



CASE REPORT

Dexamethasone to prednisolone rotation relieved hiccups in colorectal cancer patient continuing teleworking during anticancer therapy

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Key Clinical Message

We present a case of chemotherapy-induced hiccups that were alleviated by steroid rotation. Hiccups are often overlooked, but they have an impact on the patient's quality of life. In the COVID-19 era, web-based teleworking has become an important tool, hiccups during a teleconference should be noted as a concern for patients.

KEYWORDS

colorectal cancer, dexamethasone, hiccups, prednisolone, steroid rotation, teleworking

1 | INTRODUCTION

Hiccups induced by anticancer therapy occur in approximately 16%–25% of patients receiving chemotherapy.^{1–3} Most cases improve within 7 days,⁴ but some last longer, significantly decreasing the patient's quality of life (QOL). It is not uncommon for patients to continue working in a web-based fashion during cancer treatment, especially in the COVID-19 era. In this case report, we present our experience with a cancer patient undergoing web-based telework who developed hiccups associated with chemotherapy. The hiccups were well controlled by switching from dexamethasone to prednisolone as an antiemetic regimen. We obtained written informed consent for publication of this case report.

2 | CASE HISTORY

A 49-year-old man (weight: 103.9 kg, height: 167.5 cm, body surface area: 2.119 m²) with hypertension was undergoing chemotherapy (7.5 mg/kg bevacizumab and 150 mg/m² irinotecan on day 1 and combined capsule of 120 mg tegafur/34.8 mg gimeracil/117.6 mg oteracil on days 1–14 of a 21-day cycle) after surgery for transverse colon cancer with lung metastasis as a second-line anticancer therapy.⁵ Palonosetron and dexamethasone were adopted for chemotherapy-induced nausea and vomiting (CINV); the patient received an injection of 0.75 mg/day palonosetron and 9.9 mg/day dexamethasone on Day 1 and orally 8 mg/day dexamethasone on Days 2–4 during chemotherapy.⁶ At the 7th course of chemotherapy, he

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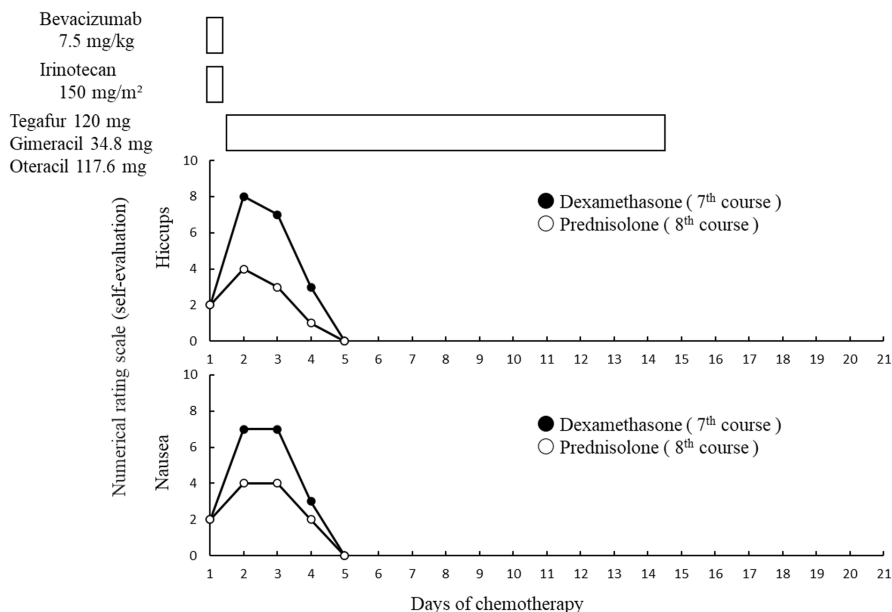


FIGURE 1 Severity of hiccups and nausea with dexamethasone and prednisolone.

complained of severe hiccups during an online meeting for his work, with one hiccup per word during the meeting. Therefore, we started 25 mg chlorpromazine and 2.5 g shakuyakukanzoto as needed for 21 days; however, his hiccups did not improve. To retain his ability to work and his QOL, at the 8th course, we changed the 8 mg dexamethasone to 60 mg prednisolone for 2 days, according to the literature by Kang et al.⁷ after obtained informed consent from him as advanced choice considering his QOL. When the patient was receiving dexamethasone, the severity of hiccups and nausea peaked on Day 2 at grades 8 and 7, respectively (0: no symptoms to 10: severe) (Figure 1). However, when he was receiving prednisolone, his symptoms peaked on Day 2 at grade 4 for both hiccups and nausea. He was satisfied that he could smoothly continue his online meetings after changing to prednisolone to prevent CINV. We continued prednisolone during the 9th course of chemotherapy to ensure the patient's QOL but decreased the dose to 30 mg/day for 2 days after chemotherapy. His hiccups and nausea were well controlled at this dose. He was administered pyridoxal (60 mg/day), vonoprazan (20 mg/day), mecobalamin (1.5 mg/day), amlodipine (5 mg/day), ambroxol (45 mg/day), and magnesium oxide (990 mg/day); these were not changed throughout the treatment period.

3 | DISCUSSION

We presented our experience with severe hiccups associated with chemotherapy that were improved by steroid rotation from dexamethasone to prednisolone for CINV. The patient's nausea was also well controlled after the

change. Hiccups are known to occur in patients treated with dexamethasone.³ In our case, some of the patient's other medicine may have caused hiccups, including irinotecan (frequency of hiccups, <5%), bevacizumab (1%–5%), and palonosetron (<1%–10%).^{8–10} Because we did not want to reduce either the anticancer or antiemetic effects of the patient's therapy, we first tried chlorpromazine and shakuyakukanzoto. However, these drugs did not improve his hiccups; therefore, we changed dexamethasone to prednisolone at a 1:7.5 titer (dexamethasone vs. prednisolone: 8 mg vs. 60 mg).^{7,11}

The mechanism of hiccups caused by dexamethasone is reported to be the stimulation of the steroid receptors and the central part of the hiccup reflex arc and a decrease in the synaptic transmission threshold in the midbrain. Steroid receptors are highly expressed in the central part of the hiccup reflex arc.^{12,13} Dexamethasone has been reported to be more potent than methylprednisolone in inducing hiccups, and steroids have different hiccup-inducing effects depending on their potency.¹⁴ Dexamethasone when administered in high doses can cross the blood–brain barrier and activate steroid receptors in the hypothalamus,¹⁵ and dexamethasone crosses the blood–brain barrier better than prednisolone.¹⁶ The hiccup reflex arc is also inhibited by γ -aminobutyric acid (GABA), and GABA antagonists are thought to induce hiccups. It has been suggested that steroids may be potent GABA antagonists at the hiccup reflex arc.¹⁷

Rotation within the same drug class is generally conducted to control adverse events or increase efficacy.¹⁸ Although our patient's hiccups may be partially explained by the rotation in steroids, they cannot be explained solely by differences in steroid potency and blood–brain barrier

passage. Further studies are needed to determine the best method for controlling hiccups in cancer patients.

4 | CONCLUSION

The present case has afforded us a new perspective on hiccups, an adverse event that is often overlooked due to its seemingly benign nature, despite its negative impact on patients' QOL, particularly in the context of the COVID-19 pandemic and the shift toward remote work for half of the working population.¹⁹ As a matter of fact, adverse events experienced by cancer patients have been described as a "missing voice" in the literature.²⁰ This study contributes to the existing body of evidence highlighting the critical importance of medical staff's awareness of overlooked adverse events that can significantly impair patients' QOL.

In conclusion, COVID-19 has drastically changed to the web-based working style. In cancer patients, web-based working is desirable to avoid physical burdens and decrease infection risks. However, randomly occurring hiccups are a considerable concern for those working online especially as videoconferencing becomes an important part of their life. Hiccups will become a primary concern for cancer patients continuing to work online during their treatment. Currently, steroid rotation is not intended to replace standard treatment methods. Effective and high-quality studies are necessary to reduce hiccups in cancer patients undergoing chemotherapy.

AUTHOR CONTRIBUTIONS

Takuya Nagata: Data curation; investigation; writing – original draft. **Ayako Watanabe:** Conceptualization; data curation; investigation; writing – original draft. **Kenji Momo:** Conceptualization; methodology; project administration; supervision; validation; writing – original draft. **Yuka Kashiwabara:** Project administration; supervision. **Misa Saeki:** Data curation; investigation; validation. **Yuji Oto:** Methodology; validation. **Takeshi Uchikura:** Methodology; validation. **Kouji Kobayashi:** Data curation; supervision. **Hirokazu Toshima:** Methodology; supervision. **Ken Shimada:** Project administration; supervision. **Katsumi Tanaka:** Project administration; supervision.

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None.

CONFLICT OF INTEREST STATEMENT

The Department of Hospital Pharmaceutics, School of Pharmacy, Showa University received funds from Ono for a contract research project according to a collaborative research agreement. YO's kin is employed from

Mitsubishi Tanabe Pharma. KS is a medical adviser of Ono, Taiho, and Sawai. As a potential conflict of interest, Hospital Pharmaceutics received research grants from Daiichi Sankyo, Mochida, Shionogi, Ono, Taiho, Nippon-kayaku, and Bayer. TN received an honorarium fee for presentations from Sanofi. KM received an honorarium fee for presentations from Nippon-Kayaku and Abbvie Inc. YK received an honorarium fee for presentations from Daiichi Sankyo. HT received an honorarium fee for presentations from Daiichi Sankyo, Taiho, Bristol-Myers. KS received an honorarium fee for presentations from Daiichi Sankyo, Ono, Taiho, Yakult, Bristol-Myers. KT received an honorarium for presentations at AYUMI, Daiichi Sankyo, TERUMO, Chugai, Towa, and Taisho. The other authors declare no conflict of interest associated with this manuscript.

DATA AVAILABILITY STATEMENT

Author elects to not share data.

CONSENT

We obtained written informed consent for publication from the patient.

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