Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Vaccine-induced immune thrombotic thrombocytopenia (VITT)

On March 11, 2020, the World Health Organization declared COVID-19 (coronavirus disease, 2019) a global pandemic. Caused by a novel coronavirus, SARS-CoV-2 (abbreviation for *severe acute respiratory syndrome coronavirus 2*), COVID-19 to date has killed over 6 million people worldwide through severe respiratory illness, thrombotic events, and other complications. An enormous scientific and clinical research response led to the unprecedented development of highly effective vaccines to mitigate this enormous toll of mortality and morbidity. On December 8, 2020, only nine months after the pandemic was declared, a 91-year-old Englishwoman became the world's first recipient (outside of clinical trials) of a novel vaccine based on mRNA technology (manufactured by BioNTech/Pfizer). Approximately 4 weeks later, on January 4, 2021, an 82-year-old Englishman was the first recipient of an adenovirus vector vaccine, ChAdOx1 nCoV-19 (Oxford/AstraZeneca). The world breathed a tentative, collective sigh of relief.

However, by late February 2021, European media reported on otherwise healthy individuals who developed highly unusual thrombotic events, including cerebral venous strokes, abdominal vein thromboses (including adrenal vein thrombosis and hemorrhage), and arterial occlusions, together with thrombocytopenia and disseminated intravascular coagulation, beginning 1 or 2 weeks following vaccination with ChAdOx1 nCoV-19. Similar reports emerged several weeks later in the United States in some recipients of another adenovirus vector vaccine, Ad26.COV2.S (Johnson & Johnson/Janssen). A similar disorder was not seen among recipients of the mRNA vaccines, despite many more doses given.

On April 9, 2021, 2 reports appeared in the *New England Journal of Medicine*, revealing this prothrombotic thrombocytopenic disorder triggered by vaccination with ChAdOx1 nCoV-19 to be explained by platelet-activating antibodies directed against platelet factor 4 (PF4), a highly cationic protein found within platelets previously implicated as the target protein in the well-known antibody-mediated prothrombotic thrombocytopenic disorder, heparin-induced thrombocytopenia (HIT). Unlike HIT, where heparin usually enhances platelet activation by the pathogenic HIT antibodies, in the case of the novel disorder—named "vaccine-induced immune thrombotic thrombocytopenia," or VITT, platelet activation by VITT antibodies was usually inhibited by heparin. Several hundred studies on VITT have subsequently been published.

Eight papers in this issue of *Seminars in Hematology* address different aspects of VITT. The first article categorizes VITT as the fourth (and latest) addition to a group of anti-PF4 disorders encompassing classic HIT, autoimmune HIT, and spontaneous HIT (Warkentin). The second article discusses case definitions and the epidemiology of VITT (Pai). The third paper reviews the dramatic clinical and laboratory picture of VITT (Chen and Pavord). The fourth article discusses laboratory testing for VITT antibodies, highlighting similarities but also key differences compared with testing for HIT antibodies (Warkentin and Greinacher). Treatment of VITT is discussed in the fifth paper, including the striking consensus recommendation to treat VITT with up-front high-dose intravenous immune globulin (IVIG); the controversy as to whether heparin is a safe treatment for VITT is also addressed (Gabarin et al.). The sixth paper presents numerous intriguing concepts regarding VITT pathogenesis (Greinacher et al.). Longitudinal aspects of VITT, including the timeline of antibody persistence and treatment implications, as well as safety of subsequent COVID-19 vaccination in affected patients, are covered in the seventh paper (Schönborn and Greinacher). The final article addresses the emerging issue of psychiatric and psychological trauma afflicting VITT patients (Carpenter et al.).

Although rare, the clear association between VITT and 2 adenovirus vector vaccines has led to almost exclusive use of mRNA vaccines in Europe and North America. Thus, the "mini-epidemic" of VITT seen in many parts of the world has disappeared. So, why should we still care about VITT? First, adenovirus vector vaccines will continue to be used, especially in low and middle income countries where the lack of cold chain delivery systems makes widespread use of mRNA vaccines infeasible. Second, insights into VITT will heavily influence scientific understanding of HIT, which remains one of the most important adverse drug reactions in medicine. For example, clinicians now better appreciate the important role for high-dose IVIG in treating patients with severe HIT. Third, VITT is reminiscent of spontaneous HIT, a HIT-mimicking anti-PF4 disorder that (like VITT) is not triggered by preceding exposure to heparin, and which (also like VITT) features a high frequency of unusual thrombi such as cerebral venous strokes and adrenal hemorrhage. Awareness of the short-lived VITT mini-epidemic will help prompt clinicians world-wide to add "spontaneous HIT" to the differential diagnosis when evaluating patients with thrombosis and thrombocytopenia. Serendipity is sometimes a crucial part of the scientific journey, and the sudden and unexpected emergence of the HIT-mimicking disorder, VITT, as an indirect consequence of the COVID-19 pandemic, has shaken HIT researchers the world over, and has provided new insights into the expanding family of profoundly prothrombotic, platelet-activating anti-PF4 disorders.

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