Metastatic Prostatic Ductal Adenocarcinoma Successfully Treated with Docetaxel Chemotherapy: A Case Report

Ryo Fujiwara a Susumu Kageyama a Keiji Tomita a Eiki Hanada a Teruhiko Tsuru a Tetsuya Yoshida a Mitsuhiro Narita a Takahiro Isono b Akihiro Kawauchi a

aDepartment of Urology and bCentral Research Laboratory, Shiga University of Medical Science, Otsu, Japan

Key Words
Chemotherapy · Docetaxel · Prostatic ductal adenocarcinoma

Abstract
A 68-year-old man presented with gross hematuria. A papillary urethral tumor adjacent to the verumontanum was found by cystourethroscopy. Serum prostate-specific antigen (PSA) was 3.246 ng/ml. A transurethral biopsy specimen was most suggestive of a primary urothelial carcinoma of the prostate, for which a radical cystoprostatectomy was performed. The final pathology was prostatic ductal adenocarcinoma with very focal acinar features (Gleason score 5 + 4 = 9, pT3bN0M0). Local recurrence and pelvic bone metastases developed 17 months later, and his PSA rose to 10.806 ng/ml. He was treated with combined androgen blockade and radiation. Two years later, the lesion showed progressive growth. Treatment followed with docetaxel (70 mg/m² every 3 weeks) and prednisolone 5 mg twice daily. After 10 cycles of chemotherapy, all lesions disappeared and PSA decreased to <0.005 ng/ml. Three years after chemotherapy, he maintains a complete response without any additional treatments. Docetaxel chemotherapy can be an effective treatment for patients with recurrent prostatic ductal adenocarcinoma.

© 2015 S. Karger AG, Basel

Susumu Kageyama, MD, PhD
Department of Urology, Shiga University of Medical Science
Seta Tsukinowa-cho, Otsu, Shiga 520-2192 (Japan)
E-Mail kageyama@belle.shiga-med.ac.jp
Introduction

Prostatic ductal adenocarcinoma is relatively uncommon, accounting for 0.4–0.8% of all prostate cancers [1]. It usually occurs in the prostatic urethra around the verumontanum, and its prognosis is generally thought to be worse than for acinar adenocarcinoma [2]. Although there are a few reports concerning systemic chemotherapy for prostatic ductal adenocarcinoma, the effect on recurrent prostatic ductal adenocarcinoma remains unknown. We report a case of a metastatic recurrent prostatic ductal adenocarcinoma that was successfully treated with docetaxel chemotherapy.

Case Report

In November 2006, a 68-year-old man presented with gross hematuria and visited the community hospital. Although cystourethroscopy and diagnostic imaging were performed, no abnormal findings were detected in the urinary tract. A transrectal prostate biopsy was also performed because of a slight elevation of prostate-specific antigen (PSA; 4.26 ng/ml), and the specimens revealed no malignancy. One year later, he presented with recurrent gross hematuria, and a repeat cystourethroscopy revealed a papillary tumor adjacent to the verumontanum. The histopathologic diagnosis of the biopsy specimen revealed grade 2 urothelial carcinoma. The patient was then referred to our hospital.

Digital examination disclosed no hard nodule on the prostate. PSA was 3.246 ng/ml, and an urothelial tumor was indicated by urine cytology. A tumor arising from the transitional zone to the periurethral region adjacent to the verumontanum was seen with contrast-enhanced magnetic resonance imaging (MRI) (fig. 1). Transrectal ultrasonography showed no abnormality. A computed tomography (CT) and a bone scan showed no evidence of metastases. The repeat biopsy of the periurethral lesion in the prostatic urethra and urine cytology also suspected urothelial carcinoma, and the clinical diagnosis of primary urothelial carcinoma of the prostate was made. Therefore, a cystoprostatectomy was performed with an ileal conduit diversion in February 2008. Histopathologic examination of the specimen revealed a ductal adenocarcinoma spreading into the lumen of the prostatic ducts with comedonecrosis and cribriform mixed with a focal acinar adenocarcinoma, and a Gleason score of 5 + 4 = 9 (pT3bN0M0) (fig. 2).

Seventeen months after surgery, he developed perineal pain. CT and MRI confirmed local recurrence in the prostate bed with metastases to the ischium and pubis, and his PSA was now 10.806 ng/ml. In July 2009, he was started on combined androgen blockade with bicalutamide and goserelin, and radiation treatments of 66 Gy were delivered to the pelvis and prostate bed. This resulted in a decrease in size of the local recurrence and bone metastases.

Combined androgen blockade combined with radiation was effective in the first 6 months, and PSA decreased to 0.01 ng/ml. However, the PSA value gradually increased to 0.931 ng/ml despite alternative antiandrogen therapy. It appeared, therefore, that the disease had become resistant to androgen deprivation therapy, and intravenous docetaxel 70 mg/m² every 3 weeks in combination with oral prednisolone 5 mg twice daily began to be administered in July 2011.

Following three cycles of docetaxel, the recurrent and metastatic lesions became undetectable on radiological images and his PSA decreased to <0.005 ng/ml. Ten cycles of docetaxel chemotherapy were completed without any adverse event, and luteinizing hormone-releasing hormone analog administration was interrupted in December 2013. He maintains a complete response 3 years and 6 months after completion of the chemotherapy (fig. 3).
Discussion

Prostatic ductal adenocarcinoma was first reported as an endometrial carcinoma of the prostatic utricle in 1967 [3]. Unlike acinar adenocarcinoma, ductal adenocarcinoma appears macroscopically as exophytic papillary or polypoid masses arising into the urethra around the verumontanum. Histopathologically, it is characterized by tall columnar cells, which form a single or pseudostratified layer reminiscent of endometrial carcinoma [2]. Due to the location of the tumor, predominant symptoms are gross hematuria and dysuria, and digital examination often reveals negative findings. PSA is not necessarily elevated [2]. In ductal adenocarcinoma patients, serum PSA elevation may be lower than in typical acinar adenocarcinoma patients because the lesions occur around the prostatic duct that provide a route of egress for PSA [2, 4]. Changes of the PSA value, however, may correlate with the clinical course in some cases, even if small changes in PSA are observed. Therefore, even if our case did not satisfy the diagnostic criteria of castration-resistant prostate cancer (CRPC), he was treated in the same way as if having CRPC.

Although the standard treatment of prostatic ductal adenocarcinoma is similar to that of acinar adenocarcinoma, radical prostatectomy for a localized prostatic ductal adenocarcinoma does not necessarily achieve a complete resection [1]. Prostatic ductal adenocarcinoma is often a more advanced pathological stage when compared with a clinical stage. Orihuela and Green [1] suggested that radiation and hormone therapy as the treatment for localized prostatic ductal adenocarcinoma is more effective than prostatectomy. Iğdem et al. [5] showed that 3-year biochemical recurrence-free survival was found in 79% of the radiation group and in 65% of the prostatectomy group. Hormone therapy reputedly has as good a response in metastatic ductal carcinoma as in acinar adenocarcinoma, but an appropriate therapy for recurrent ductal adenocarcinoma is undetermined [1]. There are only two case reports available for metastatic ductal adenocarcinomas treated with docetaxel [6, 7]. In these reports, the patients achieved partial response as early results, but both died of cancer. To the best of our knowledge, this is the first reported case that achieved complete response with docetaxel for metastatic prostatic ductal adenocarcinoma. In our case, pathological information on the recurrent lesion was inadequate because of a lack of biopsy of the recurrent tumor. Although we cannot completely exclude the possibility that the recurrent lesion may contain an acinar adenocarcinoma component, ductal adenocarcinoma was likely to be dominant because acinar adenocarcinoma of the primary lesion was a quite tiny part of the specimen.

Several papers on predictive clinical factors of the therapeutic effects of docetaxel for CRPC have been published. Armstrong et al. [8] showed that the following 4 independent pretreatment factors predict overall survival: visceral metastases, pain, anemia (hemoglobin <13.0 g/dl) and development of new bone lesions. Our case had none of the risk factors mentioned above. It has recently been reported that polymorphisms of the cytochrome P450 1B1 (CYP1B1) C>G (Leu432Val) gene show variability in the response of prostatic acinar adenocarcinoma to docetaxel chemotherapy as a genetic characteristic [9, 10]. Another study in non-small cell lung cancer also showed that CYP1B1 4326 C>G polymorphism could be a predictive marker of the activity and efficacy of docetaxel [11]. The CYP1B1 4326CC or 4326GC genotype causes an impaired production of metabolites, which attenuate the efficacy of docetaxel by interfering with the binding of docetaxel with tubulin, compared with 4326GG. Therefore, it is speculated that positive clinical responses are experienced at a higher rate in patients with 4326CC or 4326GC single nucleotide polymorphisms because docetaxel is apt to bind to tubulin more favorably. Thus, the CYP1B1 4326GG patients had shorter overall survival rates as well as poorer prognoses than patients carrying the CYP1B1.
4326GG or 4326CC genotypes [10]. We performed a genetic examination of our patient after obtaining informed consent, and his genotype was revealed to be 4326CC, which has been shown to give a favorable response with docetaxel chemotherapy. Conceivably, the CYP1B1 single nucleotide polymorphism may be one of the predictive biomarkers for the patient with ductal adenocarcinoma treated with docetaxel.

There are only a few reports of the effectiveness of docetaxel in metastatic prostatic ductal adenocarcinoma because of its rarity. Further studies are needed to elucidate appropriate treatments as well as disease behaviors for this entity.

**Statement of Ethics**

The authors declare that all examinations and interventions have been examined and approved by the appropriate ethics committee of Shiga University of Medical Science and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

**Disclosure Statement**

There are no potential conflicts of interest.

**References**

Fig. 1. Contrast-enhanced MRI. The lesion was shown as a low-intensity area with circular enhancement near the verumontanum (arrow).

Fig. 2. Histopathology of a ductal adenocarcinoma: comedonecrosis and cribriform pattern seen in the specimen. HE stain. ×400.
Fig. 3. Longitudinal PSA values during treatment. LH-RH = Luteinizing hormone-releasing hormone.