Journal of MedVerse Research & Practice

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A Case Study: Abiraterone-Induced Cardiac Arrhythmia and Heart Failure.

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Submission Date: 23.11.2024	Accepted Date: 20.12.2024	Published Date: 30.12.2024
DOI: 10.65188/nurexus.1008		

Abstract

Advancements in cancer therapy have significantly improved survival rates, but with an aging population, the co-occurrence of cancer and cardiovascular disease has become increasingly common. Additionally, certain cancer treatments can cause myocardial damage and other cardiovascular complications.

An 80-year-old male patient receiving treatment for late-stage prostate cancer requested a cardiac assessment after experiencing rapid heartbeat during nighttime hours. This case study examines the patient's situation and medical evaluation. His medical history included prostatectomy and orchiectomy performed 15 years earlier, along with hypertension and dyslipidemia. The patient had undergone treatment with abiraterone and goserelin for a period of two years. His current medication regimen included metoprolol, chlorthalidone, and rosuvastatin. During the physical examination, the patient exhibited high blood pressure, a slow heart rate, and irregular heartbeats were detected through listening to his heart sounds. The cardiac electrical activity assessment showed a slow heart rhythm, impaired conduction in the right bundle branch, the presence of a U wave, and a single premature beat originating above the ventricles. Blood tests indicated low potassium levels (2.9 mg/dL), while continuous heart monitoring over 24 hours detected persistent rapid atrial rhythm, particularly during nighttime hours.

A cardiac ultrasound revealed a decrease in ejection fraction and enlargement of the left atrium and ventricle when compared to findings from two years earlier. As discontinuation of hormonal therapy was not an option, the treatment plan included switching to spironolactone, potassium supplementation, ramipril, and continued use of metoprolol. Within 30 days, the patient experienced symptomatic improvement, and his ventricular function recovered over six months. He lived for two more years before passing away due to complications from a fall.

The cardiovascular effects of abiraterone are likely linked to its action on the adrenal glands, where it inhibits the synthesis of sex hormones and cortisol. This inhibition can lead to an overproduction of mineralocorticoids, resulting in hypokalemia, arrhythmias, and decreased cardiac function due to the lack of negative feedback from cortisol. Clinicians should be vigilant about these potential cardiovascular risks when managing patients receiving abiraterone.

Keywords: abiraterone, cardio-oncology, heart failure, arrhythmia

Introduction

Advancements in cancer treatment have saved countless lives and contributed to an aging population. Consequently, medical professionals now face the challenge of caring for cancer survivors who may

experience long-term effects from their illness as well as potential side effects from their treatments. Over the past decade, medical guidelines have increasingly emphasized cardio-oncology, reflecting heightened awareness among cardiology organizations regarding the cardiovascular care and monitoring of cancer patients. This trend underscores the growing importance of addressing heart health in individuals undergoing cancer therapy [1].

For more than 60 years, researchers have studied the impact of anthracyclines on the cardiovascular system. In recent years, there has been a marked increase in publications highlighting the cardiac toxicity associated with cancer therapies, driven by extensive research in this field. Additionally, newer treatment modalities, including agents targeting the HER2 receptor, have been shown to adversely affect heart function [2]. A key advancement in hormonal blockade therapies occurred in 1941, but the most extensive studies emerged in the 1980s with the introduction of complete hormonal blockade. This approach combined androgen suppression with luteinizing hormone-releasing hormone (LHRH) agonists to inhibit androgen production from both testicular and adrenal sources. Early research on safety and efficacy indicated that the most common adverse reactions were gynecomastia in males and transient hot flashes, with minimal cardiovascular effects [3–5]. However, in recent years, individual case reports and case series have documented cardiovascular adverse events associated with this therapeutic strategy [6–10].

Objective

Given the increased longevity of individuals following cancer diagnosis and treatment, cardiologists have developed a focused interest in the cardiovascular consequences of cancer therapies. The objective of this research is to present a clinical case of an 80-year-old male patient diagnosed with late-stage prostate cancer who was receiving hormonal suppression therapy and subsequently developed cardiac complications. This case aims to illustrate the importance of vigilant cardiovascular monitoring and management in elderly cancer patients undergoing long-term hormonal therapy.

Case report

A cardiologist evaluated an elderly man, aged 80, who was receiving treatment for late-stage prostate cancer. The patient's primary concern during the visit was a sensation of irregular heartbeats. The individual's clinical background encompassed two prior operations, namely a prostatectomy and orchiectomy, conducted 15 years earlier. Additionally, he had been subjected to multiple treatment protocols for late-stage prostate cancer. Over the past two years, the patient had been administered Abiraterone and Goserelin. Simultaneously, the individual was receiving treatment for high blood pressure and abnormal lipid levels. The current medication plan included daily doses of Metoprolol (100 mg), Chlorthalidone (25 mg), and Rosuvastatin (10 mg). The clinical assessment showed an elevated blood pressure of 176/100 mmHg and a low heart rate of 48 bpm. Auscultation detected extrasystoles, but no murmurs or other notable findings were observed during the examination. Analysis of the electrocardiogram (ECG), as shown in Figure 1, revealed several cardiac abnormalities. These included a slower-than-normal heart rate (sinus bradycardia), impaired electrical conduction in the right bundle branch, and the presence of a U wave. Additionally, a single premature beat originating from above the ventricles (supraventricular extrasystole) was observed.

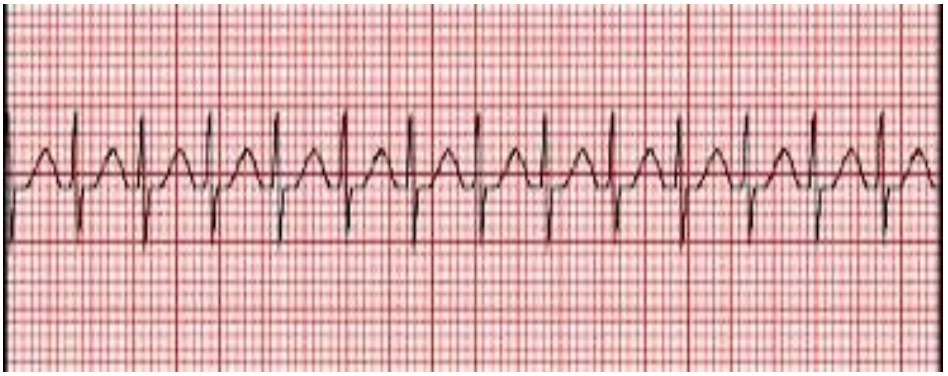

Figure 1. Initial ECG.

The laboratory results from the biochemical evaluation showed regulated lipid levels. The patient's fasting blood sugar measured 109 mg/dL, while their HbA1c was 6.2%. The creatinine level was found to be 1.27 mg/dL. Electrolyte analysis indicated a sodium concentration of 145 mEq/L and a potassium level of 2.9 mEq/L. Additionally, the thyroid-stimulating hormone (TSH) was determined to be 1,592 mU/L. Four months ago, a 24-hour Holter monitoring revealed persistent atrial tachycardia for the majority of the nighttime hours. Additionally, an echocardiogram performed two years prior demonstrated normal systolic function. The updated treatment plan involved discontinuing chlorthalidone and introducing spironolactone and enalapril, while maintaining metoprolol therapy. After two weeks, the patient experienced symptom resolution, with potassium levels normalizing to 4.2 mEq/L, blood pressure reaching 140/90 mmHg, and heart rate stabilizing at 60 bpm. The physical examination revealed no notable abnormalities. A follow-up echocardiogram showed reduced systolic function, while a new 24-hour Holter monitor identified sporadic atrial tachycardias, each with a duration under 5 seconds (Figures 2 and 3. Table 1). The cancer specialist focusing on urological issues indicated that few feasible alternatives existed beyond maintaining the patient's existing course of treatment.

Figure 2. Atrial tachycardia in the first 24-hour Holter. Source: the authors.

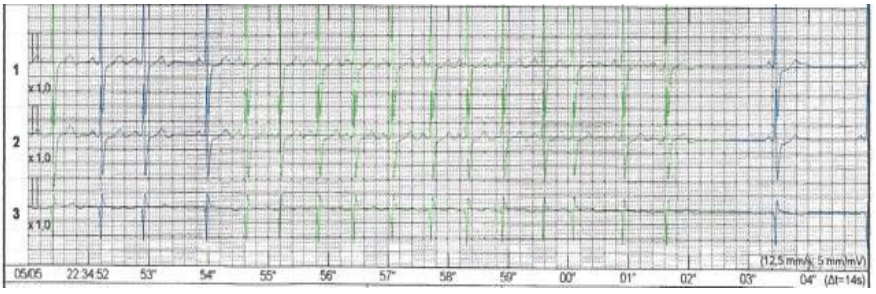

Table 1. Sequential echocardiograms Source: the authors

	2019	2020	2021
Left atrium (mm)	40	44	42
Aorta (mm)	38	39	39
Right ventricle (mm)	12	12	12
Septum (mm)	12	14	14
Posterior wall (mm)	16	16	15
Left ventricle diastolic diameter (mm)	48	44	44

Left ventricle systolic diameter (mm)	22	34	31
Left ventricle shortening (%)	46	23	30
Left ventricle ejection	72	48	63

The patient remained asymptomatic for the next two years. Unfortunately, he then suffered a serious accident at home, leading to significant trauma-related complications. After spending three days in the hospital, the patient died from his injuries. During his hospitalization, medical tests showed no irregularities in his metabolic or cardiac functions.

Discussion

Abiraterone acetate acts as an inhibitor of androgen and corticosteroid synthesis by targeting the CYP17 enzyme in the adrenal glands, thereby significantly reducing androgen production, as demonstrated by James et al. [4]. Clinical trials have generally reported a low incidence of cardiovascular adverse effects associated with Abiraterone therapy, as outlined by Lyon et al. and Thorpe et al. [2,5]. However, emerging pharmacovigilance data have suggested an association between Abiraterone use and reduced ventricular function as well as cardiac arrhythmias, as reported by Bretagne et al. [6]. Cone et al. further demonstrated that patients receiving Abiraterone had a 12% higher risk of hospitalization due to atrial fibrillation compared with those treated with enzalutamide [9]. Several case reports and series have documented cardiovascular toxicity related to Abiraterone, and a recent meta-analysis by Iacovelli et al. suggested a potential association between Abiraterone use and cardiac complications [10].

The occurrence of uncontrolled hypertension accompanied by hypokalemia, as observed in the present patient, has been variably reported across studies. While James et al. described this combination as uncommon [4], Cone et al. reported a higher prevalence [9]. This clinical presentation is believed to result from mineralocorticoid excess secondary to impaired cortisol-mediated negative feedback, leading to renal potassium loss, as explained by Tsugu et al. [8]. Bretagne et al. cautioned against the concurrent use of thiazide diuretics with Abiraterone, as this combination may precipitate severe hypokalemia [6], a mechanism consistent with the findings in this case. Following modification of antihypertensive therapy, potassium levels normalized and blood pressure improved, resulting in symptomatic relief within two weeks. The patient exhibited cardiac dysfunction, atrial arrhythmia, hypertension, hypokalemia, and corresponding electrocardiographic abnormalities.

The luteinizing hormone-releasing hormone (LHRH) agonist goserelin acetate, used as part of this patient's treatment, has been associated with fewer cardiovascular adverse effects compared with adrenal androgen synthesis inhibitors. Thorpe et al. reported cardiovascular adverse events in 1.1% of patients receiving goserelin alone and 2.2% of those treated with cyproterone, with comparable rates observed in combination therapy; however, severe reactions necessitating treatment discontinuation occurred in nearly half of the affected patients [5]. Anti-androgen therapy has also been associated with metabolic disturbances, including insulin resistance and dyslipidemia, particularly among overweight individuals, as noted by Bahl et al. [11]. In the present case, dyslipidemia was observed without accompanying obesity or hyperglycemia.

Long-term retrospective studies and meta-analyses conducted by Efstathiou et al. and Nguyen et al. have demonstrated that LHRH agonists do not significantly increase cardiovascular mortality [12,13]. Nevertheless, Smith et al. reported that men with pre-existing cardiovascular disease receiving LHRH agonists exhibited a 30% increased risk of cardiovascular events compared with those not undergoing

androgen deprivation therapy [14]. Despite conflicting evidence, current clinical guidelines recommend that patients be counseled regarding potential cardiovascular and metabolic risks and that modifiable risk factors be proactively managed.

Elderly patients with advanced prostate cancer require particularly vigilant monitoring due to age-related cardiovascular vulnerability and polypharmacy, as emphasized by Efstathiou et al. [12]. Individuals predisposed to atrial arrhythmias appear especially susceptible to the cardiotoxic and metabolic effects of hormone-blocking agents, as reported by Scailteux et al. and Lu-Yao et al. [15,16]. Cardiologists should remain aware of these risks, as they frequently manage patients with concurrent malignancy and cardiovascular disease. Ongoing surveillance should include regular assessment of ventricular function and arrhythmia monitoring, as recommended by Hajjar et al. and Lyon et al. [1,2].

Patients receiving hormone-blocking therapies such as Abiraterone should undergo comprehensive cardiovascular risk evaluation prior to and during treatment, and medications that predispose to hypokalemia should be avoided, as emphasized by Bretagne et al. [6]. The development of atrial tachyarrhythmias, particularly atrial fibrillation, remains a significant clinical concern, as highlighted by Bretagne et al. and Iacovelli et al. [6,10]. In cases where continuation of hormonal therapy is necessary, close multidisciplinary collaboration among cardiologists, urologists, and oncologists is essential to ensure optimal and safe patient management, as advocated by Hajjar et al. [1].

Conclusion

The medication abiraterone can potentially cause cardiac dysfunction, rapid heart rhythms, low potassium levels, and elevated blood pressure, as illustrated in this instance. Healthcare providers must vigilantly observe patients receiving hormonal suppression treatment for late-stage prostate cancer.

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