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Title:

HIT and VITT: is there a bridge?

Abstract:

Heparin-induced thrombocytopenia (HIT) and vaccine-induced immune thrombotic thrombocytopenia (VITT) are among the most prothrombotic disorders (thrombosis frequency >50%). HIT and VITT are "clinical-pathological" disorders, that is, positive testing for the causing anti-platelet factor 4 (PF4) antibodies - together with a compatible clinical presentation – are the mainstays of diagnosis. HIT and VITT are caused by platelet-activating anti-PF4 antibodies, forming PF4/IgG-containing immune complexes. These immune-complexes crosslink FcγIIa receptors on platelets and leukocytes, resulting in strong cell activation and a self-enhancing prothrombotic cascade. In HIT, heparin crosslinks several PF4 molecules, while in VITT anti-PF4 antibodies alone crosslink PF4. Sufficient levels of circulating anti-PF4 antibodies are needed to create a sufficient amount of immune complexes on platelet surfaces for platelet activation. Therefore free antibodies are always detectable in patients' sera. This explains why antigen assays are highly sensitive for detecting HIT/VITT antibodies, while the sensitivity of antigen assays in autoimmune thrombocytopenia is much lower. Heparin (low concentrations) enhances HIT antibody-induced platelet activation, but platelet activation by VITT sera is usually inhibited by heparin. In HIT and VITT, PF4-dependent enzyme-immunoassays (EIAs) using a microtiter plate format and PF4-enhanced platelet activation assays show high sensitivity (>99% and >95%, respectively). However, rapid immunoassays have only high sensitivity for HIT (>90-97%) but poor sensitivity (<25%) for VITT. HIT and VITT antibodies are directed at distinct sites on PF4: solid-phase EIAs and platelet activation assays obviously provide both epitopes, while rapid immunoassays do not.