Eight-year survival and continuation of therapy in a patient suffering from prostate cancer with metastases and pathological fractures of vertebrae

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KEY WORDS

carcinoma of prostate • metastases • pathological fractures

ABSTRACT

Prostate cancer (PCa) is a major health problem and one of the main causes of cancer mortality in men [1]. In patients with PCa, bone metastases manifest in 100% of patients when the PSA level exceeds 100 ng/ml causing pains and posing a risk for pathological fractures [2]. We report a case of a 70-year-old male with PCa and pathological fractures of the vertebrae, in whom we observed long-term regression and an 8-year-survival while undergoing continuous therapy. As far as we know, this is the first reported case in literature with such an unexpected outcome.

INTRODUCTION

In patients suffering from carcinoma of prostate (PCa), bone metastases manifest in 100% of patients when the PSA level exceeds 100 ng/ml causing pains and posing a risk for pathological fractures [2]. Fractures of the vertebral body are the most threatening, causing spinal cord compression leading to an unfavorable survival time – median up to 3 years [3]. PCa progression with metastases occurs after 18–36 months when inhibited with complete androgen blockade (CAB) [4]. Intermittent androgen blockade (IAB), on the other hand, is an alternative to continuous hormone therapy (HT) with the potential for reduced morbidity and a delay in progression to hormone refractory PCa (HRPC) [5]. Concurrent therapy with zoledronic acid (ZA), an inhibitor of osteoclast-mediated bone resorption, is the standard of care for the prevention of skeletal-related events (SREs) associated with bone metastases from PCa and may extend the survival period [6].

CASE REPORT

In autumn 2002, the patient A.K., aged 62 years, had severe bone pains in the chest that were treated symptomatically. In July 2003, examination revealed a PSA level of 150 ng/ml and TRUS showed that a lesion 8.3 x 11 x 8.5 mm in the peripheral part of the right lobe developing beyond the prostate. A biopsy performed on August 4th, 2003 showed adenocarcinoma (G1eason 6), which indicated treatment with flutamide. However, an intolerance to this treatment was observed (diarrhea and vomiting), which led to its discontinuation after one week. The patient was without treatment for some time until the patient was hospitalized in the Institute of Psycho-Neurology in March of 2004 due to flaccid paralysis of lower limbs. Magnetic resonance imaging (MRI) showed pathological foci of vertebral bodies L1, T11, T10, and T9 with fracture of the lamina limitans. In the vertebral body of T2, the posterior part indented into the spinal canal compressing the spinal cord with similar spinal cord compression by the vertebral arches. The patient refused to undergo surgical castration and he was not qualified to radiotherapy and surgical decompression of the spinal cord based on the decision of a consultant.

My treatment of this patient started on April 14th, 2004 – the patient presented with paresis of the lower limbs and sensation disorders from the feet to the epigastric zone; bilateral Babinski response; dysfunction of contractors; and level of PSA at 131 ng/ml.

After inclusion of mCAB (combined androgen blockade – Zoladex LA and Casodex 50 mg with finasteride), the administration of ZA (Zometa 4 mg i.v.) every 4 weeks, Cardura XL 4 mg, BioSe+Zn, leucopenes, Bio-Marine, vitE 400 mg, and a strict diet; the functions of the contractors returned gradually and after 3-months the patient regained his limb functions, while after 6-months he was able to sit, stand and, some time later, able to walk without help. Periodically, the PSA level even reached below 0.1 ng/ml. These results prompted the conversion to IAB (intermittent androgen blockade – when PSA levels approach zero androgen blockade is paused to allow androgenic cells to replicate) therapy with abandonment of finasteride, Zometa, and other drugs. Imaging controls with MRI were carried out every year; the last time on October 26, 2010. The results are presented by Dr. Renata Poniatowska, M.D., Ph.D. In March 2004, an MRI of the spinal fragments C-T and L-S showed a pathological fracture of the fragmented T2 core with the inclusion of infiltration of the vertebral arches and epidural indentation to the spinal canal with spinal cord compression, concurrently from the back (Fig. 1). The posterior part of the core indented to the spinal canal compressing the spinal cord. The foci of osteosclerotic metastases are of a lower signal in time T1 and heterogenic T2, localized in cores T1-4, T9-11 and L1 with fracture of the superior lamina limitans. Until 2009, in MRI scans, we could see fractures of the spinal bodies without features of compression on the cord. The size of the metastatic changes in the bodies of thoracic vertebrae did not show new foci (no progression), which previously revealed a heterogenic signal in time T2. However, the foci were substantially reduced, weighing in favor of sclerotization of the changes. Subsequent examinations, including the latest, did not show new foci nor progression, but quite the opposite, a profound regression of changes. The spinal cord is without focal changes and, at present, modifications of the posterior part of the vertebral body of T2 can be observed (Fig. 2).

Since 2007, the patient has been moving without assistance and driving a car. His pains have regressed and he is in a good general physical condition. Until the autumn of 2010, the PSA level was between 1.4 and 2.4 ng/ml while the patient has been medicated.
on an irregular basis. However, in November of 2010, the PSA level increased to 10.0 ng/ml and, after inclusion mCAB, Zometa 4 mg, and other medications, we observed a decrease in February of 2011 to 4.0 ng/ml, which is still lasting and the patient is in good clinical and general condition.

DISCUSSION

Prostate cancer is the most common genitourinary tract malignancy, with an estimated 192,280 new diagnoses and approximately 27,360 related deaths in the USA in 2009 alone [7]. For men with metastatic PCa, the median overall survival has been 2- to 3-years. Endocrine treatment delays clinical progression in all PCa stages [8]. Pathological fracture and spinal cord compression predict poor prognosis in men with PCa [9]. A series of meta-analyses found a statistically significant survival benefit in patients who received CAB [10] and finasteride the addition of bicalutamide provides additional intracellular androgen blockade [11]. Intermittent CAB is used to prolong response to HT and to improve patients' quality of life [4]. Furthermore, bisphosphonate treatment is incorporated in the treatment of PCa with bone metastases in order to reduce the risk of developing bone complications when combined with ZA's anti-proliferative and apoptotic effects [12]. ZA has also been shown to be efficacious in preventing bone loss in men undergoing androgen deprivation therapy [13].

In our case, no important adverse events presented during long-term therapy. We also believe that ZA has the potential to prevent additional skeletal complications. Our use of the combination treatment was well tolerated with complete reduction of bone pain and improved quality of life, altogether showing promising effects. Also, one can assume that doxazosin could have had a beneficial effect on our patient with PCa. Indeed, since the discovery of the fact that quinazolines exhibit an inhibitory effect on cell proliferation, a doxazosin impact study on the development of prostate cancer was initiated. The modified structure of the doxazosin molecule, DZ-50, inhibits apoptosis and stimulates neangiogenesis in the tumor. It has been shown in vitro that DZ-50 reduces cell adhesion to extracellular matrix, i.e., has an impact on the development of metastatic tumor cells by blocking their migration through the endothelium and, as a result, inhibits tumor growth and reduces occurrence of metastases [14]. Also studied, was doxazosin's effect on the expression of clusterin from the group of adhesion proteins and its effect on apoptosis in hormone-refractory prostate cancer. It was found that DNA fragmentation occurs in the nuclei of these cells including an increase in clusterin mRNA expression and the consequent protein as well as the increase in prostate cancer cells undergoing apoptosis [15]. There are also works of other authors demonstrating a proapoptotic impact of doxazosin on cancer cells.

CONCLUSION

The case history was presented due to the lack of a similar case description in the available literature as well as the extremely long survival period accredited to the applied treatment, which produced an unexpected successful outcome.

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