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OXALIPLATIN-INDUCED IMMUNE THROMBOCYTOPENIA IN A PATIENT WITH PANCREATIC CANCER

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ABSTRACT

Oxaliplatin-induced immune thrombocytopenia is a rare but potentially serious complication of chemotherapy. We present the case of a 55-year-old man with stage 4 pancreatic carcinoma who developed immune thrombocytopenia during the 18th cycle of folinic acid, fluorouracil, irinotecan, and oxaliplatin (FOLFIRINOX) chemotherapy, immediately after oxaliplatin infusion. Despite treatment with methylprednisolone and platelet infusion, the patient's platelet count remained low. Subsequent plasmapheresis and continued steroid therapy resulted in a gradual improvement in platelet count and resolution of symptoms. This case highlights the importance of considering immune thrombocytopenia in patients receiving oxaliplatin-based chemotherapy, and the potential role of plasmapheresis in refractory cases. Further research is needed to elucidate the optimal management of this rare complication.

KEYWORDS

Oxaliplatin, oxalipatin-induced immune thrombocytopenia, thrombocytopenia

LEARNING POINTS

- Oxaliplatin-induced immune thrombocytopenia is a rare but potentially life-threatening side effect of chemotherapy.
- Management of drug-induced immune thrombocytopenia involves discontinuation of the offending drug and the use of steroids.
- Monitoring and follow-up are crucial in patients receiving oxaliplatin-based chemotherapy to promptly detect and manage potential hematologic emergencies, including immune thrombocytopenia.

INTRODUCTION

Oxaliplatin, a third-generation platinum derivative, is among the chemotherapeutic agents widely used in the treatment of pancreatic cancer. Drug-induced acute thrombocytopenia is a very rare side effect that can occur immediately after oxaliplatin infusion[1]. Oxaliplatin-induced immune thrombocytopenia cases have been rarely reported in the literature[2]. Drug-induced immune thrombocytopenia is the result of accelerated platelet destruction caused by drug-induced platelet antibodies. We present a case of immune

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thrombocytopenia occurring at the onset of oxaliplatin infusion in a patient undergoing folinic acid, fluorouracil, irinotecan, and oxaliplatin (FOLFIRINOX) chemotherapy.

CASE DESCRIPTION

A 55-year-old man with stage 4 pancreatic carcinoma, who had received 17 cycles of FOLFIRINOX chemotherapy, developed immune thrombocytopenia during the planned 18th cycle incorporating oxaliplatin, folinic acid, and 5-fluorouracil (FOLFOX). Prior to treatment, his hemoglobin level was 10.8 g/dl, white blood cell count was 3,930/ml, and platelet count was 241,000/ml. In 15 minutes after oxaliplatin infusion began, he experienced shivering and a body temperature of 37.4°C, followed by petechiae on his trunk and arms. Subsequent blood tests showed a platelet count of 2,000/ml, elevated white blood cell count of 8,190/ml, and hemoglobin level of 10.7 g/dl, with no coagulation abnormalities. There was no sign of venous thromboembolic disease or disseminated intravascular coagulation (INR 1.26; aPTT 27.1s and fibrinogen 301 mg/dl; D-dimers 18.36 mg/ml). Peripheral smear revealed low platelets, anisocytosis, and hypochromia in erythrocytes, but no schistocytes or micro spherocytes. Treatment with methylprednisolone (100 mg) and platelet infusion failed to raise platelet levels, leading to initiation of daily plasmapheresis and continued methylprednisolone therapy. Following this treatment, the platelet count improved to over 50,000/ml in 4 days. The platelet count improved to normal level just in week (over 150,000/ml). The patient was discharged 7 days after oxaliplatin infusion, with resolution of petechial lesions.

DISCUSSION

In our case, other possible etiologies were considered for this patient who developed symptomatic thrombocytopenia right at the beginning of the oxaliplatin infusion. Drug-induced immune thrombocytopenia is caused by the immune destruction of platelets by drug-induced antibodies[3]. The presence of drug-induced antibodies capable of reacting with platelet surface glycoprotein IIb/IIIa was detected in the serum of a patient with oxaliplatin-associated thrombocytopenia[4].

Cases of acute thrombocytopenia with or without hemolysis during or after oxaliplatin infusion have been reported in the literature. James et al.[5], reported oxaliplatin-induced thrombocytopenia developing in 3 cases without hemolysis during the 10th, 17th and 28th cycles of FOLFOX chemotherapy. Taleghani et al.[6] also reported a case of oxaliplatin-induced immune pancytopenia and showed oxaliplatin-dependent antibodies against red blood cells, platelets, and neutrophils. Beg et al.[7] reported two more cases of oxaliplatin-induced acute immune-mediated thrombocytopenia developed following the 12th and 17th cycles of FOLFOX chemotherapy. Bencardino et al.[8] published a study of 61 patients who developed oxaliplatin-induced immune syndrome. Oxaliplatin immune-induced syndrome is defined as a rare but life-threatening side effect. It encompasses a variety of immune reactions such as acute immune thrombocytopenia, immune-hemolytic anemia, thrombotic microangiopathies, and Evan's syndrome. It usually occurs after an average of 16 oxaliplatin cycles. In our case, it occurred during the oxaliplatin infusion during the 18th cycle of FOLFOX chemotherapy.

The Naranjo adverse drug reaction probability scale (Naranjo scale) was created to standardize the evaluation of causality for all adverse drug reactions. It was specifically designed for use in controlled trials and registration studies of new medications, rather than for routine clinical practice. Using traditional definitions and probabilities of definite, probable, possible and suspected adverse drug reaction results in wide variability in assessment[9]. Several case reports have documented oxaliplatin-induced thrombocytopenia. In the case of our patient, platelet levels were within normal range prior to the oxaliplatin infusion. However, an adverse reaction manifested 15 minutes into the infusion. Following this adverse event, oxaliplatin treatment was discontinued, and thrombocytopenia resolved by the fifth day of follow-up. The patient did not receive subsequent oxaliplatin treatment. Typically, thrombocytopenia occurs after an average of 16 cycles of oxaliplatin. In this instance, it developed during the oxaliplatin infusion administered as part of the 18th cycle of FOLFOX chemotherapy. There are no alternative causes of the reaction. Considering these conditions, our patient's Naranjo scale score was determined to be 8. A score of 5-8 indicates a probable adverse drug reaction.

In the treatment of drug-induced immune thrombocytopenia, the first step is discontinuation of the drug. Steroids are typically used to treat drug-related thrombocytopenia. In previous studies, thrombocytopenia has been shown to improve with steroid treatment. However, in our case, a rapid response was not achieved with steroid therapy alone. Therefore, plasmapheresis was initiated as an adjunctive treatment alongside steroid therapy. This approach was successful in improving the patient's platelet count and resolving symptoms.

CONCLUSION

The efficacy of methylprednisolone in drug-induced immune thrombocytopenia remains uncertain. Clinicians should be aware of the possibility of developing oxaliplatin-induced immune thrombocytopenia at any time during treatment with the oxaliplatin-based chemotherapy protocol. This case underscores the rare yet critical possibility of oxaliplatin-induced immune thrombocytopenia, highlighting the challenges in managing this hematologic emergency. In addition to high-dose steroid treatment, plasmapheresis should also be considered.

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