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Case discussion: 66-year-old man with low-volume prostate cancer

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JASON M. HAFRON, MD

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+ CASE SUMMARY

A 66-year-old man is found to have a firm bilateral prostate nodule of 1.8 mm on his routine physical exam. The clinical work-up includes a prostate-specific antigen (PSA) level of 136.8 ng/dL. The patient has a family history of prostate cancer in his father and uncle. A transrectal ultrasound-guided prostate biopsy confirms advanced adenocarcinoma of the prostate, with a Gleason score of 8, 4 + 4 or grade group 4. A technetium bone scan was negative for bone involvement. However, an MRI was negative for pelvic lymph node involvement but positive for one 1.2-cm mediastinal paraoesophageal lymph node. His clinical stage was T2b N0M1A and his ECOG performance status was 1. Initial treatment starting in April 2022 included leuprolide, abiraterone (Zytiga), and prednisone. He was scheduled for a physical exam, PSA assessment, and imaging every 3 months.

Q. What risk group would this patient be in, and what would his prognosis be?

HAFRON: Risk group identification is a very important clinical factor that urologists need to determine when evaluating [patients with] metastatic castration-sensitive prostate cancer [CSPC]. This patient would be considered [as having] low-volume prostate cancer or [being] low risk. This is based on the CHAARTED [NCT00309985] definition, which showed that low-volume disease is fewer than 4 bony metastases and no presence of visceral metastases. This patient has 1 lymph node positive and no bony metastases, so essentially that would put him in the low-volume or low-risk group.

The prognosis for patients with this disease can vary, and it's very important that these patients are treated according to National Comprehensive Cancer Network [NCCN] guidelines. If you treat patients with androgen deprivation therapy [ADT] monotherapy, according to SEER [Surveillance, Epidemiology, and End Results Program] data their 5-year median survival [rate] is about 30%. But if you treat them with combination therapy—doublet or even triplet therapy—you can potentially extend their median survival beyond 5 years. That's why it's critical that urologists treat these patients according to NCCN guidelines.

Q. Would you have ordered any other tests besides ultrasound, bone scan, and MRI for this patient prior to initiating therapy?

HAFRON: In addition to the bone scan, I would order a CT of the chest, abdomen, and pelvis. I definitely would have ordered germline and somatic testing. This patient has metastatic disease and based on NCCN guidelines, he should at least have germline testing. I also like to order somatic testing at the time of diagnosis. I think it is very helpful to have their complete genetic profile (germline and somatic results) up front. This information will influence my discussion about expectations, outcomes, and future therapies when I discuss their short- and long-term treatment plan.

Q. What is the rationale for adding abiraterone and prednisone to ADT for first-line treatment of metastatic CSPC?

HAFRON: The basis for adding abiraterone to ADT was [data from] a trial called LATITUDE [NCT01715285]. [The results were] published in *Lancet Oncology*,[1] and it was a large, randomized trial of [more than] 1200 patients with newly diagnosed high-risk metastatic hormone-sensitive prostate cancer. In LATITUDE, they defined high risk as greater than 3 bone metastases, Gleason 8 or higher, or visceral metastases. So this is not exactly high-risk disease according to LATITUDE, but the STAMPEDE trial [(NCT00268476) data] validated that in low-volume or high-volume disease, the use of abiraterone in combination with ADT will significantly improve survival. It is a very robust signal and is the basis for our use of abiraterone in this patient population, whether they are low volume or high volume or high risk.

Q. Given the available treatment options for metastatic CSPC, which treatments would you have selected for this patient?

HAFRON: If this was my patient, I would have considered any of the oral therapies: abiraterone, enzalutamide [Xtandi], or apalutamide [Erleada]. All of these are reasonable choices. Additionally, darolutamide [Nubeqa] in combination with docetaxel recently received FDA approval and should also be considered. This is where the art of medicine comes in [when] trying to decide what's the best therapy. I think it's very important to discuss with the patient and his family the adverse events of each of these drugs and weigh that against their improvement

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in survival. I help patients decide, based on the evidence, how they want to be treated. Additionally, patients need to be aware of the financial impact of these drugs, which will also unfortunately impact treatment decisions.

Q. What clinical factors influence your decision between various ADT regimens?

HAFRON: With low-volume disease, you're going to be less likely to use chemotherapy and more likely to use abiraterone, enzalutamide, or apalutamide. With high-volume disease, you would consider chemotherapy as well as the oral agents. In addition, and this is hard to generalize,…you need to evaluate what is the patient's fitness for chemotherapy. Are they a good chemotherapy candidate? Are they a good candidate for oral therapy? Which oral therapy? Do they have specific comorbidities such as seizures or neurologic disorders where I would be less likely to consider enzalutamide or apalutamide? As opposed to abiraterone, where [in] patients with a significant history of cardiac disease, diabetes, or liver disease I might not utilize this therapy. You have to look at the nuances and comorbidities of each patient to determine their fitness or their tolerability of each of these agents. What is also important in this situation is to determine whether this is de novo disease, or progressive oligometastatic disease from failure of primary therapy. This also might guide how aggressively you treat these patients.

Q. In your practice, how do patients with metastatic CSPC generally fare on leuprolide, abiraterone, and prednisone? Do they have stable disease or improved survival?

HAFRON: Generally, patients do very well with this combination of ADT, abiraterone, and prednisone. That's why, as a urologist, I've been very comfortable treating these patients. Urologists can use these drugs and combinations of these drugs quite easily in their practice. I find this area of urology quite rewarding because typically the patients will have a robust initial response that will last for a few years without significant [adverse] effects. With decent predictability, on an everyday basis we can extend the lives of these patients. Obviously, you can't say everybody, but typically patients respond very well to these therapies. It is also important for urologists to [make] clear to their patients that these therapies are not curative but will extend their life without a significant impact on their quality of life.

Q. What clinical pearls do you have for community oncologists who are treating patients with metastatic CSPC?

HAFRON: The key to the proper treatment of metastatic CSPC is combination therapy. Even though patients respond to ADT monotherapy and do well, they won't do well for long. If you look at the SEER data, again, the 5-year survival rate is 32% for de novo CSPC. For a urologist, this is the most lethal cancer they have in their office. So if you're going to treat these patients, you need to treat them with ADT plus oral and/or ADT plus chemotherapy. If you are going to remember anything about this case, you need to strongly consider combination therapy or treatment intensification for patients with metastatic CSPC. ●

REFERENCE

1. Fizazi K, Tran N, Fein L, et al. Abiraterone acetate plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive prostate cancer (LATITUDE): final overall survival analysis of a randomised, double-blind, phase 3 trial. *Lancet Oncol.* 2019;20(5):686-700. doi:10.1016/S1470-2045(19)30082-8