Paclitaxel therapy and immune thrombocytopenic purpura: Coincidence or association?

Paclitaxel tedavisi ve immun trombositopeni: Rastlantı mı, ilişki mi?

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To the Editor,

Thrombocytopenia is defined as a platelet count <150,000 μL^{-1}. Primary causes of thrombocytopenia are decreased production of platelets in the bone marrow and increased destruction of platelets in the spleen [1]. Thrombocytopenia is most commonly observed in cancer patients as a result of direct tumor infiltration in the bone marrow, and bone marrow toxicity due to chemotherapy and/or radiotherapy. Clinical diagnosis of drug-induced thrombocytopenia can be made when thrombocytopenia is reversed following withdrawal of the suspected drug and doesn't develop during follow-up.

Drug-induced thrombocytopenia can be caused by various medications. Drug-induced thrombocytopenia is the result of bone marrow suppression and destruction of platelets in peripheral blood due to immune or non-immune mechanisms [1,2]. Paclitaxel-induced thrombocytopenia percentage is reported to be 4-20%, and 1-7 % if the grade of trombocytopenia is grade 3-4. [3]. Our aim was to present a rare case of immune thrombocytopenic purpura (ITP) following paclitaxel treatment.

Modified radical mastectomy was performed in a 47-year-old female patient following a biopsy of a mass in the upper lateral quadrant that was diagnosed as invasive ductal carcinoma. The tumor was grade II, T3N0M0 invasive ductal carcinoma. CerbB2 score was 1, level of estrogen receptor expression was 60% and progesteron receptor expression was 60%. The patient was treated with 4 courses of cyclophosphamide, epirubicin, and 5-fluorouracil, as well as radiotherapy to the surgical area, followed by weekly treatment with paclitaxel. After taking paclitaxel for 7 weeks the patient presented with rashes on her leg. The patient's hemogram results were as follows: leukocyte count: 5700 μL^{-1}; hemoglobin: 11.9 g dL^{-1}; platelet count: 7000 μL^{-1}. Paclitaxel treatment was discontinued due to suspicion of drug-induced bone marrow suppression. Written informed consent was obtained from the patient.

The patient did not come for regular follow-up visits, but presented 2 months after paclitaxel treatment was withdrawn; hemogram results at that time were as follows: leukocyte count: 6270 μL^{-1}; hemoglobin: 12.9 g dL^{-1}; platelet count: 9740 μL^{-1}. She was hospitalized. Peripheral blood smear did

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doi:10.5152/tjh.2011.35

not show atypical cells, but several single platelets were observed. Aggregated platelets were not observed. Brucella agglutination, salmonella group agglutination, ANA, TORCH panel, HBsAg, anti-HCV, anti-HIV, and urea breath test results were negative. Thyroid function test and abdomen ultrasonography results were normal. Bone marrow biopsy was performed on the third day of hospitalization. Analysis of the biopsy specimen showed an increase in the number of hematopoietic cells of erythroid, myeloid, and megakaryocytic lineage. Findings for blastic cell infiltration and carcinoma metastases were negative. Due to the persistence of thrombocytopenia 2 months after the discontinuation of paclitaxel and lack of any other cause for ITP, the patient was diagnosed with immune thrombocytopenic purpura (ITP) and prednisolone treatment (1 mg kg^{-1}) was initiated. The patient's platelet count began to increase within 24 h. After 1 week of prednisolone treatment the platelet count reached 150,000 μL^{-1}.

ITP is an acquired disorder caused by antibodies against platelets and progresses as platelet destruction increases [1]. The literature contains only a few cases of ITP that developed following paclitaxel-containing chemotherapy [4]. The occurrence of ITP in the presented case during the period in which the disease was controlled ruled out the diagnosis of malignancy-related paraneoplastic syndrome. The patient's bone marrow was not hypocellular; therefore, diagnosis of bone marrow suppression secondary to drug use was also eliminated. There was no clear explanation for the patient's persistent ITP 2 months after paclitaxel was withdrawn. There is an association between paclitaxel 's elimination half-life and the time to platelet recovery in cases of drug-induced thrombocytopenia [5,6]. As the mean elimination half-life of paclitaxel is 5.8 h, one could expected that platelet recovery after discontinuation of paclitaxel would normally occur within 1 week; however, case reports describe thrombocytopenia persisting beyond the traditional 4-5 half-lives of the drug. Quinidine's half-life is approximately 6 h, but in 1 report recovery time was as long as 15-30 d following withdrawal of the drug. It was theorized that the antibody originally directed against the drug-protein complex might have broadened its spectrum so that an antigen on the platelets became the target [5].

The presented patient's ITP might have been related to a paclitaxel-induced immunological mechanism or coincidence. There is a need for further clinical studies involving large numbers of patients to more fully understand this subject. In conclusion, great care should be exercised in patients using paclitaxel, with regard to ITP and neutropenia [6].

Conflict of interest statement

The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

References

1. Hillman RS, Ault KA, Rinder HM. Thrombocytopenia. In: Hematology in clinical practice. 4th ed. New. York: McGraw-Hill, 2005:339-56.
2. Casciato DA. Hematologic complications. Casciato DA, Territo MC(Ed) Manual of clinical oncology. 6th ed. Lippincott Williams&Wilkins,2009:658-83.
3. Solimando DA. Drug ınformation handbook for oncology. 6th ed. Lexİ- Comp Inc, 2007;804-9.
4. Demirer T, Celebi H, Arat M, Ustün C, Demirer S, Dilek I, Ozcan M, Ilhan O, Akan H, Gürman G, Koç H. Autoimmune thrombocytopenia in a patient with small cell lung cancer developing after chemotherapy and resolving following autologous peripheral blood stem cell transplantation. Bone Marrow Transplant. 1999;24:335-7.
5. Hackett T, Kelton JG, Powers P. Drug-induced platelet destruction. Semin Thromb Hemost 1982;8:116-37.
6. Rowinsky EK, Eisenhauer EA, Chaudhry V, Arbuck SG, Donehower RC. Clinical toxicities encountered with paclitaxel (Taxol). Semin Oncol. 1993;20:1-15.