FDA-approved for use in metastatic castrate-resistant prostate cancer. We report an elderly patient who tolerated Abiraterone well but had significant cardiovascular morbidity following treatment with enzalutamide.

Case presentation

Our patient is an 82-year-old Caucasian man who had non-metastatic prostate cancer in 2007 and was treated with radiation to the prostate and androgen deprivation therapy. In January 2019, he had a detectable serum prostate-specific antigen (PSA) in surveillance blood work. Imaging studies showed an anterior right seventh rib lesion and retroperitoneal lymphadenopathy. Treatment was initiated with Abiraterone and GnRH agonist, and his PSA steadily improved. Nevertheless, in September 2021, his PSA started rising. Computerized tomography showed persistent retroperitoneal lymphadenopathy, and a bone scan revealed a single new abnormal area in the left ilium. Treatment was switched to Enzalutamide from Abiraterone by the Oncologist.

Two weeks after starting enzalutamide, he presented to the emergency room with acute onset shortness of breath. An echocardiogram demonstrated new cardiomyopathy, reduced left ventricular (LV) systolic function with an ejection fraction of 20%, and severe diffuse hypokinesis. Left heart catheterization showed moderate atherosclerosis of the mid and distal portion of the left anterior descending artery, and cardiomyopathy was considered disproportionate to his coronary artery disease. He had well controlled hypertension and no history of alcohol use. Enzalutamide was discontinued since it was the only preceding event before his onset of heart failure. He was started on guideline-directed medical therapy with Carvedilol and Entresto. The patient declined spironolactone due to concern for side effects. A repeat echocardiogram after three months showed improvement in LV systolic function with an ejection fraction of 45%. Our patient decided to continue ADT therapy alone since he is not symptomatic from his metastatic cancer.

Discussion

To our knowledge, this is the first case reported that has a direct correlation of enzalutamide to cardiomyopathy. Men treated with ADT have been well shown to have increased cardiovascular risk, and one study predicted a 20% increase in serious cardiovascular morbidity [3]. Enzalutamide is an androgen receptor inhibitor, and it binds to the androgen receptors with a higher affinity than older inhibitors like bicalutamide [4]. A pharmacovigilance study by Eugene B et al. in 2021 found lower cardiac events in patients with Enzalutamide compared to Abiraterone [5], and investigators suggested that enzalutamide may be better suited for patients with known cardiac comorbidities. Our observation is contrary to the fact the patient had excellent tolerance to Abiraterone but not to Enzalutamide. A meta-analysis by Lee HY et al. in 2020 reported a total of 7103 patients from seven RCTs and found Abiraterone had a higher probability of cardiac events than Enzalutamide, but the incidence of hypertension was higher in patients treated with Enzalutamide [6]. Another meta-analysis in 2018 studied a total of 8660 patients and reported a similar result with an increased incidence of hypertension in patients treated with Enzalutamide [7]. These observations concord with the higher incidence of hypertension in patients with Enzalutamide [13% vs. 4%], as observed in the landmark trial comparing enzalutamide with placebo [8]. An interesting observation was made by Moreira R et al., who reported no increased risk of cardiovascular events with Enzalutamide compared to Abiraterone [9]. With regards to specific cardiovascular events, a study in 2020 reported hypertension (10.6%) as the most common cardiovascular event in the Enzalutamide group, followed by ischemic heart disease (1.88%) and atrial fibrillation (0.39%) [10].

Conclusion

We understand from this review that men treated with ADT have a higher risk for cardiovascular adverse events, and the risk increases with the addition of novel anti-androgen treatments. Overall, Abiraterone appears to have a higher incidence of cardiovascular events, and data are conflicting in patients treated with Enzalutamide. An increase in hypertension has been well documented in patients treated with Enzalutamide. Treating physicians must be prudent in using novel anti-androgen treatments in elderly patients with a detailed discussion about potentially serious side effects of these agents. More prospective research is needed to see if initiating cardioprotective medications will reduce the risk of cardiovascular events in this patient population.

Abbreviations

ADT	Androgen deprivation therapy
GnRH	Gonadotropin releasing hormone
PSA	Prostate specific antigen
LV	Left ventricular

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