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Case Report

A case of oxaliplatin-induced immune thrombocytopenia followed by complete remission of metastatic colon cancer

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Abstract:

An 87-year-old male underwent laparoscopic left hemicolectomy for adenocarcinoma of the descending colon in December 2021. Lung metastasis was found in the left upper lobe 6 months postoperatively, and it increased in size after 9 months from the surgery. S-1 plus oxaliplatin (SOX) was started in October 2022. The lung metastasis was shrinking within 23 cycles of SOX therapy. The 24th cycle of SOX (only oxaliplatin) was administrated in April 2024, the catheter of venous infusion line of right forearm was removed after finishing the infusion, however bleeding did not stop. The platelet count was rapidly dropped into 2,000/μl from 131,000/μl (pretreatment) within 7 hours and hemoglobin levels decreased from 10.9 to 8.9 in the same period, furthermore, dropped into 6.2 g/dl in next 24 hours. PA-IgG was significantly high (204.0 ng/107 cells; normal < 30.2). Transfusion of platelet, red blood cell concentrate, steroid pulse therapy, antibiotic treatment with multiple agents and non-invasive positive pressure ventilation (NPPV with oxygen were performed. As a result, the patient's platelet count was increased and his DIC score was decreased to 3 points (normal range) in April 2024. The patient's general condition gradually improved, and he was discharged from hospital on the 35th day of hospitalization. CT scan after discharge showed complete remission of the lung metastasis. Possible mechanisms and approach to treatment are discussed.

Key words: oxaliplatin, OIIS, thrombocytopenia, Evans syndrome

Introduction

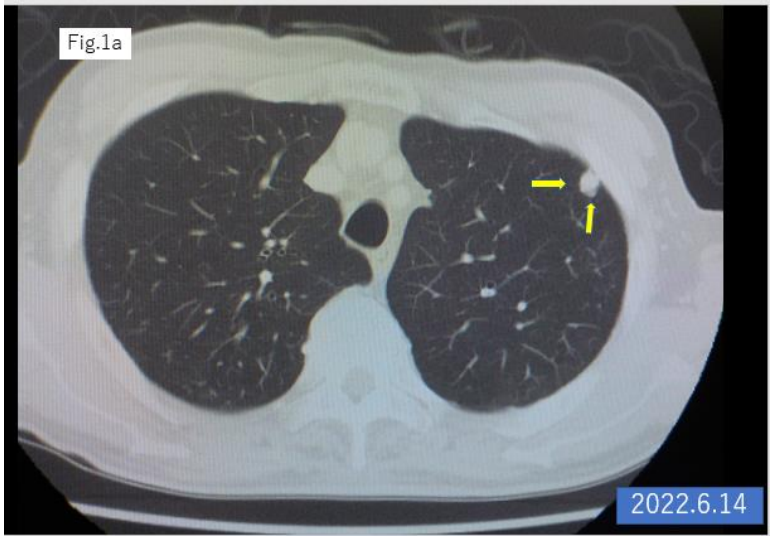
Hematological disorders are common adverse effects of anticancer chemotherapeutic agents. Among them, thrombocytopenia is a frequently experienced complication during chemotherapy and sometimes is remained even after the chemotherapy is terminated. Chemotherapy-induced thrombocytopenia sometimes cause chemotherapy delays, dose reductions, and discontinuation of chemotherapy, and have negative influences on treatment outcomes. There is no approved agent available to manage thrombocytopenia [1].

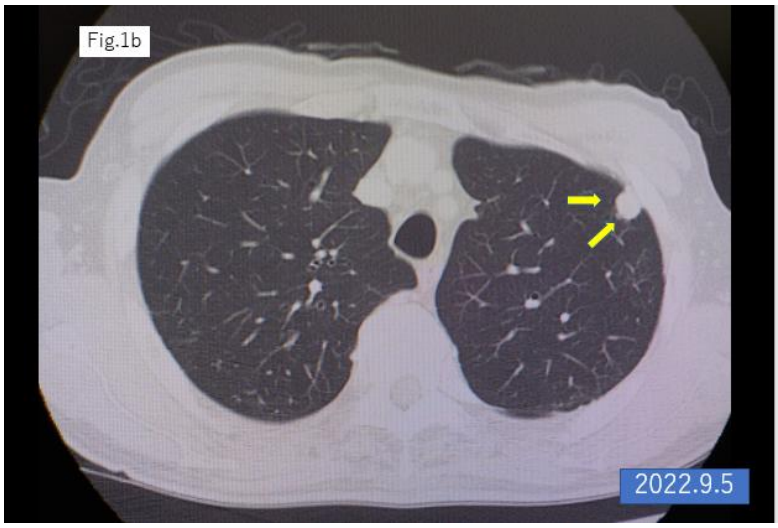
Oxaliplatin, a third generation platinum analog binding to DNA forming cross-links that inhibit DNA replication and transcription, is a standard component of 5-fluorouracil-based chemotherapy for gastrointestinal cancers, prolonging progression-free survival and overall survival in multiple clinical studies [2,3]. Several trials have shown the feasibility and efficacy of S-1 plus oxaliplatin (SOX) as an upfront chemotherapy for metastatic colorectal cancer [4,5.] Other than the common adverse effects such as bone marrow suppression and gastrointestinal symptoms, neurotoxicity including cold-induced parenthesias of distal extremities become sometimes serious, leading to motion disorder when the administration was continued [6]. Allergic reaction is also a common complication that occurs after several courses of oxaliplatin-containing regimen, and is usually manageable with steroid therapy [7,8]. Drug-

induced immune thrombocytopenia (ITP) is another uncommon side effect of oxaliplatin therapy. We herein present a case of oxaliplatin-induced ITP occurring after 24 courses of SOX therapy in which complete remission of the lung metastasis was demonstrated after thrombocytopenia is recovered.

Case presentation

An 87-year-old male underwent laparoscopic left hemicolectomy with a diagnosis of adenocarcinoma of the descending colon in December 2021. Lung metastasis was found in the left upper lobe 6 months postoperatively, and it increased in size after 9 months from the surgery (Figures 1a,b). The patient began S-1 plus oxaliplatin (SOX) treatment with first-line chemotherapy consisting of oral S-1 (a mixed drug of tegafur, gimeracil, and oteracil potassium) at a dose of 50 mg twice daily for 2 weeks following by 1-week off schedule, and intravenous oxaliplatin (100 mg/m^2) given on day 1 of a 3-week cycle [2,3], was started in October 2022.The lung metastasis was shrinking within 23 cycles of SOX therapy (Figures 1c–f). The 24th cycle of SOX (only oxaliplatin) was administrated in April 2024, the catheter of venous chemotherapy line of right forearm was removed after finishing the infusion, however bleeding did not stop. The patient had vomiting, chill and pale face, and was transferred to the intensive care unit. The platelet count was rapidly dropped into 2,000/μl from 131,000/μl (pretreatment) within 7 hours and hemoglobin levels decreased from 10.9 g/dl to 8.9 g/dl in the same period, furthermore, dropped into 6.2 g/dl in next 24 hours. Disseminated intravascular coagulation (DIC) score was 8 points, and platelet-associated IgG (PA-IgG) was significantly high (204.0 ng/10^7 cells; normal < 30.2 ng/10^7 cells; Figure 2). CT scan revealed alveolar hemorrhage. Transfusion of platelet, red blood cell concentrate, steroid pulse therapy, antibiotic treatment with multiple agents and non-invasive positive pressure ventilation (NPPV) with oxygen were performed in the hospitalization. Nutritional management was done by intravenous hyperalimentation. The platelet count was increased to 133,000/μl, and DIC score was decreased to 3 points (normal range) in April 2024. Oral intake was started, leading to gradual improvement of the patient's general condition, and discharge from hospital 35 days after admission. CT scan after discharge showed complete remission of the lung metastasis (Figures 1 e,f). Steroid treatment was tapered, and at the time of writing, the patient is being carefully followed up in an outpatient clinic without any of anticancer therapy in a good condition.





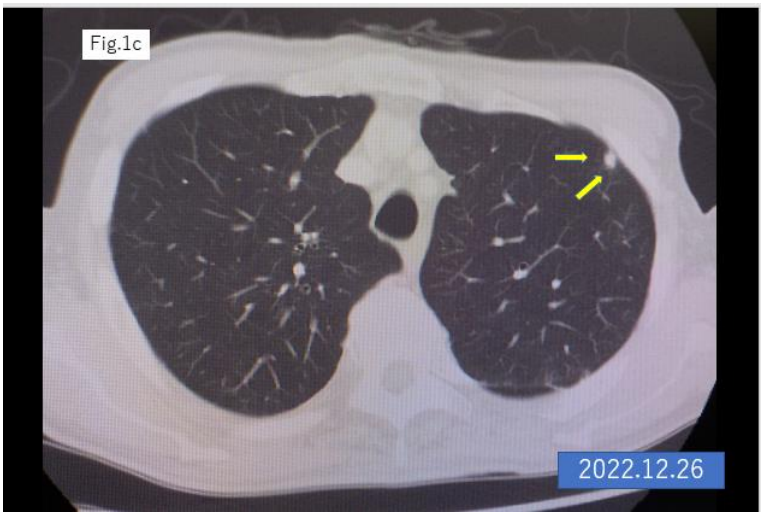


Fig.1c
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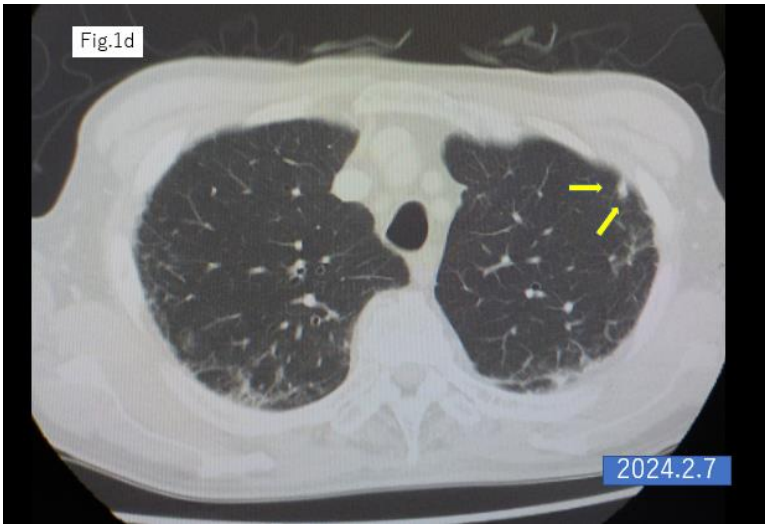
Fig.1d
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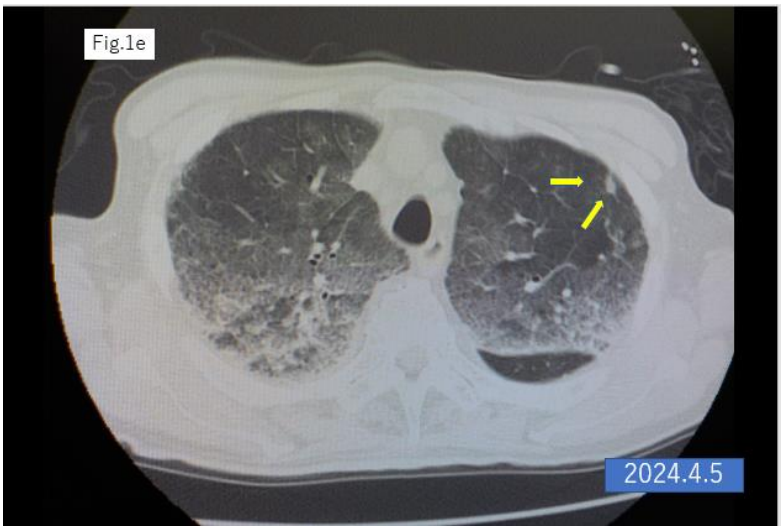
Fig.1e
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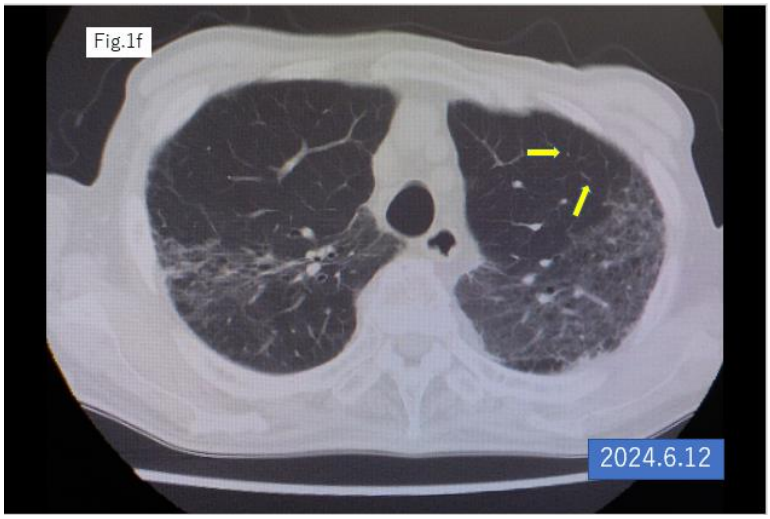

Figure 1: CT scan of the lung

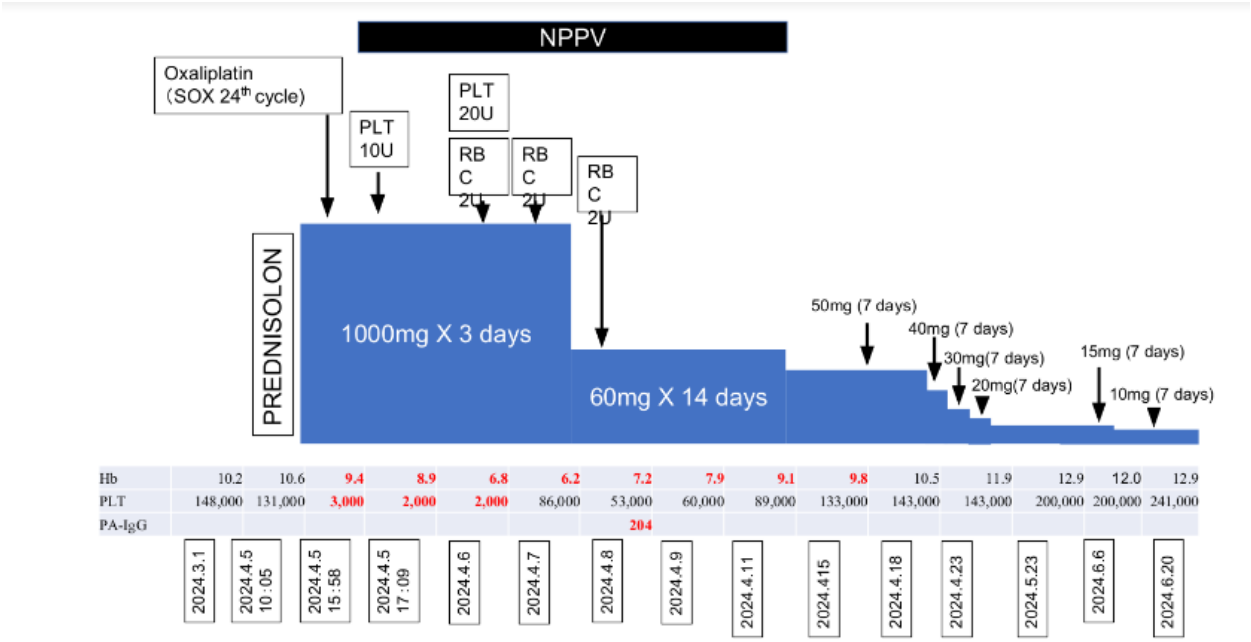

Figure 2: Clinical course of the patient

NPPV, non-invasive positive pressure ventilation

PLT 10U, platelet transfusion of 10 units

RBC 2U, transfusion of red blood cell concentrate of 2 units

Hb, hemoglobin (g/dl)

PLT, platelet count (/μl)

PA-IgG, platelet associated IgG (ng/10^7 cells)

Discussion

Allergic hypersensitivity has been reported to occur in 10–23.8% of patients who have undergone oxaliplatin therapy, known as a type I hypersensitivity reaction involving IgE mediated release of antibodies, is well known complication and is usually well-managed with using steroid [9-11]. Oxaliplatin-induced ITP, as shown by our case, is a type II hypersensitivity reaction involving release of IgG antibodies binding tos

platelet surface [12-15]. These two types of allergic reaction are known as oxaliplatin induced immune syndrome (OIIS) and the latter, as shown in the present case, has been reported to present hyperacute thrombocytopenia is recommended to be treated with steroid pulse therapy and platelet transfusion. In the present case, although DIC score was high and sufficient for DIC diagnosis, anticoagulation therapy was not selected but steroid pulse as well as infusions of platelets and concentrated red blood cells were performed, and alveolar bleeding and pneumonia were successfully managed followed by recovery. Although no anticancer therapy was administered since the onset of thrombocytopenia, the nodule of lung metastasis was disappeared after the recovery, and the mechanisms of this anti-tumor reaction are not clear. Given that oxaliplatin has been reported to induce immunogenic cell death in the tumor microenvironment [16,17], anti-tumor immune reactivities including in immunological memory may exist, and some mechanisms of immunosuppression might be altered by chain of immunological events occurred to this patient.

Evans syndrome, first reported in 1951 [18], is an uncommon condition characterized by ITP combined with autoimmune hemolytic anemia (AHA) with a positive direct antiglobulin test (DAT) and a positive direct Coombs test [19]. In the present case, since hemoglobin levels were dropped from 10.6 into 6.2 g/dl within 2 days combined with thrombocytopenia, the underlying pathophysiology of our case might be included in Evans syndrome. Rousseau et al. reported that there are two mechanisms, hapten-specific and neoantigen-dependent (immune complex), that are involved when Evans syndrome is induced by oxaliplatin [20]. In the second mechanism especially, the complement system may be activated, and the disappearance of metastatic nodule in our case might be associated with complement-dependent cytotoxicity against cancer cells.

Conclusion

Although this entity of pathophysiology is uncommon and has not been described well in the past reports, appropriate managements such as steroid pulse and blood transfusion may succeed. This life-threatening symptom should motivate physicians to refer to specialized laboratory examination for OIIS and Evans syndrome during and after oxaliplatin therapy.

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References

1. Al-Samkari H and Soff GA. (2021). Clinical challenges and promising therapies for chemotherapy-induced thrombocytopenia. Exp Rev Hematol 14(5): 437-448.
2. Andre T, Boni C, Navarro M, Tabernero J, Hickish T, Topham C, et al.(2009). Improved overall survival with oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment in stage II or III colon cancer in the MOSAIC trial. J Clin Oncol 27(19): 3109-3116.
3. De Gramont A, Figer A, Seymour M, Homerin M, Hmissi A, Casidy J, et al. (2000).Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. J Clin Oncol 18(16): 2938-2947,.
4. Hong YS, Park YS, Lim HS, Lee J, Kim TW, Kim K-P, et al. (2012). S-1 plus oxaliplatin versus capecitabine plus oxaliplatin for first-line treatment of patients with metastatic colorectal cancer: a randomized, non-inferiority phase 3 trial. Lancet Oncol 13(11): 1125-1132
5. Baba H, Yamada Y, Takahari D, Matsumoto H, Yoshida K, Nakamura M, et al. (2017). S-1 and oxaliplatin (SOX) plus bevacizumab versus mFOLFOX6 plus bevacizumab as forst-line treatment for patients with metastatic colorectal cancer: updated overall survival analyses of open-label, non-inferiority, randomized phase III: SOFT study.ESMO Open.;2(1): e000135.
6. Argyriou AA, Cavaletti G, Briani C, Velasco R, Bruna J, Campagnolo M, et al. (2013).Clinical pattern and association of oxaliplatin acute neurotoxicity: a prospective study in 170 patients with colorectal cancer. Cancer 119(2): 438-444
7. Mori T, Nishimura T, Kitano T, Yoshimura K, Matsumoto S, Kanai M, et al. (2010).Oxaliplatin-free interval as a risk of hypersensitivity reaction among colorectal cancer patients treated with FOLFOX. Oncology 79(1-2): 136-143
8. Shen Y, Li C, Liu W, Mao W, Qian H, and Xu, Q. (2018).Clinical analysis of hypersensitivity reactions to oxaliplatin among colorectal cancer patients. Oncol Res 26 : 801-807
9. Kim BH, Bradley T, Tai J, and Budman DR.(2009). Hypersensitivity to oxaliplatin; an investigation of incidence and risk factors, and literature review. Oncology 76(4):231-238.
10. Seki K, Senzaki K, Tsuduki Y, Ioroi T, Fujii M, Yamauchi H, et al. (2011).Risk factors of oxaliplatin-induced hypersensitivity reactions in Japanese patients with advanced colorectal cancer. Int J Med Sci 8(3) : 210-215.
11. Gowda A, Goel R, Berdzik J, Leichman CG, and Javle M. (2004).Hypersensitivity reactions to oxaliplatin: incidence and management. Oncology (Williston Park) 18(13):1671-1675; discussion 1676,1680, 1683-1684. [PubMed: 15648298]
12. Stack A, Khanal R, and Denlinger CS.(2021).Oxaliplatin-induced immune thrombocytopenia: A case report and literature review. Clin Colorectal Cancer 20(1): e1-e4.
13. Suh SE, Jang MJ, Chong SY, Aster RH, Curtis BR, Oh D. A case of oxaliplatin-induced immune-mediated thrombocytopenia. Blood Res 49(1), :61-64.
14. Jardim DL, Rodrigues CA, Novis YAS, Rocha VG, Hoff PM (2012.). Ann Oncol 23:1937-1942.
15. Bencardino K, Mauri G, Amatu A, Tosi F, Banazzina E, Palmeri L, et al. (2016).Oxaliplatin immune-induced syndrome occurs with cumulative administration and rechallenge: Single institution series and systematic review study. Clin Colorectal Cancer 15(3): 213-221
16. Wang J, Zhang H, Yin X, Bian Y. (2022).Oxaliplatin induces immunogenic cell death in human and murine laryngeal cancer. J Oncol
17. Tesniere A, Schlemmer F, Boige V, Kepp O, Martins I, Ghiringhelli F, et al. (2010) Immunogenic death of colon cancer cells treated with oxaliplatin. Oncogene 29: 482-491.
18. Evans RS, Takahashi K, and Duane RT. (1951).Primary thrombocytopenic purpura and acquired hemolytic anemia. Evidence for a common etiology. AMA Arch Intern Med 87(1):48-65,
19. Norton A, and Roberts I.(2006) Management of Evans syndrome. Br J Haematol 132(2):125-137,

20. Rouseau C, Nguyen TN, Rebibou JM, Bastie JN, Audia S, Darut-Jouve A, and Legendre M. (2020).Oxaliplatin-induced Evans syndrome: a possible dual mechanism. Clin Colorectal Cancer 19(1): 57-60.

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