PSA, which including leuprorelin, goserelin, flutamide. Nevertheless, the serum level of testosterone was maintained at castration level, but serum levels of PSA still elevated. Until February 22, 2016, the pelvic MRI showed a nodule in the prostate and should be further confirmed whether it was a local recurrence (Fig. 1). After MDT discussion, the current diagnoses of this patient were:
(1) Postoperative PCa, high risk;
(2) CRPC;
(3) local recurrence.

According to the absence of clear guidelines, treatment options at this stage are difficult to choose. Generally, there are several possible treatment options as follows:

Figure 1. Pelvic MRI (2016-2-22). Follow-up MR images acquired 9 years after initial RP, T2WI MR images (A, B, C) and DW image (D) reveal an irregular nodule (arrow) with high intensity located on resected prostate tumor bed. MRI = magnetic resonance imaging. RP = radical prostatectomy.
(1) continuous androgen-deprivation therapy (ADT);
(2) secondary surgery;
(3) salvage radiation therapy (SRT);
(4) systemic treatment with docetaxel or other medicine, or
(5) other treatments.

In our institution, PCa MDT was carried out for this patient, and then the SRT was suggested for the patients. Therefore, the patient underwent pelvic RT from March 10, 2016 to May 3, 2016 with a total dose of 200cGy/37F = 7400cGy. The target area was the prostate tumor bed area + local recurrence area. Each stage of field modification was based on diffusion images of the patient with MR, in order to minimize the doses of organs at risk, while maximizing the radiation doses of locally recurrent lesions. After 37 fractions of RT treatment, he underwent follow-up examinations every 3 months. The serum levels of PSA were all between 0 and 0.007ng/ml, and serum levels of testosterone were between 41.9 and 188.7ng/dl. After 1 year of RT, the pelvic MRI scan in June 26, 2017 showed no evidence of nodules in the prostate region and no enlarged lymph nodes were found in the pelvic cavity (Fig. 2). And EPIC26 scale assessment revealed leak-free urine, good urine control, no defecation abnormalities or blood in the stool, no breast tenderness and breast enlargement significantly improved. The patient now has no adjuvant therapy, including endocrine therapy. Quality of life intact, and is still under follow-up, the specific course of disease and related treatment shown in Figure 3.

3. Discussion
How to manage patients with PCa with BCR following primary curative treatment is a controversial issue. The options for treatment of recurrence after RP are, according to the EAU, RT at least to the prostatic bed, complete or intermittent ADT, or observation.[2] This patient adopted continuous ADT when he presented to his local urologist. Until he was diagnosed with CRPC and MRI demonstrated local recurrence did he came to our radiation oncology center for advice. Through multidisciplinary discussion, we found that systemic treatment with docetaxel or other medicine for him has little overall survival benefit, but high economic costs.[3–7] So we began to turn to the local treatments. For local treatments, choose secondary surgery or SRT? It is reported that locally recurrent postoperative PCa may have a possible secondary surgical removal of the recurrent focal, but most of the cases of recurrent tumor produced obstruction complications at the same time, such as the involvement of ureteral causing kidney seep, or involvement of the bladder urethral anastomotic causing dysuria, and so on.[8] However, the patient was 77 years old with a single recurrent focus and no local obstruction, and the patient and his families both refused surgery. Therefore, after evaluating the patient’s systemic symptoms and reviewing the relevant literature, we believe that the patient is considered unsuitable for second surgery. Finally, pelvic local SRT was performed for him. For this patient, in the positioning before RT and before each RT, bladder volume was used to measure the urinary volume in the bladder, which was basically controlled at the same level to reduce the internal target volume and further protect the organ at risk. For patients with good prognosis, although RP can achieve better results, but there are still about 40% of patients relapse after surgery, of whom approximately 15% will eventually die of local recurrence or distant metastasis.[9,10] PSA monitoring can prompt the relapse 6 to 48 months in advance, the serum PSA
levels more than 2 consecutive ≥0.2 ng/ml defined as BCR. Therefore, patients with PCa after radical surgery may appear PSA gradually increased, BCR, and then enter the CRPC stage, and finally the recurrence of PCa and distant metastasis process.

In conclusion, the patient has been progression-free for 30 months up to now. Therefore, we have reasons to believe that pelvic SRT for patients with locally recurrent PCa can restore the same radical effect as RP. Accordingly, for such postoperatively recurrent PCa, it should be actively carried out early pelvic SRT, thereby blocking the progression of PCa, so that patients regain the effect of cure, and expect to get a better prognosis. And more importantly, under MDT mechanism, it can effectively improve patient prognosis and survival, reduce patient diagnosis and treatment waiting time, and greatly improve patient satisfaction. 

Author contributions

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