A case of rapidly progressing prostate cancer diagnosed 20 months after holmium laser enucleation of the prostate

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Received: 10 January 2018 / Accepted: 28 March 2018 / Published online: 6 April 2018
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Abstract

A 65-year-old man presented for treatment of benign prostatic hyperplasia. His prostate volume was 50 cm³ and serum prostate-specific antigen was 1.93 ng/mL. Digital rectal examination showed no malignant nodules on the surface of the prostate. Holmium laser enucleation of the prostate was performed. The enucleated tissue was 21 g and pathological examination revealed no malignancy. Serum prostate-specific antigen had increased continuously to 6.38 ng/mL and prostate biopsy was performed 20 months after holmium laser enucleation of the prostate. Pathological examination confirmed an adenocarcinoma of the prostate with a Gleason score of 9 (4 + 5). Computed tomography and bone scintigraphy demonstrated multiple bone metastases and we made a diagnosis of prostate cancer, cT2aN0M1b. After 3 months on androgen deprivation therapy, he developed castration-resistant prostate cancer and died within 13 months after diagnosis of prostate cancer, despite receiving sequential therapy including enzalutamide, docetaxel and abiraterone. In our case, prostate-specific antigen was not measured until 13 months after holmium laser enucleation of the prostate, after which prostate-specific antigen rose from 1.93 to 4.09 ng/mL. This report provides an important implication of continuous monitoring of prostate-specific antigen after holmium laser enucleation of the prostate to detect prostate cancer early.

Keywords Prostate cancer · Holmium laser enucleation of the prostate

Introduction

Several studies have reported the rate of incidental detection of prostate cancer (PCa) from the enucleated tissue at the time of holmium laser enucleation of the prostate (HoLEP) as being 8.1–13% [1–3]. In the case of transurethral resection of the prostate (TUR-P), many cases of dissemination of cancer cells have been reported [4, 5]. However, only one case of aggressive PCa after HoLEP has been reported [6]. In that report, preoperative serum prostate-specific antigen (PSA) level was 3.78 ng/mL and the patient was incidentally diagnosed with PCa from the enucleated tissue at the time of HoLEP. Approximately 2 weeks after HoLEP, serum alkaline phosphatase rapidly increased from 230 to 3654 IU/L and bone scintigraphy showed multiple bone metastases. Dissemination of cancer cells is thought to occur during the

surgery of HoLEP. We herein report another case of rapidly progressing PCa after HoLEP. In our case, no malignant cells in the enucleated tissue and PCa were discovered 20 months after HoLEP because of an increase in serum PSA from 1.93 to 6.38 ng/mL. At the time of diagnosis, bone scintigraphy showed multiple bone metastases and the patient died within 13 months after diagnosis of PCa. To our knowledge, this is the first report of a highly aggressive newly diagnosed PCa during the follow-up period of HoLEP.

Case report

A 65-year-old Japanese man with history of benign prostatic hyperplasia (BPH) was referred to our hospital for treatment of BPH in April 2014. His International Prostate Symptom score/quality-of-life score was 19/6. Digital rectal examination showed no malignant nodules on the surface of the prostate. Uroflowmetry showed that the maximum flow rate was 16.5 mL/s, with 280 ml of residual urine. The prostate volume was 50 cm³ and serum PSA was 1.93 ng/mL. HoLEP was performed in June 2014.

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The enucleated tissue weighed 21 g and pathological examination revealed no malignant cells. Serum PSA had increased continuously after surgery to 4.09 ng/mL in July 2015 and 6.38 ng/mL in February 2016. T2-weighted magnetic resonance imaging (MRI) showed no abnormal finding (Fig. 1a); however, diffusion-weighted MRI showed a high signal intensity in the right lobe of the prostate (Fig. 1b). Prostate biopsy confirmed an adenocarcinoma of the prostate with Gleason score 9 (4 + 5) in 3 of 10 cores (Fig. 1c). Cancer cells were positive for PSA according to immunohistochemical staining (Fig. 1d). Surprisingly, computed tomography (CT) and bone scintigraphy showed multiple bone metastases defined as extent of disease (EOD) 3 and no evidence of lymph node and visceral metastasis (Fig. 1e). We diagnosed the patient with PCa, cT2aN0M1b. Serum PSA increased rapidly to 23.01 ng/mL in March 2016 and degarelix and bicalutamide treatment was initiated, which was later substituted with enzalutamide for the treatment of castration-resistant PCa 3 months after initial treatment at the serum PSA level 5.1 ng/mL. He then underwent 3×10 Gy (total dose, 30 Gy) palliative radiation therapy for bone metastasis in the third lumbar vertebra in October 2016 at the serum PSA level 5.5 ng/mL. CT demonstrated multiple lung and liver metastases; however, he received two cycles of docetaxel after radiation therapy, which was substituted with abiraterone in February 2017 at the serum PSA level 120.5 ng/mL. He died in March 2017 within 13 months after diagnosis of PCa (Fig. 2).

Fig. 2 The clinical course of the patient. The solid line showed the change in serum PSA level. *Bic* Bicalutamide, *ENZ* Enzalutamide, *DOC* Docetaxel, *Abi* Abiraterone

Discussion

In our case, no malignant cells in the enucleated tissue were evident and PCa was discovered 20 months after HoLEP as a result of an increase in serum PSA from 1.93 to 6.38 ng/mL. Therefore, there is no clear association between HoLEP and multiple bone metastases. A recent study demonstrated that in high grade PCa (Gleason score 8–10), low PSA PCa (PSA ≤ 2.5 ng/mL) has a very high risk for PCa death and may not respond well to androgen deprivation therapy [7]. In our case, it is possible that low PSA, high grade PCa originally existed before

Fig. 1 **a** T2-weighted magnetic resonance imaging showed no abnormal finding. **b** Diffusion-weighted magnetic resonance imaging showed high signal intensity in the right lobe of prostate (white arrow). **c** Pathological examination showed adenocarcinoma with

Gleason score 4 + 5 (hematoxylin-eosin, $\times 200$). **d** Immunohistochemical staining showed adenocarcinoma positive for PSA. **e** Bone scintigraphy showed multiple bone metastases defined as extent of disease (EOD) grade 3

HoLEP, and that cancer cells had disseminated as a result of the HoLEP procedure. There has only been one report of PCa diagnosed during the follow-up period of HoLEP [8]. In that study, nine patients (2.7%) of 335 were newly diagnosed with PCa 3 or 4 years after HoLEP. The author reported that in the PCa patients, the PSA reduction rate was significantly lower (47.49 vs 75.39%, $p < 0.001$) and PSA velocity (PSAV) was significantly higher at 1-year (1.28 vs 0.13 ng/ml, $p < 0.022$) and 3-year follow-up (2.40 vs 0.09 ng/ml, $p < 0.001$) compared with the benign disease group. The author concluded that if the reduction of PSA was less than 50%, the patient should be followed up more carefully with regular PSA measurements every 3–6 months for the first 2–3 years to allow earlier detection of PCa [8]. In our case, PSA was not measured until 13 months after HoLEP and PSA rose from 1.93 to 4.09 ng/mL. Thus, we were unable to evaluate the nadir of the PSA level, nor the precise reduction rate of PSA and PSAV. Up to 20 months after HoLEP, PCa with multiple bone metastases was discovered; however it is unclear when the PCa cells had metastasized to bone. If we had monitored PSA more closely and had prostate biopsy been performed earlier, PCa could have possibly been diagnosed and treated earlier. To our knowledge, this is the first report of a highly aggressive newly diagnosed PCa during the follow-up period of HoLEP. We conclude that it is important to continuously monitor PSA after HoLEP to detect PCa earlier.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent The patient provided a written informed consent for his case report to be published anonymously.

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