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Case Study

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Severe thrombocytopenia related to trastuzumab infusion

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Marina Mantzourani[ABDE], Helen Gogas[DEF], Aikaterini Katsandris[DEF], John Meletis[ABDE]

1st Department of Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, Laiko General Hospital, Athens, Greece

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Summary

Background: Trastuzumab is a humanized, monoclonal antibody that interferes with the HER2/neu receptor and binds selectively to the HERB2 protein which causes uncontrolled proliferation of malignant breast cells.

Case Report: We report a case of severe thrombocytopenia related to trastuzumab administration. Three days after the first dose of single-agent trastuzumab, the patient was admitted to the hospital with nose bleeding, petechiae and platelet counts of 5×10^9/L.

Conclusions: The patient showed a self-limiting trastuzumab-related thrombocytopenia. Among the reported cases of trastuzumab-induced severe thrombocytopenia, this patient is the only one who did not interrupt trastuzumab treatment. It is possible that our patient showed progressive reduction of immune-mediated thrombocytopenia caused by trastuzumab administration.

key words: thrombocytopenia • trastuzumab

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Author's address: John Meletis, 1st Department of Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, Laiko General Hospital, 17 Agiou Thoma, Goudi, Athens 11527, Greece, e-mail: imeletis@med.uoa.gr

Background

The HER receptors are proteins that are embedded into the cell membrane and communicate molecular signals regulating gene functions. They also regulate cell growth, survival, adhesion, migration and differentiation functions that are amplified or silenced in cancer cells. Trastuzumab is a humanized, monoclonal antibody that interferes with the HER2/neu receptor and binds selectively to the HERB2 protein. When binding to defective HER2 proteins, the HER2 protein no longer causes uncontrolled proliferation of malignant breast cells, and thus the drug increases the survival of women with breast cancer.

Trastuzumab is approved by the US FDA for the treatment of early- and late- stage HERB2-positive breast cancer, as it provides survival advantage in both metastatic and adjuvant disease [1,2]. The most common reported adverse-effects include a flu-like syndrome, hypersensitivity reaction and nausea; the most serious adverse effect is cardiac dysfunction. We report a patient with breast cancer and severe thrombocytopenia that was related by trastuzumab therapy [2].

Case Report

A 56-year-old woman presented at our oncology department with a 3-month history of a mass in her right breast. One month later the patient had a resection of the right breast mass and the biopsy showed ductal carcinoma of the breast, grade II, negative for estrogen and progesterone receptors but positive for HER2 (3+ positivity). The patient had 11 lymph nodes removed from the right axilla and none of them had a positive biopsy for metastasis.

Adjuvant therapy with trastuzumab was started at a loading dose of 8 mg/kg. Her full blood laboratory examination was normal. Three days after trastuzumab initiation, she noticed a petechiae rash covering her whole body and nose bleeding started the same day. She went to the hospital, where a severe thrombocytopenia (platelets counts of 5×10^9/l) was revealed. The patient was admitted for the management of thrombocytopenia. She was treated for immune thrombocytopenic purpura and received therapy with intravenous immunoglobulin (IVIGs) 0.5 g/kg for 5 days with good response. Her symptoms and platelets counts recovered to within normal range on the fifth day of treatment and the patient was released.

The patient was admitted in our department for continuation of her treatment with trastuzumab and daily blood examination. After 21 days after the first cycle, a second cycle of trastuzumab at dose of 6 mg/kg was administered. Three days later, her platelets had dropped to 28×10^9/l. Disseminated intravascular coagulation was excluded based on normal levels of fibrinogen, fibrin degradation products and the cross-linked fragment, D-dimer. She was negative for human immunodeficiency virus and serological testing did not reveal other viral infections (HBV, HCV, CMV, EBV, Parvovirus B19, Herpes zoster virus, Herpes virus 1 and 2). Bone marrow aspirate and trephine biopsy showed no abnormalities, with normal megakaryopoiesis and no infiltration by tumor cells. Additional laboratory tests provided no evidence of secondary thrombocytopenia, suggesting a diagnosis of ITP, according to the American Society of Hematology criteria. The platelet counts very soon recovered (50×10^9/l on the 6th day), and 10 days later their number was within normal limits. During the third cycle of trastuzumab, the platelet counts dropped to 128×10^9/l on the third day after trastuzumab infusion, and then the patient continued and completed the treatment with trastuzumab without thrombocytopenia and without any other adverse event.

Discussion

Several medications are implicated to drug-induced thrombocytopenia, but the diagnosis is usually made by exclusion [3]. In our case, treatment with trastuzumab led to severe thrombocytopenia and the same phenomenon reoccurred twice, but stopped after the third cycle of treatment. Although there are reports in the literature of 3 patients who had thrombocytopenia after treatment with trastuzumab, none of them could continue on trastuzumab therapy [4–7]. The exact pathogenesis of drug-induced thrombocytopenia is unknown. However, there are several models that try to explain this phenomenon and implicate hapten-induced antibodies, drug-dependent antibodies, glycoprotein IIb/IIIa inhibitors or direct bone marrow toxicity [3,8]. In our patient, the time of onset of thrombocytopenia is directly connected with the infusion of trastuzumab and could be attributed to classic drug-induced immune-mediated thrombocytopenia. Management of drug-induced thrombocytopenia includes immunoglobulin therapy, or corticosteroids and platelets transfusion in cases of severe hemorrhage. Our patient had a course of IVIGs at the first episode of thrombocytopenia and continued on trastuzumab treatment without other problems.

Conclusions

In conclusion, our patient showed a self-limiting trastuzumab-related thrombocytopenia. There are 3 other cases reported in the literature of trastuzumab-induced severe thrombocytopenia, but this patient is the only one who did not interrupt trastuzumab treatment. We do not know why our patient showed progressive reduction of this possible immune-mediated thrombocytopenia that was caused by trastuzumab.

Competing interests

The authors declare that they have no competing interests.

Consent

Written consent was obtained from the patient for publication of this case report.

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