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CASE REPORT

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Acute kidney injury in villous cancer patients treated with vancomycin and tazobactam/piperacillin

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Villous cancer occurs due to abnormal growth of the placental cytotrophoblasts in pregnant women. It is rare with an incidence of 1.5:1 million.[1] The remission rate is reported to be above 80% with high-intensity chemotherapy, which includes methotrexate, actinomycin D, and etoposide (MAE). Patients treated with chemotherapy frequently suffer from febrile neutropenia or severe infections requiring antibiotic treatment.

We previously reported that acute kidney injury (AKI) is observed in approximately 25% of patients with hematological malignancies treated with vancomycin (VCM) and tazobactam/piperacillin (TAZ/PIPC).[2] This proportion is higher than that with co-administration of VCM with cefepime (8.6%) and meropenem (2.6%), although the VCM trough levels were not affected. One possible yet unclear mechanism of drug–drug interactions inducing AKI is VCM-induced cell necrosis associated with acute interstitial nephritis due to TAZ/PIPC. In this report, we present the case of a patient with villous cancer who developed AKI after co-administration of VCM and TAZ/PIPC.

A 37-year-old woman with villous cancer was admitted to the Showa University Hospital in May 2021. We administered MAE (methotrexate 450 mg/body every 3 weeks on day 1, actinomycin D 0.5 mg/body every 3 weeks from day 1 to 5, and etoposide 100 mg/body every 3 weeks from day 1 to 5) as adjuvant chemotherapy after total abdominal hysterectomy. On day 14 after starting MAE therapy, she developed cellulitis of the left facies digiti manus with a confirmed gram-positive organism being cultured from the wound. Cefepime 6 g/day was started as empiric therapy. On day 0, we made an incision on her left facies digiti manus and changed the antibiotics to TAZ/PIPC 18 g/day and VCM 2–3 g/day as the causative bacteria was confirmed to be *Staphylococcus aureus*. One day after starting TAZ/PIPC and VCM, a grade 2 rash appeared whole body. We added fexofenadine 120 mg/day orally. On day 1, serum creatinine drastically increased from 0.45 mg/dL to 0.88 mg/dL. On day 2, the rash was under control, but serum creatinine increased to 1.62 mg/dL, and the trough concentration of VCM was at toxic levels at 37.7 μg/mL. Subsequently, we discontinued TAZ/PIPC and VCM on the same day. On day 3, the trough concentration of VCM decreased to 8.6 μg/mL, and we restarted VCM at 1.5 g/day. On day 7, VCM was increased to 2 g/day because of its low trough concentration of 9.9 μg/mL, and subsequently, it reached the target range of 13 and 15.9 μg/mL on days 9 and 11, respectively. On day 17, the patient was discharged as the cellulitis had reduced (Figure 1).

In this report, we present a young patient with villous cancer whose renal function drastically worsened after co-administration of TAZ/PIPC and VCM. We previously reported similar drug–drug interactions in patients

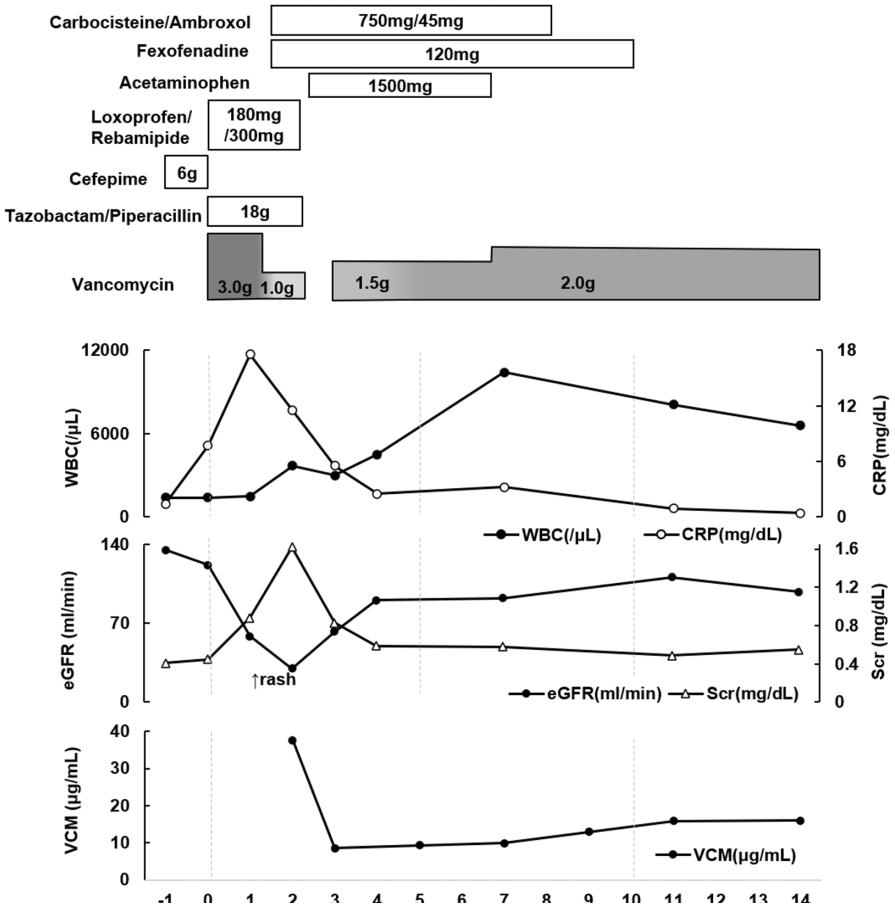

FIGURE 1 Clinical course of the present case

with hematological cancer with bone marrow suppression.[2] The AKI risk for VCM co-administered with TAZ/PIPC is higher than that of VCM co-administration with cefepime.[3-5] Our patient showed drastic worsening in renal function after co-administration of VCM and TAZ/PIPC within 24 hours of starting both drugs. Conversely, renal function was not affected when cefepime was administered alone. This suggests that renal toxicity in our case may have been caused by the co-administration of VCM and TAZ/PIPC. In addition, we did not observe renal toxicity upon restarting VCM in the absence of TAZ/PIPC. The VCM levels were therapeutic at 13 μg/ml on day 9. In previous reports, AKI was higher in VCM and TAZ/PIPC combination therapy than in VCM monotherapy.[6,7] The affinity of TAZ/PIPC for renal transporters is high, and it might competitively inhibit renal tubular secretion, thereby reducing the renal clearance of other antibiotics.[8] To date, pharmacokinetic drug–drug interactions of VCM and TAZ/PIPC have not been reported. These results suggest that the cause of AKI was (1) TAZ/PIPC and VCM drug–drug interaction and (2) higher VCM concentrations following co-administration of both drugs, inducing renal toxicity.

In conclusion, our case suggests that TAZ/PIPC and VCM co-administration should be avoided due to its potential nephrotoxic effects. The mechanism requires further investigation to be validated.

AUTHOR CONTRIBUTIONS

All authors met the ICMJE recommendations. KM and KN contributed to the study concept and drafted the manuscript. KN collected the raw data. TS, EY, and TM performed the clinical interpretation. KM and KN conducted the study. All authors participated in the discussion during manuscript preparation. All authors have agreed to publish this manuscript.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

The authors elect to not share the data.

CONSENT

We obtained written informed consent from the patient for publication of this report.

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