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Heparin-induced Thrombocytopenia in Patients Receiving Plasma Exchange

To the Editor:

Heparin-induced thrombocytopenia is a rare complication of heparin use. Based on pathogenesis, it is classified into 2 types. Type 1 thrombocytopenia is a transient decrease in platelet count, which improves spontaneously, even with continuation of heparin. Heparin-induced thrombocytopenia Type 2, which is more severe, is caused by the formation of an antibody to the heparin-platelet factor 4 complex. The binding of the antibody to the complex results in platelet activation and widespread thrombosis by platelet consumption.[1] Heparin-induced thrombocytopenia is a clinical diagnosis. A 4T score (**T**iming, degree of **T**hrombocytopenia, **T**hrombosis, other causes of **T**hrombocytopenia) is used to assess the likelihood of heparin-induced thrombocytopenia.[1] It is treated by the discontinuation of heparin and the initiation of a nonheparin anticoagulant. We describe 2 cases of heparin-induced thrombocytopenia that arose in patients receiving heparin while on treatment with plasma exchange for other indications.

Patient 1 was a 33-year-old man admitted to our hospital with newly diagnosed acute inflammatory demyelinating polyradiculopathy. Starting on day 3 of admission, he underwent 5 sessions of plasmapheresis, on alternating days. Thrombocytopenia was noticed on day 11. A 4T score of 5 was calculated, and subcutaneous heparin, which was being used for deep vein thrombosis prophylaxis, was discontinued. Heparin antibody assay was positive, with >50% inhibition and level >0.4 optical density units. The patient was started on bivalirudin. Platelets recovered to normal range (150-450 $\times$ 10^9/L) by day 19 (**Figure**).

Patient 2 was a 55-year-old woman diagnosed with neuromyelitis optica and received 5 sessions of plasmapheresis, on alternating days, starting on day 10 of hospitalization. The patient had received subcutaneous heparin since day 1 of admission. Three days after initiation of plasma exchange, she developed thrombocytopenia. With a 4T score of 4, heparin-induced thrombocytopenia was suspected. Platelets continued to decrease and troughed at 44 $\times$ 10^9/L on day 17. Heparin was discontinued at this time. Heparin antibody returned positive, with >50% inhibition. At this time, argatroban was started for treatment of heparin-induced thrombocytopenia. Platelets count normalized by day 27 (**Figure**).

Both patients received heparin to flush dialysis catheter. Acid citrate dextrose solution-A was the anticoagulant used during each session of plasmapheresis.

DISCUSSION

As is typical of heparin-induced thrombocytopenia Type 2, both patients developed thrombocytopenia between days 4 and 14 after initiation of heparin therapy.[1] Patients received unfractionated heparin for deep vein thrombosis prophylaxis and for catheter flushes during plasmapheresis. The fact that thrombocytopenia developed after beginning plasmapheresis in both cases indicates that the heparin used for flushes has likely contributed to the heparin-induced thrombocytopenia, though subcutaneous heparin may have played a role. The rapid decrease in platelets after stopping apheresis in patient 1 makes us believe that plasmapheresis delayed the presentation of thrombocytopenia by removal of heparin antibodies.[2]

Clinicians should maintain a high level of suspicion for heparin-induced thrombocytopenia in patients developing thrombocytopenia or thrombosis while on any form of heparin. In addition, heparin-induced thrombocytopenia should be considered in the differential diagnosis of decreasing or inadequate recovery of platelet count while on plasmapheresis. Future use of heparin in these patients should be considered with caution and only after exclusion of heparin antibodies. In cases with nondiagnostic heparin antibody levels, serotonin release assay can confirm the diagnosis. In patients who have a history of heparin-induced thrombocytopenia, use of citrate-based anticoagulant solution to flush catheters is recommended, instead of heparin.

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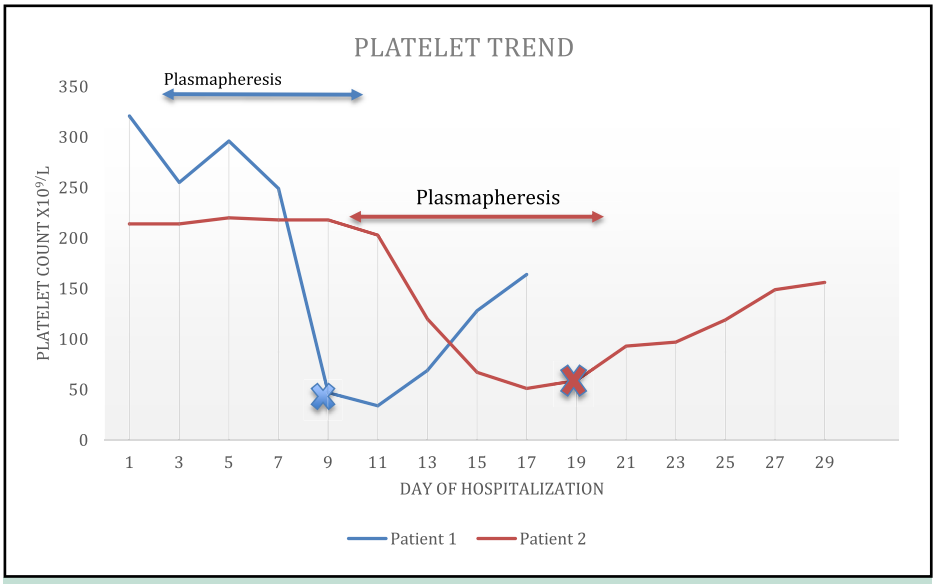

Figure The trend of platelet count during hospitalization. The symbol X (blue/red) marks the day when subcutaneous heparin was discontinued.

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