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CASE REPORT

Clinical course involving thrombocytosis and thrombocytopenia in a patient with bladder cancer treated with gemcitabine and cisplatin

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Abstract

Gemcitabine induce thrombocytopenia and thrombocytosis as toxicity. In this report, we show detailed time-course for platelet fluctuation. Our case emphasis attention to monitor see-saw-like toxicity on platelet count.

KEYWORDS

gemcitabine, thrombocytopenia, thrombocytosis, time-course, toxicity

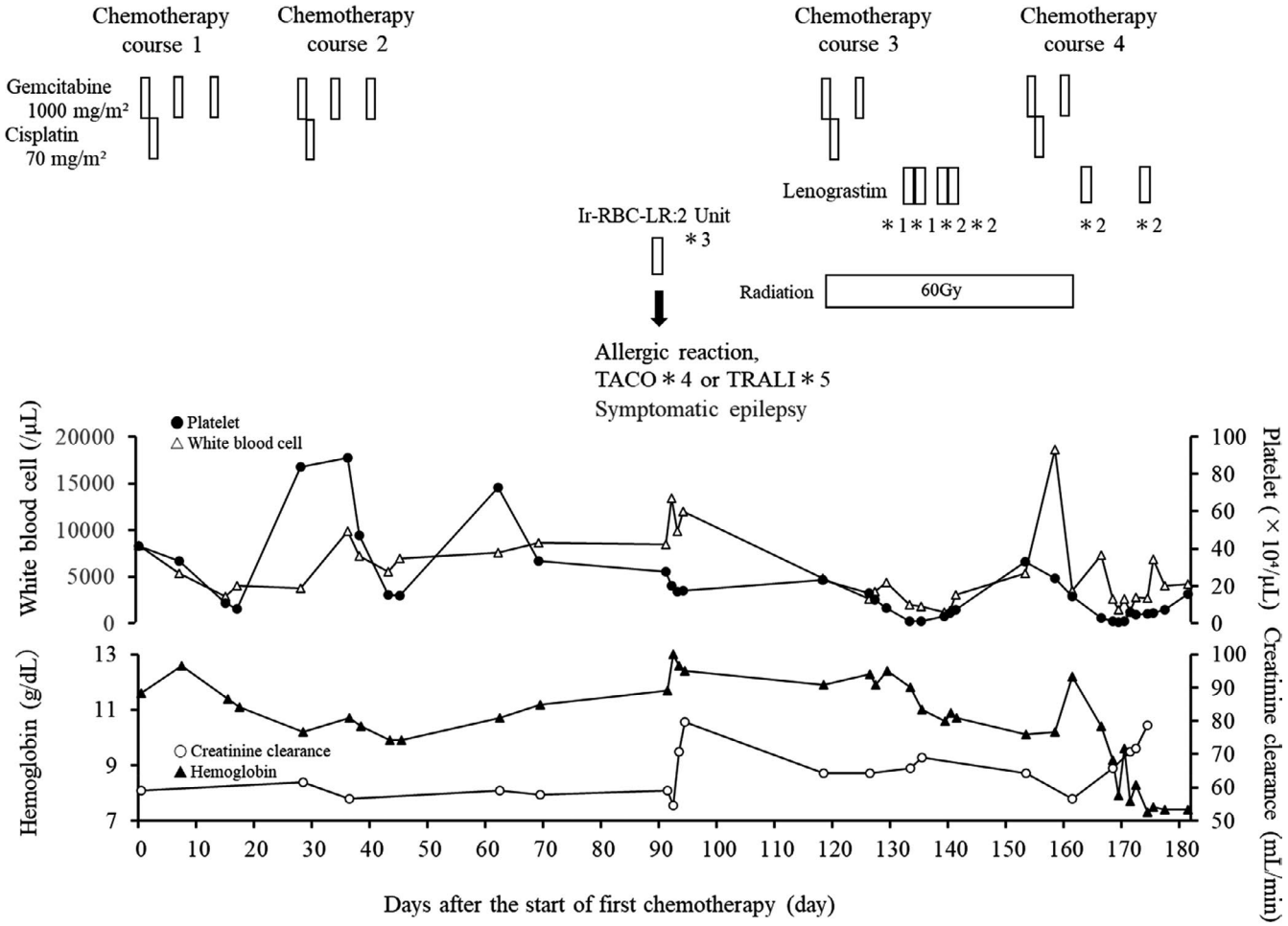
1 | INTRODUCTION

Platelet fluctuation such as thrombocytopenia is usually observed in clinical settings caused by chemotherapy-induced toxicity. Thrombocytopenia caused by gemcitabine and cisplatin has been reported approximately 71% and 57%.[1,2] On the contrary, thrombocytosis is reported only some chemotherapy agents such as gemcitabine, vinca alkaloids, and irinotecan.[3] Thrombocytosis in chemotherapy with gemcitabine alone or in combination with cisplatin or carboplatin has been reported as 49% and 46%.[4,5] However, time-course information in chemotherapy-induced thrombocytosis and thrombocytopenia is lacking. We, herein, present the case of a patient with thrombocytosis who had a repeated history of gemcitabine and cisplatin (GC)-based chemotherapy for bladder cancer.

A 69-year-old woman with Class III urine cytology was admitted to Showa University Koto Toyosu Hospital for clinical investigation. Transurethral resection of the bladder tumor (TUR-Bt) was performed to confirm the pathology. After stage II bladder cancer (invasive urothelial carcinoma, pT2, G2>G3, LVIx) was detected, we started 2 cycles of GC therapy (1000 mg/m^2 gemcitabine on days 1, 8, and 15 and 70 mg/m^2 cisplatin on day 2 for each 28 days) as neoadjuvant chemotherapy. During the first course of GC therapy, myelosuppression, such as leucopenia and thrombocytopenia, was observed. On the contrary, her platelet count temporarily increased from 7.8×10^4/μl to 88.7×10^4/μl at 36 days after GC therapy. A tendency of a temporary increase in the platelet count (from 15.1×10^4/μl to 72.6×10^4/μl at 34 days after GC therapy) was repeatedly observed in the second course of GC therapy (Figure 1).

After she completed her planned neoadjuvant chemotherapy, she was admitted to our hospital on day 91 to undergo total cystectomy. She developed transfusion-associated circulatory overload (TACO), or transfusion-related acute lung injury (TRALI), and symptomatic epilepsy due to preoperative red blood cell transfusion. Therefore, we did not perform the operation and planned to continue GC therapy and radiation therapy (total dose: 60 Gy). During the third course of GC therapy, she developed severe myelosuppression, that is, leucopenia (grade 3), anemia (grade 2), and thrombocytopenia (grade 4). During the fourth course of GC therapy, myelosuppression, including thrombocytopenia was observed 16 days after GC therapy.

Our patient had a repeated history of thrombocytosis, but the magnitude gradually decreased, and finally, the platelet count decreased to the thrombocytopenia level during the third and fourth courses of chemotherapy. This unique time-course of temporal platelet enhancement and change in magnitude has been rarely reported. We diagnosed thrombocytopenia due to gemcitabine and cisplatin, thrombocytosis due to gemcitabine. The mechanism underlying gemcitabine-induced thrombocytosis is currently unknown; however, chemotherapy is reported excessive platelet production as a toxicity,[6,7] and the platelet gains higher reactivity by injuring the vascular endothelium by chemotherapy.[7] These may partially explain chemotherapy inducing thrombocytosis in our case. Red blood cell transfusion is known to have an immunosuppressive effect.[8,9] In our case, thrombocytopenia was observed after TRALI, though thrombocytosis observed only



＊1: Lenograstim 200 μg intravenous infusion
＊2: Lenograstim 100 μg subcutaneous injection
＊3: Irradiated Red Blood Cells, Leukocytes Reduced
＊4: Transfusion-associated circulatory overload
＊5: Transfusion-related acute lung injury

FIGURE 1 Clinical course in the present case

before TRALI. Immunosuppression by red blood transfusion may affect to enhance the magnitude for reduction of platelet count by repeated chemotherapy-based cytotoxicity. So, therefore, we think that TRALI and thrombocytopenia are not related interactively in our case.

In conclusion, the platelet rebound and see-saw-like reaction accompanies with gemcitabine-based chemotherapy is complex. These situations alter bone marrow function and may cause exhaustion over repeated chemotherapy treatments.[10] Platelet enhancement sometimes occurs; however, this may not have been observed continuously.

Our case emphasis intensively to need closely monitoring for platelet because of drastic change from thrombocytosis to thrombocytopenia in a case treated with gemcitabine-based chemotherapy.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

All authors meet the ICMJE recommendations. Especially, KM and AW contributed to the study conception and drafted the manuscript. AW, RK, and TN collected raw data. MM interpreted clinically. KT and TS completed the study. All authors took part in the discussion during manuscript preparation. All authors have agreed to publish this manuscript.

ETHICAL APPROVAL

None.

CONSENT

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

DATA AVAILABILITY STATEMENT

Author elects to not share the data.

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REFERENCES

1. Kaneko G, Kikuchi E, Matsumoto K, et al. Neoadjuvant gemcitabine plus cisplatin for muscle-invasive bladder cancer. *Jpn J Clin Oncol*. 2011;41:908-914.
2. von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. *J Clin Oncol*. 2000;18(17):3068-3077.
3. Vo QT, Thompson DF. A review and assessment of drug-induced thrombocytosis. *Ann Pharmacother*. 2019;53:523-536.
4. Canova S, Cicchiello F, Agustoni F, et al. Gemcitabine-induced thrombocytosis as a potential predictive factor in non-small cell lung cancer: analysis of 318 patients. *Tumori*. 2017;103:143-147.
5. Ahmed S, Shahid RK, Bhatt H, Lee-Ying R, Lim J. Chemotherapy-related thrombocytosis: does it increase the risk of thromboembolism? *Oncology*. 2012;82:327-332.
6. Swieboda-Sadlej A, Kraj L, Krawczyk J, Nita E, Dwilewicz-Trojaczek J. Thrombocytosis in patients with pancreatic cancer treated with gemcitabine - does it have clinical significance? Description of 6 cases. *Contemp Oncol (Pozn)*. 2012;16:353-355.
7. Zecchina G, Ghio P, Bosio S, Cravino M, Camaschella C, Scagliotti GV. Reactive thrombocytosis might contribute to chemotherapy-related thrombophilia in patients with lung cancer. *Clin Lung Cancer*. 2007;8:264-267.
8. Remy KE, Hall MW, Cholette J, et al. Pediatric critical care blood research network (blood net). Mechanisms of red blood cell transfusion-related immunomodulation. *Transfusion*. 2018;58:804-815.
9. Opelz G, Terasaki PI. Improvement of kidney-graft survival with increased numbers of blood transfusions. *N Engl J Med*. 1978;299:799-803.
10. Georgiou KR, Foster BK, Xian CJ. Damage and recovery of the bone marrow microenvironment induced by cancer chemotherapy - potential regulatory role of chemokine CXCL12/receptor CXCR4 signalling. *Curr Mol Med*. 2010;10:440-453.

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