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CASE REPORT

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Abiraterone, a rare cause of severe perioperative hypokalemia with unusual presentation as aphonia and quadriparesis: a case report

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Abstract

Background Oral Abiraterone acetate is a novel antineoplastic agent approved by the FDA for the treatment of metastatic prostate cancer. Abiraterone is an irreversible inhibitor of the 17α-hydroxylase (CYP17) enzyme complex resulting in a reduction of androgens and corticosteroids. It may cause mineralocorticoid excess syndrome; hence, it is prescribed with steroids. Here we describe a case of postoperative severe hypokalemia with unusual presentation in a patient after spine surgery in which abiraterone with prednisolone was continued preoperatively. Anesthetic concerns about the perioperative administration of abiraterone have not been reported in the literature.

Case presentation An 80-year-old male with a known case of metastatic prostate cancer was posted for spine surgery under general anesthesia. Surgery was uneventful and the patient was extubated after ensuring adequate muscle power and respiratory parameters. Postoperatively, the patient developed aphonia, quadriparesis, and respiratory distress leading to reintubation. After evaluation, severe grade 4 hypokalemia was found to be the causative factor. The patient recovered well after potassium and steroid supplementation. Low potassium and cortisol levels indicate a diagnosis of abiraterone-induced hypokalemia.

Conclusion Patients on abiraterone require more stringent and vigilant monitoring of potassium and cortisol levels. In such circumstances, it might be advantageous to add additional steroids or substitute alternative steroids.

Keywords Abiraterone, Hypokalemia, Anesthesia, Case report, Mineralocorticoids

Background

Oral abiraterone acetate is a novel antineoplastic agent approved for the treatment of metastatic castration-resistant prostate cancer (mCRPC). It works by irreversible inhibition of CYP17, a key enzyme for the biosynthesis of androgens (Feng et al. 2022). Abiraterone may lead to many adverse effects including hypokalemia, cardiac arrhythmias, hepatotoxicity, and adrenocortical insufficiency. However, severe Grades 3 and 4 hypokalemia is extremely rare. After written informed consent, we describe a case of severe hypokalemia postoperatively with unusual presentation of quadriparesis, aphonia, and respiratory distress in a metastatic prostate cancer patient after spine surgery owing to preoperative administration of Abiraterone acetate. To the best of our knowledge, anesthetic implications of perioperative abiraterone have not been described in the literature.

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Case presentation

An 80-year-old male, weighing 70 kg, BMI 24.2 kg/m^2 known case of metastatic prostate cancer presented with chief complaints of lower back pain radiating to lower limbs, weakness, and numbness in bilateral lower limbs for 10 days. There was no history of diabetes, hypertension, or any other chronic illness. He had a history of prostate surgery along with orchidectomy 1 year back. On examination power in bilateral lower limbs was 4/5 (MRC grade) (Dyck et al. 2005). There was impaired touch/pain/temperature sensation in the bilateral lower limb below T10 (50% decrease), the rest systemic examination was normal. MRI spine revealed compression fracture at D9 and D11, suggestive of metastasis. He was posted for D9, D10 decompressive laminectomy. Preoperative electrolytes were also within normal limits (136 meq/l sodium and 3.8 meq/l potassium). His preoperative medications included Tab Abiraterone acetate 1000 mg OD and tab prednisolone 5 mg BD (started 5 days back) which were continued until the morning of surgery. In OT, induction was done with an injection of fentanyl(150 mcg), propofol, and vecuronium (6 mg), and intubated with a flexometallic 8.0 mm tube followed by prone positioning. Anesthesia was maintained with O_2, N_2O (1:1), sevoflurane (MAC 1–1.2), and vecuronium (1 mg repeated based on clinical parameters). The patient was ventilated on VCV mode (TV = 500 ml, RR = 14/min, I: E ratio 2:1, PEEP 5 cm of H_2O). For analgesia, inj fentanyl 100 mcg and paracetamol 1 g were given. Dexamethasone 4 mg was given at induction of anesthesia. Surgery was completed in 3 h with an uneventful intraoperative course and then the patient was made supine. Neuromuscular blockade was reversed with inj neostigmine (3 mg) and inj glycopyrrolate (0.6 mg) after ensuring adequate muscle power and respiratory parameters as neuromuscular monitoring is not available at our institute. The patient was then extubated and shifted to the post-anesthesia care unit (PACU). Postoperatively after half an hour, the patient became restless along with aphonia and quadriparesis (power 3/5 in all four limbs). Injection of neostigmine and glycopyrrolate was repeated in PACU due to the possibility of inadequate reversal, but muscle power did not improve. He gradually developed drowsiness and shallow breathing with a saturation of 93% on oxygen at 6 L/min. Arterial blood gas revealed severe respiratory acidosis (pH 7.05, pCO2 88, K+ 2.0). He was shifted to OT and reintubated in view of altered sensorium and CO_2 retention. Differential diagnoses of cervical spine injury, cerebrovascular accident, electrolyte imbalance, hypokalemic periodic paralysis, hypothyroid myopathy, and thyrotoxic periodic paralysis were considered. Serum electrolytes and thyroid samples were sent. After intubation, the patient was shifted for CT brain, CT cervical spine, CT thorax, and MRI brain, all were found to be normal. After radiological investigations, the patient was transferred to ICU. He was put on mechanical ventilation in VCV mode (FiO_2 0.5, TV 500 ml, RR 14/min, PEEP 5 cm of water). ECG was done and was suggestive of hypokalemic changes (Fig. 1). Serum electrolytes revealed severe hypokalemia (potassium 1.9 (3.5–5.2 meq/l)); however, sodium and magnesium were

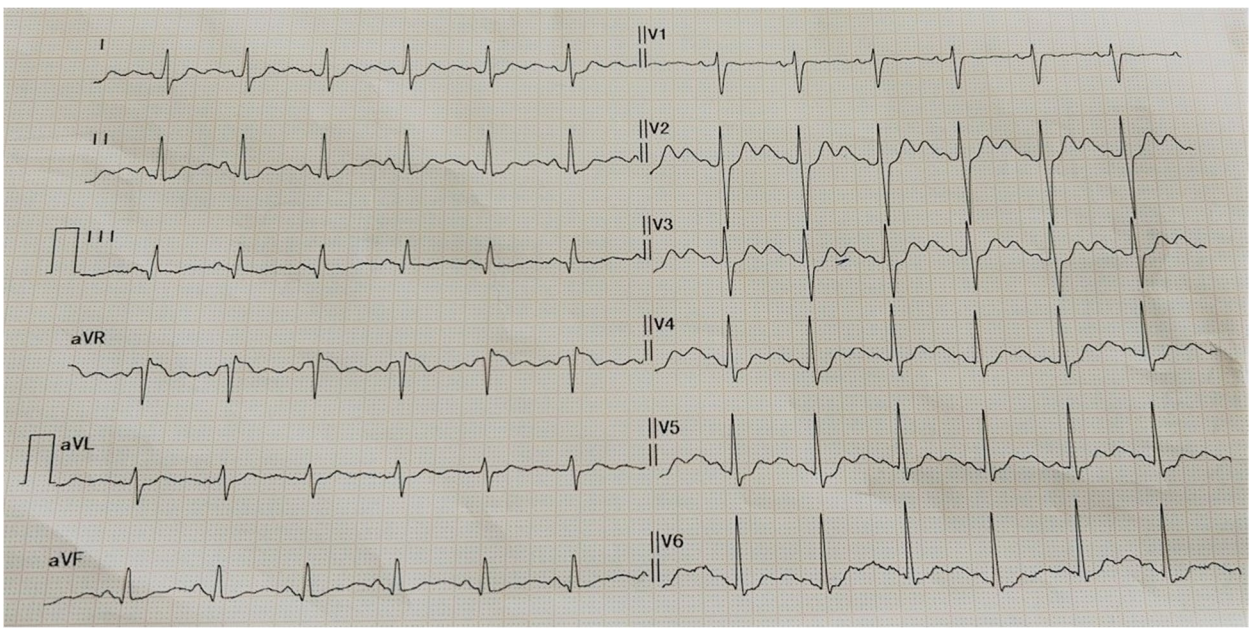

Fig. 1 ECG changes suggestive of hypokalemia

normal. He was started on IV potassium supplementation of 40 meq over 2 h followed by 10 meq/h and magnesium 2 g over 20 min. His thyroid function tests were normal. His serum cortisol levels were investigated and found to be 5 (10–20 mcg/dl). He was administered 8 mg dexamethasone intravenously followed by 8 hourly. Next potassium analysis was done after 6 h and was found to be 3.7 meq/l. A surgical oncology reference was sought and they advised to stop abiraterone. After the removal of the offending agent, i.e., abiraterone, correcting hypokalemia, and administering IV magnesium and steroids, his muscle power and respiration improved. Mechanical ventilation was continued for approximately 18 h and gradually weaned off and extubated the next morning. He was able to phonate with adequate muscle power (5/5 in all 4 limbs). The only cause of these symptoms was hypokalemia which could be attributed to abiraterone. There was no past or familial history of episodic paralysis, which makes hypokalemic periodic paralysis unlikely.

Discussion

Abiraterone acetate is a new androgen deprivation therapy, approved by the FDA in 2011 in combination with prednisone for mCRPC (Goldberg and Berrios-Colon 2013). Abiraterone therapy significantly prolongs overall survival and reduces tumor burden in patients with castration-sensitive prostate cancer (Fizazi et al. 2017; James et al. 2017). The median time to reach the maximum plasma concentration of abiraterone is 2 h and has an elimination half-life of 12 h (Thakur et al. 2018).

Abiraterone is a selective and irreversible inhibitor of the 17α-hydroxylase (CYP17) enzyme complex required for androgen biosynthesis. As a result, androgen levels in testicular, adrenal, and prostatic tumor tissues are reduced. CYP17 promotes the formation of dehydroepiandrosterone (DHEA) and androstenedione which are precursors of testosterone (Yamamoto et al. 2018) (Fig. 2). Abiraterone administration inhibits corticosteroid and androgen production, resulting in hypothalamic-pituitary axis (HPA) upregulation. This potentially results in an increase in ACTH levels and consequently increased mineralocorticoid production by the adrenal glands (Thakur et al. 2018). This may result in mineralocorticoid excess syndrome (MES) characterized by a triad of fluid retention, hypertension, and hypokalemia (Yamamoto et al. 2018). To prevent MES, concurrent administration of glucocorticoid is currently adopted in routine practice.

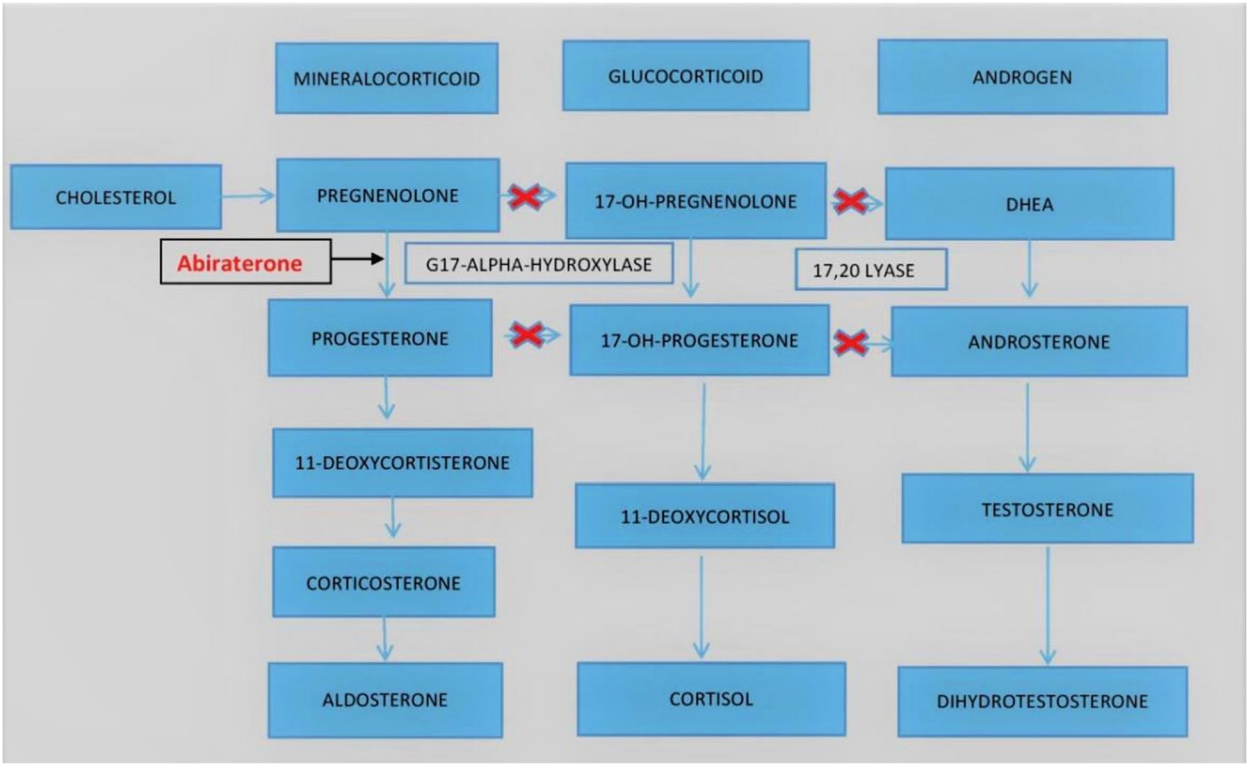

Fig. 2 Mechanism of action of abiraterone acetate

Yamamoto et al described 2 cases of severe life-threatening hypokalemia leading to convulsive seizure and severe lethargy associated with abiraterone within 2 weeks and 1 month after starting the treatment respectively (Yamamoto et al. 2018). Torsades de pointes related to Abiraterone-induced hypokalemia have also been observed in two case reports (Lee et al. 2022; Riad et al. 2021). Similar to our case, Rajvanshi et al. also observed quadriplegia secondary to abiraterone-related hypokalemia (Rajvanshi et al. 2019). However, none of the cases described were perioperative.

Hypokalemia is defined as potassium < 3.5 meq/l. It has 4 grades of severity (Clase et al. 2020) (Table 1). Hypokalemia is a known side effect of abiraterone, but severe grade 4 hypokalemia is extremely rare and reported in only 1% of patients (Fizazi et al. 2017). Severe hypokalemia may present as an ascending paralysis, intestinal paralysis, respiratory failure, or cardiac dysrhythmias. However, there is a high degree of interindividual variability, presentation of aphonia is unusual and not being described in the literature.

There is a recommendation for the continuation of antineoplastic urologic medications up to the day of surgery (Pfeifer et al. 2021). However, we observed severe grade 4 hypokalemia in our patient when abiraterone with steroids was continued preoperatively. Prednisolone, usually prescribed with abiraterone itself has mineralocorticoid activity (0.8) which may precipitate mineralocorticoid excess syndrome. It may be preferable to add dexamethasone or eplerenone when glucocorticoid supplementation is insufficient to manage abiraterone-induced hypokalemia (Yamamoto et al. 2018).

With an extensive literature search, we did not find any data on the anesthetic implications of preoperative administration of abiraterone. Meticulous preoperative examination, vigilance, and stringent monitoring of potassium, cortisol, and ACTH levels should be considered in patients on Abiraterone. Drugs causing hypokalemia should be taken into consideration. Further clinical studies are required to determine the risks and benefits of continuing abiraterone preoperatively.

Table 1 Grades of hypokalemia

Grade of hypokalemia	Serum levels of potassium (meq/l)
Grade 1	3–3.4
Grade 2	2.5–3
Grade 3	2–2.4
Grade 4	< 2

Conclusions

One should be cautious about the perioperative administration of abiraterone. Avoiding hypokalemia-causing factors, and frequent potassium and cortisol monitoring may all be considered perioperatively. It might be advantageous to supplement alternative steroids or increase the dose of steroids when abiraterone is continued perioperatively.

Abbreviations

BMI	Body mass index
MRC	Medical Research Council
VCV	Volume control ventilation
PEEP	Positive end-expiratory pressure
mCRPC	Metastatic castration-resistant prostate cancer
HPA	Hypothalamic pituitary axis
DHEA	Dehydroepiandrosterone
ACTH	Adrenocorticotrophic hormone
MES	Mineralocorticoid excess syndrome
FDA	Food and Drug Administration
CT	Computed tomography
MRI	Magnetic resonance imaging
PACU	Post anesthesia care unit

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None

Authors' contributions

ST Corresponding Author, Case management, data collection and analysis, manuscript preparation. AK contributed to case management, data analysis, and manuscript preparation. NT contributed to case management and data analysis. YCH contributed to case management, manuscript preparation.

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Availability of data and materials

Yes

Declarations

Ethics approval and consent to participate

Ethics approval is not applicable as this is a case report. Written informed consent was obtained from the patient to participate.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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