Autopsy Case Reports

Article / Clinical Case Report

Metastatic castration-resistant prostate cancer and the challenge of a patient with chronic kidney disease in hemodialysis

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ABSTRACT

At a time when the population shows increasing longevity, entities such as cancer and chronic kidney disease (CKD) are more frequently connected. In the United States, approximately 6% of the patients on hemodialysis have cancer. The challenge to manage oncologic patients with CKD in a hemodialytic program represents a great shortage of available information on the choice of the best drug, timing, dosage adjustments, dialysis method, and treatment safety. We present the case of a patient with prostate cancer and terminal CKD in hemodialysis, and the treatment sequence after the development of resistance to hormonal blockade therapy, which included docetaxel, enzalutamide, and radium-223.

Keywords
Prostate cancer; Dialysis; Docetaxel; Enzalutamide; Radium-223.

CASE REPORT

A 57-year-old Caucasian man was referred to the Oncologic Center due to the diagnosis of prostate cancer. Besides being a smoker, he denied any other known disease, cardiovascular risk factors, use of any medication, and had no family history of oncologic disorders. Eight years ago, he was diagnosed with obstructive acute renal failure due to an enlarged and heterogeneous prostate detected by ultrasound and the total prostate-specific antigen (tPSA) of 250 ng/mL (reference value: 4 ng/mL). He was treated with percutaneous nephrostomy and was submitted to a transrectal core prostate biopsy afterward. The anatomic pathologic report showed a prostatic acinar adenocarcinoma Gleason 8 (4+4). The computed tomography (CT) scan and bone scan showed metastatic lesions (mainly pelvic and in the dorsal and lumbosacral spine). Therefore, he was submitted to bilateral subalbuginea orchiectomy, and a month after the surgery his tPSA dropped to 26.34 ng/mL. Over the next 3 months, he presented a marked renal function deterioration and started regular hemodialytic treatment. The case was discussed in a multidisciplinary meeting, and it was decided to keep surveillance since the patient's neoplasia was steady.

Five years after the initial symptoms, the castration-resistant status ensued. The disease presented clinical progression and the patient complained of severe bone pain, his tPSA rose to 768 ng/mL, and a bone scan showed new lesions—parietal bone, right scapula, D4-5, 6th to 7th left costal ribs and right iliac (Figure 1).

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Eastern Cooperative Oncology Group (ECOG) performance status (PS) was 1. In face of the disease progression, antalgic radiotherapy to the dorso-lumbar spine (D3-5 and D11-L4) with total doses of 30 Gy, and chemotherapy with docetaxel 75 mg/m^2 intravenously (21-21 days), prednisolone 10 mg/day, and bisphosphonate therapy with zoledronic acid 3 mg (with the dose adjusted to the renal failure) (21-21 days) were started. The latter was withdrawn after 6 months because of symptomatic hypocalcemia, and peripheral grade-1 sensory neuropathy was observed and considered to be an adverse event of docetaxel. After completing 10 cycles of chemotherapy, the disease seemed steady, and the patient's tPSA was 231 ng/mL.

One year after he started the first chemotherapy, the patient presented a new disease progression, with worsening bone pain; the tPSA persistently increased (318 ng/mL) and the bone scan showed new lesions (8th to 11th costal ribs and right pubis) (Figure 2).

A second-line treatment with enzalutamide 160 mg per day was started. No adverse events were observed during the whole treatment. One year later, the disease was stable with the tPSA 3,9 ng/mL and the bone scan results were unchanged. However, over the following 9 months, the patient presented new biochemical (tPSA of 217 ng/mL) and radiologic progression (new bone metastasis: 3rd, 6th, 7th, and 11th right costal ribs) (Figure 3).

At the multidisciplinary meeting a third-line treatment with radium-223 (injections from 4-4 weeks) was indicated. He completed six cycles of radium-223 in the following 8 months. No adverse events were reported. In the final evaluation, the patient was without pain and ECOG PS was 0. During the treatment, the tPSA determinations remained high, and at the end of the treatment it was 2364 ng/mL. However, the alkaline phosphatase (ALP) decreased and normalized at the end of the treatment (123 U/L) (Figure 4).

Paradoxically, the bone scan showed new lesions in frontal bone, 4th to 5th left costal ribs, 8th right and left costal ribs, sternum, and the right and left femurs, but less intensity of previous parietal, costal ribs and iliac lesions (Figure 5). The CT scan was unchanged.

The patient is currently undergoing regular follow-up examinations and will repeat the imaging revaluation scan in 3 months.

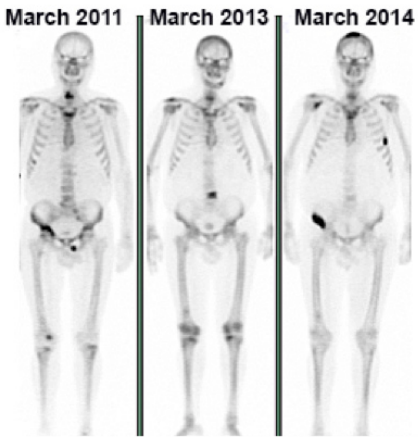

Figure 1. Bone scans in the last 4 years. Image C corresponds to the bone scan at the time of progression, with new lesions in parietal bone, right scapula, D4-5, 6th to 7th left costal ribs and right iliac.

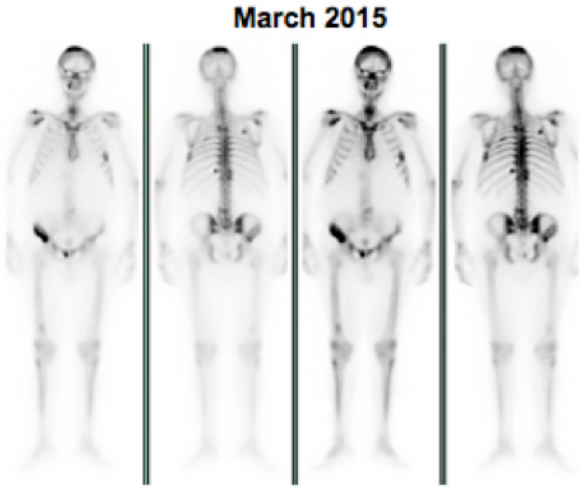

Figure 2. Bone scan in March 2015. New progression with new lesions at the 8th to 11th costal ribs and right pubis.

Figure 3. Bone scan in December 2016. New progression with new lesions in the 3rd, 6th, 7th, and 11th right costal ribs.

DISCUSSION

Due to the increasing number of patients in hemodialysis requiring oncologic treatment with chemotherapy, oncologists are now expected to face serious dilemmas. A multidisciplinary decision involving oncologists, urologists, and nephrologists is crucial to start a chemotherapeutic regimen in these types of patients. Experience with these patients is very scarce, as is the available published information. The scarcity of case reports and small case series led us to raise the importance of this theme.[1,2] The drug selection is the first critical step.

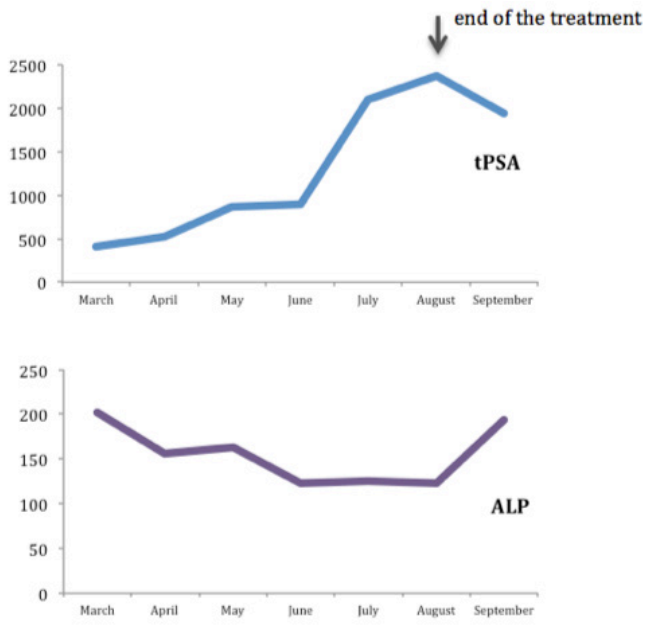

Figure 4. Behavior of the total prostate-specific antigen (tPSA [ng/mL]) and alkaline phosphatase (ALP [U/L]) determinations during and after the treatment with radium-223.

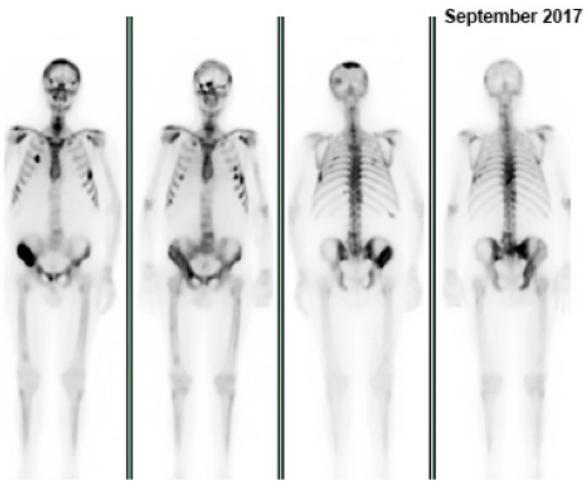

Figure 5. Evolution of bone scans through the years. The image on the right corresponds to the last evaluation, in September 2017, after the end of the treatment with radium-223.

The several therapeutic interactions and the need for treatment adjustments have to be considered. Regarding the docetaxel, although the main metabolic pathway is hepatic, and only a small part of the drug is excreted in the urine (less than 5-6%),[3,4] some authors recommend the use of a reduced dose of 65 mg/m^2 (level of evidence C).[4,5] However, we decided to use the full dose in our patient, according to the safety indicated by Ito et al.[6]

The time of the administration of the chemotherapy in the setting of a hemodialytic patient should also be taken into account to avoid drug clearance during the dialysis. In our case, the patient underwent chemotherapy after the dialysis sessions; however, since docetaxel is non-dialyzable,[3] the treatment may be administered regardless of the dialysis session. These adaptations should be carefully carried out to optimize the efficacy of the selected drug.

Concerning enzalutamide, although there is scarce information on the dose adjustments in hemodialysis patients,[7] caution is advised in patients with severe renal impairment. The drug is primarily eliminated by hepatic metabolism, and the renal excretion is insignificant.[8] Our patient received the full dose of 160 mg per day, without toxicity and with a normal and controlled tensional profile.

Regarding radium-223, it is considered a safe and well-tolerated option for castration-resistant prostate cancer (CRPC) patients with symptomatic bone metastases and no known visceral metastases. The drug is rapidly cleared from the blood and is essentially excreted into the intestine, with approximately 5% being excreted in the urine.[9] No dose adjustment is necessary for patients with renal function impairment.[9]

There are still some questions to be answered concerning the patient's evaluation during and after treatment with radium-223. In this setting, the precise value of the tPSA and ALP as biomarkers is still unclear, although there is a suggestion that ALP better represents the therapeutic response.[10] In a phase 3 radium-223 trial (ALSYMPCA), 87% of the

patients showed a decrease in ALP determination.[10] Similarly, the imaging evaluation may not accurately document the clinical response. Eventual changes in the bone scan and the CT scan have to be interpreted with caution, due to the flare phenomenon. The right timing for this evaluation is uncertain; however, according to the last Saint Gallen's consensus, the majority of the panel (41%) considered 3-4 months after the beginning of the treatment, although 27% favored the imaging study at the end, after completion of radium-223, and every 3-4 months thereafter.[11,12] In our case, we decided to do it after the end of the treatment. The results we have are certainly related to a flare situation since the patient had an optimal clinical response.

CONCLUSION

There are many problems that oncologists find in patients with chronic kidney disease, especially regarding the safety of treatments in hemodialysis patients. For patients with CRPC, the exact choice of drug, timing, and sequence of various therapies remains an inexact science, essentially depending on the clinical history and performance status of the patient. In patients progressing during or after docetaxel chemotherapy, other safe therapeutic options are available on a hemodialysis program. Cases like this are a challenge, given the lack of evidence in these types of patients. For these reasons, pharmacokinetic and pharmacodynamic studies in cancer patients undergoing renal replacement therapy, a population that is typically excluded from clinical trials, should be further investigated.

DECLARATION

This manuscript is in accordance with the institutional ethics committee, and the patient signed an informed consent.

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