

# IVIG HITs the Spot

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## History of Present Illness

A 47-year-old man with known coronary artery disease presented with acute left lower extremity pain and paresthesia. He had undergone a coronary catheterization 12 days prior and uneventful coronary artery bypass grafting 11 days prior to presentation.

## Initial Evaluation

Vital signs were notable for tachycardia. His left lower extremity was cool, pale, and without a palpable pulse. Laboratory data revealed platelets of 13 K/cu mm, decreased from 214 the day following his recent surgery. Computed tomography angiography demonstrated occlusion of the left external iliac, femoral, and popliteal arteries (figure 1), multiple pulmonary emboli, and a left atrial thrombus. He was started on a heparin drip and transferred to our hospital for further care.

## Hospital Course

Given the presentation with multiple arterial thromboses, acute thrombocytopenia, and recent heparin exposure there was concern for heparin-induced thrombocytopenia (HIT). The heparin drip was switched to a continuous argatroban infusion. Further imaging revealed right lower extremity arterial thromboses. He underwent bilateral thrombectomy and left-sided fasciotomy. Platelet factor 4 (PF4) antibody and serotonin release assay returned positive, confirming the diagnosis of HIT. The initial PF4 antibody optical density was quite high at 2.72. (A summary of the major clinical events are represented in figure 2).



Figure 1. Angiogram from 5/2 reveals complete occlusion of the left external iliac, femoral, and popliteal arteries

Despite the fact that the patient had no further heparin exposure, the thrombocytopenia persisted. He was given platelet transfusions and was empirically trialed on glucocorticoids and bivalirudin. These treatments were unsuccessful, and he developed transfusion-refractory thrombocytopenia.

Treatment with intravenous immunoglobulin (IVIG) was found to be successful in similar case reports so this was administered next. Within 48 hours the platelet count began to rise, returning to normal within four days. In total, the thrombocytopenia persisted for 19 days. There were no further clotting events during the remainder of the hospitalization.

The patient was discharged on rivaroxaban with a planned course of at least 6 months. He has continued to do well with platelet counts remaining in the normal range 120 days after IVIG treatment.

## Discussion

The atypical features of this case, including the persistence of thrombocytopenia after heparin exposure ceased, degree of thrombocytopenia, and high optical density of the PF4 antibody, were consistent with a poorly defined subtype of HIT sometimes termed “delayed-onset” or “autoimmune HIT”.

The use of IVIG, which is not beneficial in typical HIT, has been demonstrated to be efficacious in a case series of this subtype. The difference in clinical presentation and response to IVIG may be due to a distinct type of antibody interaction (figure 3). More research is needed to better understand this mechanism.

For the clinician, recognition of atypical HIT is imperative in order to avert harmful re-exposure to heparin products, which may be given reflexively in these patients who often present with thrombosis. Also important is awareness that IVIG may be used with success in certain instances of refractory HIT.

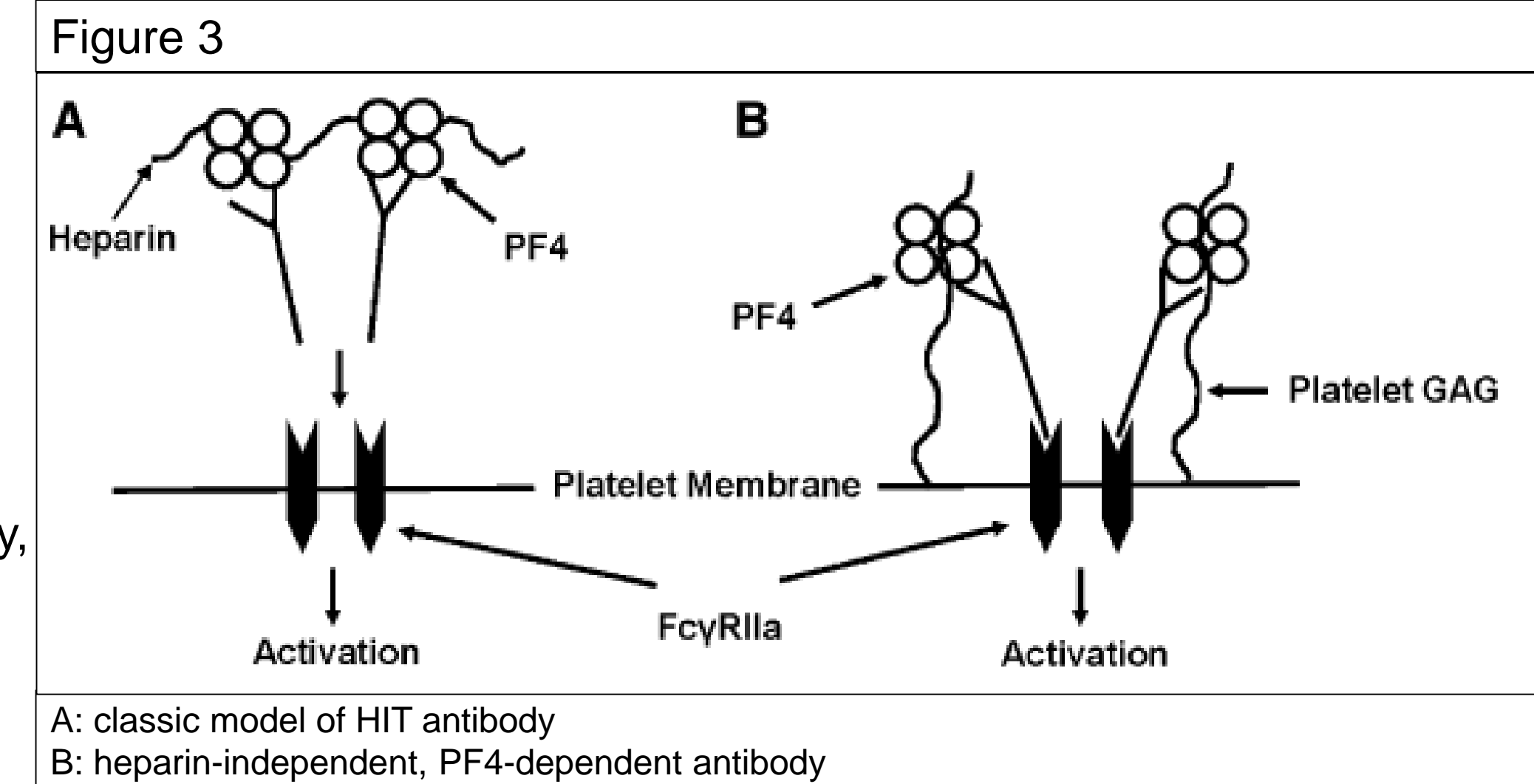
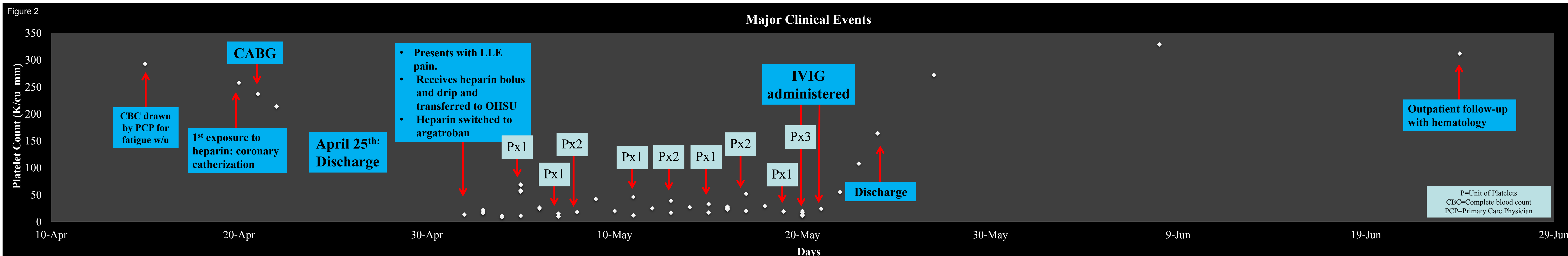


Figure 3 from Padmanabhan, A. et al. Heparin-independent, PF4-dependent binding of HIT antibodies to platelets: implications for HIT pathogenesis. *Blood*. 2015; 125(1):155-61



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