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CASE REPORT

Irinotecan-induced severe hypotension in a patient with lung cancer

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Abstract

Most hypotension during chemotherapy is caused by an allergic mechanism. Conversely, non-allergic hypotension due to chemotherapy is rare. In this case report, we present a patient who suffered severe hypotension followed by the administration of irinotecan-based chemotherapy and some supportive care such as steroids for preventing emesis. A 71-year-old man with hypertension was diagnosed with stage IV small cell lung cancer (sT1cN3M0). Severe hypotension occurred in the patient after every administration of chemotherapy. Finally, he was able to receive all four courses of chemotherapy as planned along with the medical staff's support care. This case provides that a regimen that contained irinotecan and steroid could cause hypotension and the mechanism is partially explained by inhibiting choline esterase and adrenal insufficiency. We should be careful about non-allergic hypotension when we administer irinotecan-based chemotherapy.

KEYWORDS

adverse effects, chemotherapy, irinotecan, non-allergic hypotension

1 | INTRODUCTION

Chemotherapy drugs are known to induce cardiovascular toxicity, such as arrhythmias, thrombosis, hypotension, and hypertension due to oxidative stress, cytokine release syndrome, and myocarditis.[1,2] There are several reports of chemotherapy drug-induced shock and allergic hypotension, but few of non-allergic hypotension. Here, we present a case of non-allergic severe hypotension due to irinotecan-based chemotherapy for lung cancer.

2 | CASE REPORT

A 71-year-old man (151.3 cm, 53.6 kg) with hypertension and deep vein thrombosis was diagnosed with small cell lung cancer in July 2020. We conducted thoracoscopic segmental resection of stage IV lung cancer (sT1cN3M0) on August 3, 2020. On September 1, he was admitted to the Izumi Memorial Hospital for chemotherapy. On Day 2 after admission, we started chemotherapy with irinotecan (60 mg/m^2 for 3 consecutive weeks followed by 1-week rest) and cisplatin (60 mg/m^2 on Day 1) under normal

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range blood pressure of 120–140/80–90 mmHg (shown in Figure 1). Valsartan (80 mg/day) and amlodipine (5 mg/day) had been administered for hypertension before admission, and we continued both antihypertensive drugs during chemotherapy. On Day 6, grade 2 headache, grade 2 constipation, and low blood pressure of 101/62 mmHg were observed. Chemotherapy-associated adverse events were graded according to the Common Terminology Criteria for Adverse Events v5.0. On Day 8, the patient exhibited dysphoria and low blood pressure of 88/60 mmHg, which improved by elevating the lower limbs. On Day 9, his blood pressure decreased to 83/59 mmHg. We discontinued both antihypertensive drugs and hydration with 1000 ml of lactated ringer's solution and considered dehydration with blood urea nitrogen at 40 mg/dl. In addition, we paused chemotherapy. On Day 16, his blood pressure improved to 133/84 mmHg, and irinotecan was initiated without administration of antihypertensive drugs. However, grade 2 headache and low blood pressure (84/66 mmHg) were observed again. He was discharged on Day 24 with a blood pressure of 98/64 mmHg because other chemotherapy-induced adverse effects improved. On Day 28, he was re-admitted to our hospital, and we initiated the second chemotherapy course with 50 mg/m^2 irinotecan and 50 mg/m^2 cisplatin. A low blood pressure of 90/66 mmHg, grade 2 headache, and constipation were observed again. We continued chemotherapy while the medical staff monitored the patient's safety during hospitalization. Finally, he was able to receive all four courses of chemotherapy as planned.

3 | DISCUSSION

We hypothesized that the symptoms of low blood pressure, headache, and constipation experienced by our patient might be partially explained by the cholinergic adverse effects of irinotecan, cardiotoxicity of cisplatin, and adrenal insufficiency caused by dexamethasone. Irinotecan was reported to exert depressant effects on heart rate and arterial blood pressure.[3] Cisplatin is known to be cardiotoxic and is reported to induce under 1% hypotension in the package insert. In addition, etoposide and cisplatin combination therapy induced bradycardia,[4] cisplatin, and 5-fluorouracil combination therapy inducing hypotension were reported.[5] Adrenal insufficiency was reported in cancer patients who received steroids as supportive administration against cancer chemotherapy-induced adverse effects.[6] A 60-year-old woman with fallopian tube cancer who was undergoing treatment with paclitaxel and carboplatin experienced drowsiness and hypotension after administration of 40 mg (p.o.) and 20 mg (i.v.) of dexamethasone to avoid emesis.[7] In the package inserts and a clinical trial, these drugs were reported to induce hypotension without allergic reactions at an undetectable level up to about 4%.[8] We administered dexamethasone,

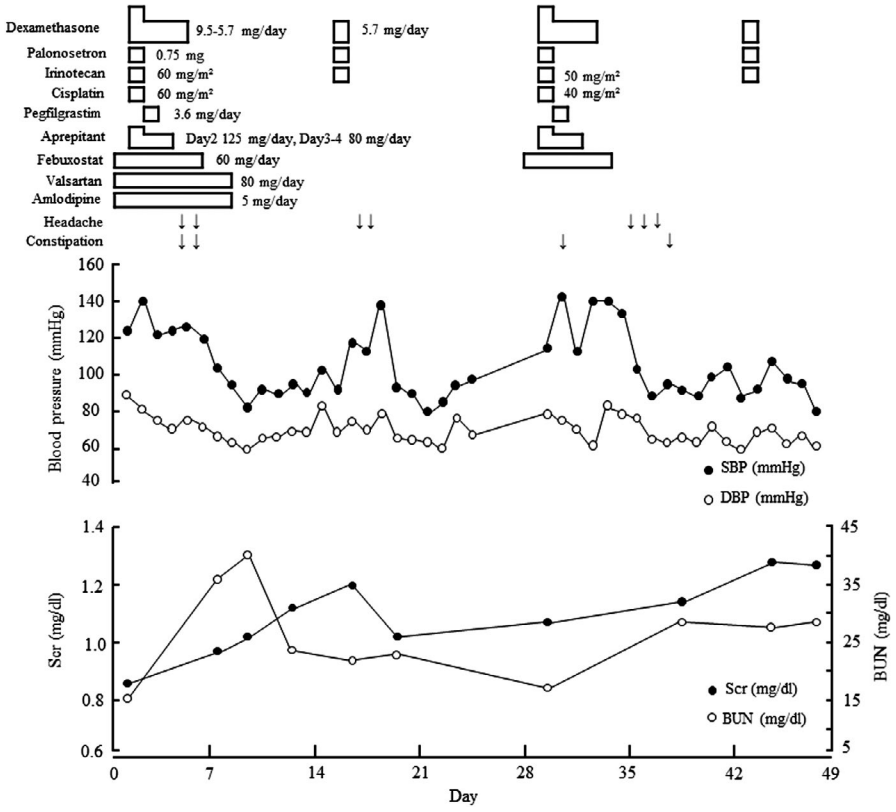

FIGURE 1 Clinical course of the present case. BUN, blood urea nitrogen, Scr, serum creatinine

palonosetron, and aprepitant to prevent emesis. The frequency of hypotension in palonosetron is less than 1% and in aprepitant is undetectable as seen in each package insert. We think that palonosetron and aprepitant are less likely to be responsible for the hypotension in our case. In our case, we repeatedly observed an increase and decrease in blood pressure after the chemotherapy. That was also observed after the discontinued antihypertensive medication. We think that antihypertensive medication may potentially affect the first course of chemotherapy. Finally, irinotecan inhibits cholinesterase and exhibits parasympathetic hyperactivity. Irinotecan was reported to affect the vagus nerve, leading to an increase in the response of the parasympathetic nervous system.[9] However, these effects are known to be transient and short-acting after irinotecan administration. In our case, the hypotension was longer than that of a typical irinotecan-inducing one. Although we did not check cortisol level and ACTH stimulation test, this may be due to an additive, synergistic effect of steroid-induced adrenal insufficiency. This observation suggests that a combination regimen of anticancer drugs and steroids, such as those with known cardiotoxicity, may lead to unexpected hypotension.

In conclusion, we report a case of repeated history of hypotension, headache, and constipation due to anticancer drugs. The symptoms that occurred in our patient were tolerated under hospitalization monitoring. However, patients treated with irinotecan could experience sudden hypotension or worsening cardiac disease. Therefore, medical staff should carefully monitor patients undergoing irinotecan-based chemotherapy for patient vitals, cholinergic reactions, and adverse effects, which require hospitalization.

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None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

AUTHOR CONTRIBUTIONS

All authors are satisfied that the ICMJE recommends four criteria. In particular, RN, KM, and AM built this study. RN and KM drafted the manuscript. RN and AM collected data. AS, KT, TU, and SN were discussed the interpretation. TS finalized the study. All authors contributed to the discussion of the manuscript. All authors agreed to the publication of this manuscript.

CONSENT

Written consent was obtained from the patient for the publication of this case report.

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REFERENCES

1. Castel M, Despas F, Modesto A, et al. Cardiotoxicity of chemotherapies. *Presse Med*. 2013;42(1):26-39. doi:10.1016/j.lpm.2012.04.014
2. Romitan DM, Rădulescu D, Berindan-Neagoe I, et al. Cardiomyopathies and arrhythmias induced by cancer therapies. *Biomedicines*. 2020;8(11):496. doi:10.3390/biomedicines8110496
3. Blandizzi C, De Paolis B, Colucci R, Di Paolo A, Danesi R, Del Tacca M. Acetylcholinesterase blockade does not account for the adverse cardiovascular effects of the antitumor drug irinotecan: a preclinical study. *Toxicol Appl Pharmacol*. 2001;177(2):149-156. doi:10.1006/taap.2001.9293
4. Kucharz J, Michalowska-Kaczmarczyk A, Zygulska AL, et al. Bradycardia as a rare symptom of cisplatin cardiotoxicity: A case report. *Oncol Lett*. 2016;11(3):2297-2299. doi:10.3892/ol.2016.4195
5. Jakubowski AA, Kemeny N. Hypotension as a manifestation of cardiotoxicity in three patients receiving cisplatin and 5-fluorouracil. *Cancer*. 1988;62(2):266-269.
6. Spiege MWE, Vigersky RA, Oliff AI, Echelberger CK, Bruton J, Poplack DG. Adrenal suppression after short-term corticosteroid therapy. *Lancet*. 1979;313(8122):932. doi:10.1016/S0140-6736(79)91420-X
7. Jeske W, Gawrychowski K, Smiertka W. Supplementation with hydrocortisone on the 3rd-5th day following dexamethasone premedicated chemotherapy eliminated severe dizziness and postural hypotension. *Kardiol Pol*. 2012;70(3):273-274.
8. Lara PN Jr, Natale R, Crowley J, et al. Phase III trial of irinotecan/cisplatin compared with etoposide/cisplatin in extensive-stage small-cell lung cancer: clinical and pharmacogenomic results from SWOG S0124. *J Clin Oncol*. 2009;27(15):2530-2535. doi:10.1200/JCO.2008.20.1061
9. Blandizzi C, De Paolis B, Colucci R, Lazzeri G, Baschiera F, Del Tacca M. Characterization of a novel mechanism accounting for the adverse cholinergic effects of the anticancer drug irinotecan. *Br J Pharmacol*. 2001;132(1):73-84. doi:10.1038/sj.bjp.0703766

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