$Fc_{\gamma}RIIa$ - Dependent Platelet Activation Identified in Covid-19 Vaccine-Induced Immune Thrombotic Thrombocytopenia-Heparininduced Thrombocytopenia, Streptokinase- and Anisoylated Plasminogen-Streptokinase Activator Complex-Induced Platelet Activation

Mustapha Abdelouahed
Department of Medical Sciences and Education, Boston University School of Medicine, Boston, MA, United States

Dana Yateem
School of Medicine, The Royal College of Surgeons in Ireland, Medical University of Bahrain, Al Sayh, Muharraq Governorate, Bahrain

Salim Fredericks
School of Medicine, The Royal College of Surgeons in Ireland, Medical University of Bahrain, Al Sayh, Muharraq Governorate, Bahrain

Abstract:

Coronavirus disease 2019 (COVID-19), which was caused by the coronavirus - severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was globally responsible for remarkable morbidity and mortality. Several highly effective vaccines for COVID-19 were developed and disseminated worldwide within an unprecedented timescale. Rare but dangerous clotting and thrombocytopenia events, and subsequent coagulation abnormalities, have been reported after massive vaccination against SARS-CoV-2. Soon after their global rollout, reports of a morbid clinical syndrome following vaccination with adenovirus-DNA-based vaccines appeared. In the spring of 2021, reports of a novel, rare and morbid clinical syndrome, with clinically devastating and fatal complication after vaccination with adenovirus-based coronavirus vaccines (Janssen/Johnson & Johnson and Astra-Zeneca vaccines) led to a brief suspension of their use by several countries. Those complications were associated with unusual cerebral and splanchnic venous thrombosis, and circulating autoantibodies directed against anti-platelet factor 4 (PF4), a protein secreted from platelets, leading to the designation: Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT). The reported VITT incidence remains very low and does not affect the overall benefit of immunization, however, if left untreated, VITT can be debilitating or even fatal. VITT

resembled specific adverse drugs' reactions that also involved the production of autoantibodies and subsequent abnormal platelet activation through platelet FcγRIIa. These unusual but well-documented drug reactions were heparin-induced thrombocytopenia (HIT), streptokinase- (SK), and anisoylated plasminogen-streptokinase activator complex- (APSAC) associated with platelet-activating antibodies. There was considerable overlapping of clinical features between VITT, COVID-19 and these adverse drugs' reactions. We review the phenomenon of VITT against the backdrop of shared and common mechanisms that underlie HIT-, SK-, and APSAC-platelet FcγRIIa-dependent platelet activation. An understanding of VITT's pathogenesis may be achieved by comparing and contrasting VITT-, HIT-, SK- and APSAC-induced platelet activation mechanisms, their respective physiopathology and similarities. Discussing these conditions in parallel provides insight into complex immunological disorders and diseases associated with abnormal hemostasis and thrombosis in particular

Keywords:

vaccine-induced immune thrombotic thrombocytopenia, COVID-19, platelet activation, FcγRIIa, heparin-induced thrombocytopenia, vaccination.