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Possibility of recovery of estrogen sensitivity following high-dose glucocorticoid therapy in a patient with hormone-refractory prostate cancer

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Abstract A 74-year-old man underwent irradiation therapy (RT) to the prostate bed because of prostate-specific antigen (PSA) failure after retropubic radical prostatectomy (RRP). Six months after the RT, a solitary bone metastasis developed in the third thoracic vertebra, and hormonal therapy (HT) was initiated. Three years later, following the loss of response to all hormonal agents, including oral estrogen and glucocorticoid therapy, paraplegia developed, due to a spinal metastasis. RT and high-dose glucocorticoid therapy were given for the spinal metastasis. Diethylstilbestrol diphosphate (DES-DP) was given continuously during this treatment, except for a 1-month period when the patient had pneumonia. After the RT and high-dose glucocorticoid therapy, his serum PSA decreased, from 308 to 36.99 ng/ml. In accordance with the 1-month discontinuation, and then resumption of DES-DP, the serum PSA levels went up and down. So we suspected that the tumor had recovered sensitivity to DES-DP with the high-dose glucocorticoid therapy. With a further decrease of serum PSA to 2.12 ng/ml, he has been alive for more than 3 years to date since the diagnosis of hormone-refractory prostate cancer (HRPCA). To our knowledge, there have been no reports showing such a marked recovery of hormone-sensitivity in HRPCA. No optimal therapy has yet been established for HRPCA; therefore, high-dose glucocorticoid therapy in combination with DES-DP warrants further study.

Key words Diethylstilbestrol diphosphate · High-dose glucocorticoid therapy · Hormone-refractory prostate cancer

Introduction

Although almost all advanced prostate cancers (PCAs) initially respond well to hormonal therapy (HT), most of them finally lose their hormone sensitivity and progress. Once the hormone sensitivity is lost, there is no effective way to make the PCA cells regain it. Without an effective therapy for hormone-refractory (HR) PCA, patients will die within approximately 12–18 months after the diagnosis of HRPCA.

Recently, a survival benefit of treatment with docetaxel-containing chemotherapy for men with advanced PCA was demonstrated in two large phase III clinical trials. However, the poor performance status of such patients often makes it impossible for them to receive cytotoxic chemotherapy. Accordingly, non-invasive therapy is needed for HRPCA.

Here, we report a patient in whom the response to treatment with diethylstilbestrol diphosphate (DES-DP) appeared to have been regained, and was retained for more than 3 years after high-dose glucocorticoid therapy.

Case report

A 74-year-old man underwent retropubic radical prostatectomy (RRP) in December 1997, after 4 months of neoadjuvant treatment with combined androgen blockade (CAB; luteinizing hormone-releasing hormone [LH-RH] analog + flutamide 375 mg/day) for clinical stage B1, well-to-moderately differentiated (Gleason score, 4 + 3), prostate adenocarcinoma. The pathological results were pT2N0, with a negative surgical margin.

Four months later, he underwent irradiation therapy (RT; 60 Gy) to the prostate bed because of PSA failure. Six months after the RT, however, a solitary bone metastasis was confirmed in the third thoracic vertebra (extent of disease [EOD], level 1) and CAB was again administered. Although the CAB stabilized his serum PSA level for the
following 3 years, the tumor proved to be HRPCA in May 2002, when his serum PSA level was 7.9 ng/ml. Despite the administration of estramustine sodium phosphate (560 mg/day) and DES-DP (300 mg/day per os), his serum PSA level increased, with serum testosterone (TS) being at castration level.

The bone metastasis gradually extended, and showed EOD level 3 on a bone scan in September 2003. One month later, he had failure of bilateral leg perception and difficulty in walking. Magnetic resonance imaging (MRI) revealed spinal compression by a metastatic tumor at the second to fourth thoracic level; therefore, oral betamethasone, 2 mg/day, was initiated immediately. However, 1 week later, paraplegia developed. RT (32 Gy) to the thoracic lesions and high-dose glucocorticoid therapy was started on November 7, when the serum PSA was 308 ng/ml. The dose schedule is shown in Fig. 1. DES-DP was continued during this treatment. After this treatment, the serum PSA decreased to 36.99 ng/ml, and the paralysis of his legs was slightly improved.

Although serum PSA increased temporarily during a 1-month cessation of DES-DP (due to his suffering from pneumonia) the serum PSA gradually decreased to 36.99 ng/ml, and the paralysis of his legs was slightly improved.