—Case Reports—

Safety of Abiraterone Acetate Administration in Elderly Patients Receiving Peritoneal Dialysis with Castration-Resistant Prostate Cancer: Two Case Reports

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We report two elderly patients receiving peritoneal dialysis with castration-resistant prostate cancer (CRPC). Herein, we show that the patients were safely treated using abiraterone acetate (750 mg/day orally once daily) and prednisolone (5 mg/day orally once daily). Although the prostate-specific antigen (PSA) level increased in both cases, there was no manifestation of disease progression (clinical and radiographic) for 22 months in case 1 and 8 months in case 2. In case 2, the only adverse event was hypokalemia, which was treated using potassium preparations. (J Nippon Med Sch 2019; 86: 135–138)

Key words: castration-resistant prostate cancer, abiraterone acetate, peritoneal dialysis

Introduction

The number of patients with prostate cancer who require dialysis is increasing in Japan owing to a rapidly aging society. In our hospital, peritoneal dialysis has been introduced for use in elderly patients.

We report on two elderly patients with castration-resistant prostate cancer (CRPC) receiving peritoneal dialysis.

Case Reports

Case 1: We present an 86-year-old man with end stage renal disease on peritoneal dialysis for 1 year and 8 months. He had a history of type 2 diabetes mellitus and hypertension. In August 2010, the patient was diagnosed with prostate cancer, and combined androgen blockade (CAB) therapy was initiated at another hospital. The initial prostate-specific antigen (PSA) level was 80.6 ng/mL and the clinical stage was TxN0M0. In April 2013, the patient was admitted to our hospital because of left femoral head fracture due to a fall. The laboratory findings were as follows: alkaline phosphatase, 482 IU/L; PSA, 2.52 ng/mL; potassium, 3.8 mEq/L; blood urea nitrogen (BUN), 25.5 mg/dL; creatinine (Cre), 3.36 mg/dL; and hemoglobin (Hb), 10.1 g/dL. The patient had been undergoing peritoneal dialysis. Computed tomography (CT) scans of the chest and abdomen and bone scintigraphy showed no evidence of metastatic disease. At first, we continued CAB therapy for 4 months. However, because the PSA level gradually increased we changed to alternative antiandrogen therapy (for 10 months) and estrogen agent therapy (for 2 months) sequentially (**Fig. 1**). In August 2014, at the age of 86 years, the patient was treated using abiraterone acetate (750 mg/day orally once daily) and prednisolone (5 mg/day orally once daily). Although the PSA level increased, his general condition remained stable and no new metastasis appeared on CT for 22 months. Furthermore, adverse events of more than grade 3 were not observed. However, the patient died because of peritonitis in June 2016.

Case 2: We present an 87-year-old man with end stage renal disease on peritoneal dialysis for 5 years. He had a history of type 2 diabetes mellitus, atrial fibrillation, and aortic regurgitation. In July 2010, the patient was diagnosed with prostate cancer, and CAB therapy was initiated at our hospital. The initial PSA level was 497 ng/mL, and the clinical stage was T2bN0M0. The laboratory findings were as follows: potassium, 4.6 mEq/L; BUN, 83.3 mg/dL; Cre, 2.64 mg/dL; and Hb, 9.3 g/dL. The pa-

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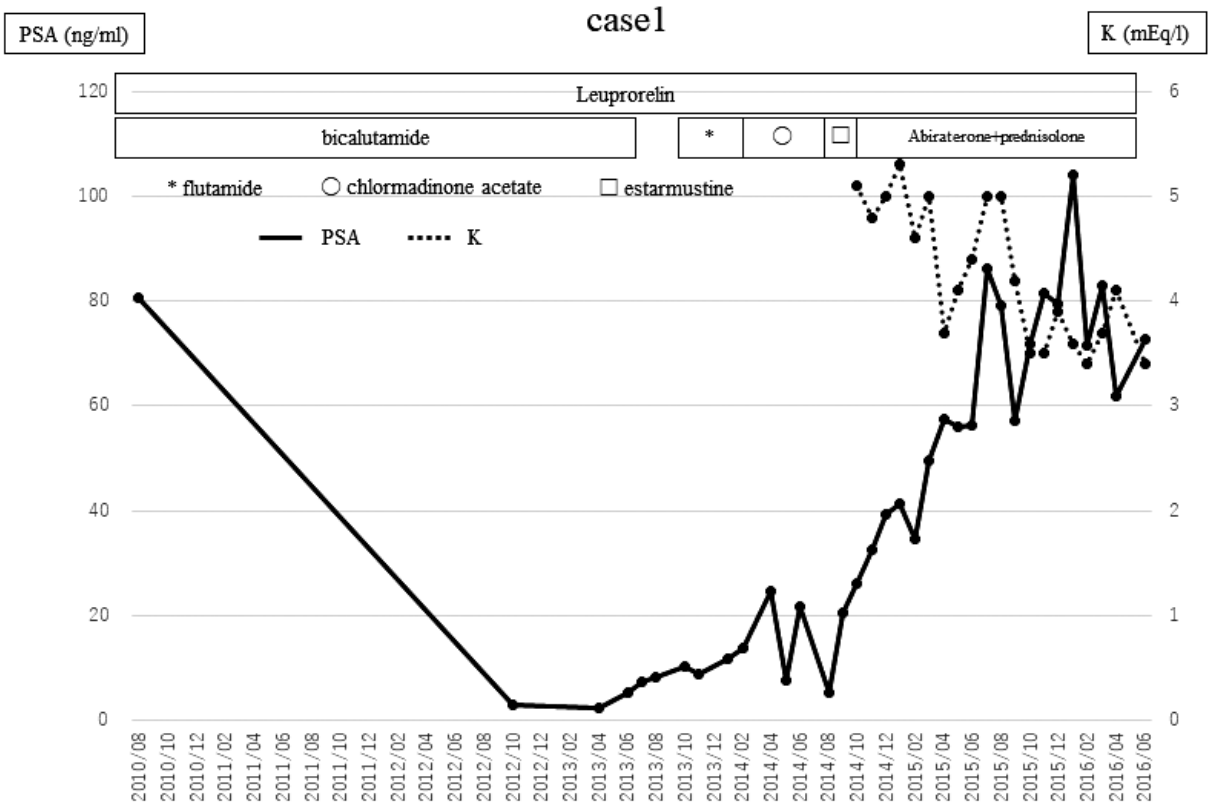

Fig. 1 Clinical course and changes in prostate-specific antigen and serum potassium levels in "Case 1"

tient had been undergoing peritoneal dialysis. CT scans of the chest and abdomen and bone scintigraphy showed no evidence of metastatic disease. At first, we continued CAB therapy for 11 months. However, because the PSA level gradually increased we changed to alternative antiandrogen therapy (for 7 months), estrogen agent therapy (for 15 months), and chemotherapy using Docetaxel (for 20 months) sequentially (**Fig. 2**). Furthermore, CT revealed a new lymph node metastasis in the pelvis. In June 2015, at the age of 87 years, the patient was treated using abiraterone acetate (750 mg/day orally once daily) and prednisolone (5 mg/day orally once daily). Although the PSA level increased, his general condition remained stable and there was no progression of lymph node metastasis and no new metastasis appeared on CT for 8 months. The only adverse event of more than grade 3 was hypokalemia, which was treated using potassium preparations. However, the patient gradually became bedridden and died because of decubitus in February 2016.

Discussion

In the urological field, abiraterone acetate and enzalutamide are novel therapeutic agents used to treat patients with CRPC[1,2]. To date, enzalutamide administration has been reported in patients receiving hemodialysis[3]. Here, we report for the first time the treatment of two elderly patients receiving peritoneal dialysis with CRPC using abiraterone acetate. Abiraterone acetate, a CYP17 inhibitor, is now a standard treatment for metastatic CRPC; it is mainly metabolized in the liver. Therefore, it is unnecessary to adjust the dose of abiraterone acetate in patients receiving peritoneal dialysis; however, in our cases, because physiological function may decrease in the elderly, the dose was reduced from 1,000 mg/day to 750 mg/day.

In both our patients, the level of PSA was not decreased after oral abiraterone acetate administration. However, we did not detect any new metastatic lesion or decreasing performance status for 22 months in case1 and for 8 months in case 2. Compared with previous reports, we found that abiraterone acetate could be useful even for elderly patients receiving peritoneal dialysis with CRPC[4].

Abiraterone acetate administration increases the levels of mineralocorticoids and may cause hypokalemia, which was observed in case 2. Since both patients were undergoing peritoneal dialysis, we thought that they were less likely to develop hypokalemia, and we reduced the dose of prednisolone from 10 mg to 5 mg. Furthermore, we

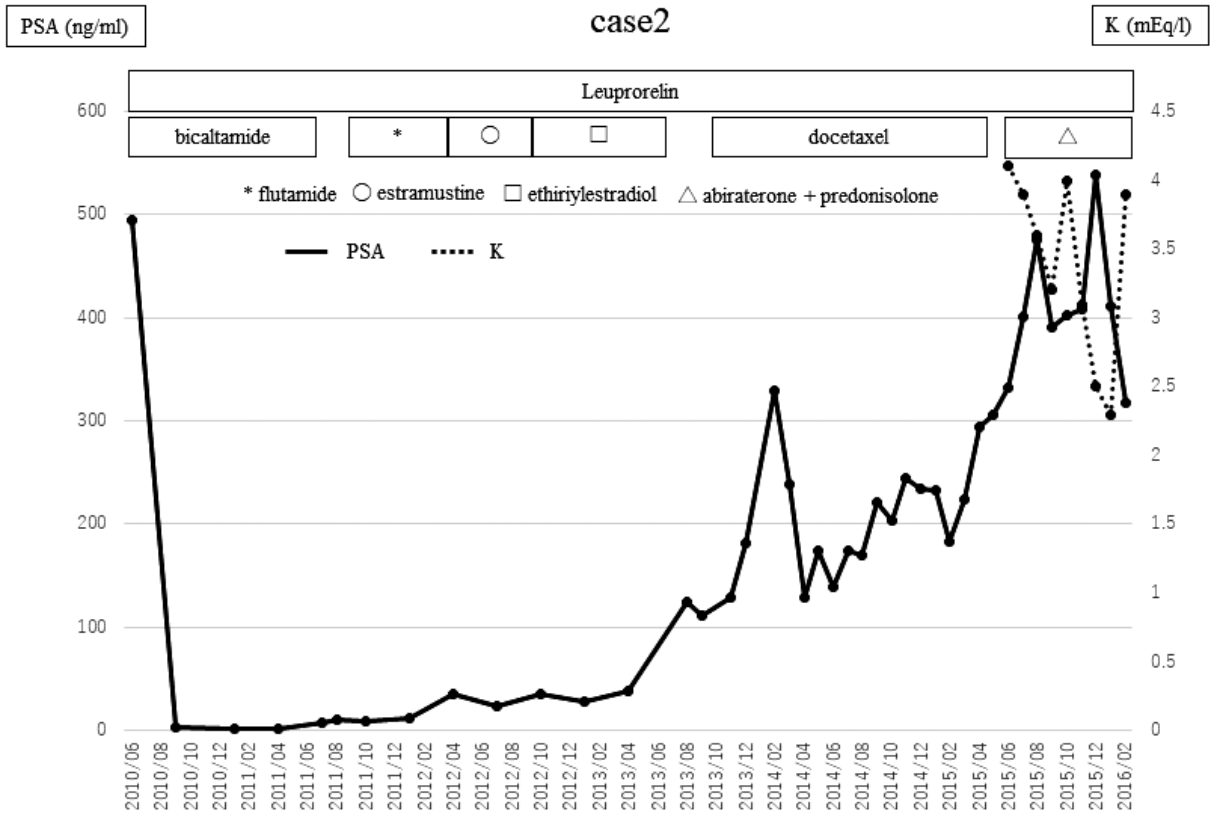

Fig. 2 Clinical course and changes in prostate-specific antigen and serum potassium levels in "Case 2"

thought that it was reduced the risk of infection. Grade 4 hypokalemia developed in case 2. The patient had no symptoms, such as weakness, vomiting, and arrhythmia, and the hypokalemia improved only after oral potassium administration. We believed that hypokalemia could not occur in patients receiving hemodialysis. However, it is possible that the residual renal function in case 2 was caused by the hypokalemia, despite peritoneal dialysis.

Nine cases (about 9%) of hypokalemia were reported in a domestic Phase II study of abiraterone acetate with 10 mg prednisolone[5,6], seven cases of which occurred within 16 weeks. In our case 2, hypokalemia occurred after 8 weeks from the start of abiraterone acetate administration; thus, this case occurred in same period as well as in the normal renal function group. In this case, urine volume was kept over 1,000 mL/day. Therefore, the patients receiving peritoneal dialysis with a volume of urine over 1,000 mL/day should have potassium monitoring during abiraterone acetate treatment. Also, we think that the administration of 10 mg prednisolone makes higher risk of infection, but hypokalemia may be avoided.

In conclusion, we described two cases of patients receiving peritoneal dialysis with CRPC who were over 85 years old and treated using abiraterone acetate. The treatment results indicate that abiraterone acetate can be considered a safe treatment option for CRPC in elderly patients receiving peritoneal dialysis.

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References

1. De Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L, Chi KN, Jones RJ, Goodman OB Jr, Saad F, Staffurth JN, Mainwaring P, Harland S, Flaig TW, Hutson TE, Cheng T, Patterson H, Hainsworth JD, Ryan CJ, Sternberg CN, Ellard SL, Fléchon A, Saleh M, Scholz M, Efstathiou E, Zivi A, Bianchini D, Loriot Y, Chieffo N, Kheoh T, Haqq CM, Scher HI: Abiraterone and increased survival in metastatic prostate cancer. N Eng J Med 2011; 364: 1995–2005.
2. Ryan CJ, Amith MR, de Bono JS, Molina A, Logothetis CJ, de Souza P, Fizazi K, Mainwaring P, Piulats JM, Ng S, Carles J, Mulders PF, Basch E, Small EJ, Saad F, Schrijvers D, Van Poppel H, Mukherjee SD, Suttmann H, Gerritsen WR, Flaig TW, George DJ, Yu EY, Efstathiou E, Pantuck A, Winquist E, Higano CS, Taplin ME, Park Y, Kheoh T, Griffin T, Scher HI, Rathkopf DE: Abiraterone in metastatic prostate cancer without previous chemotherapy. N

Eng J Med 2013; 368: 138–148.
3. Tsang ES, de Haan M, Eigl BJ: A case report of enzalutamide administration in a dialysis-dependent patient with castration-resistant prostate cancer. J Oncol Pharm Pract 2018; 24: 143–145.
4. Mulders PF, Molina A, Marberger M, Saad F, Higano CS, Chi KN, Li J, Kheoh T, Haqq CM, Fizazi K: Efficacy and safety of abiraterone acetate in an elderly patient subgroup (aged 75 and older) with metastatic castration-resistant prostate cancer after docetaxel based chemotherapy. Eur Urol 2014; 65: 875–883.
5. Matsubara N, Uemura H, Satoh T, Suzuki H, Nishiyama T, Uemura H, Hashine K, Imanaka K, Ozono S, Akaza H: A phase 2 trial of abiraterone acetate in Japanese men with metastatic castration-resistant prostate cancer and without prior chemotherapy (jpn-201 study). Jpn Clin Oncol 2014; 44: 1216–1226.
6. Satoh T, Uemura H, Tanabe K, Nishiyama T, Terai A, Yokomizo A, Nakatani T, Imanaka K, Ozono S, Akaza H: A phase 2 study of abiraterone acetate in Japanese men with metastatic castration-resistant prostate cancer who had received docetaxel-based chemotherapy. Jpn Clin Oncol 2014; 44: 1206–1215.

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