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Thrombocytopenia after COVID-19 vaccination

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Recent data suggests a link between the Oxford-AstraZeneca adenoviral (ChAdOx1) vector-based COVID-19 vaccine (AZD1222) and immune-mediated thrombotic thrombocytopenia resembling heparin-induced thrombotic thrombocytopenia (HITT) and therefore called VITT (vaccine-induced immune thrombotic thrombocytopenia) [1–3]. However, a case series of 20 patients hospitalized due to thrombocytopenia occurring 1–23 days (median 5 days) after vaccination with the PfizerBioNTech BNT162b2 mRNA Covid-19 vaccine or the Moderna mRNA-1273 SARS-CoV-2 vaccine, including a fatal intracranial hemorrhage, has also been reported [4]. Finally, emerging data has suggested that thrombocytopenia events may likely occur unevenly across the three COVID-19 vaccines, with higher events among individuals vaccinated with the Oxford-AstraZeneca vaccine relative to the PfizerBioNTech vaccine, but further data is needed [5].

Using data from the North Denmark Region (capture population≈600,000 inhabitants), we reviewed cases with thrombocytopenia and associated clinical events among healthcare personnel ≤65 years of age vaccinated with the PfizerBioNTech/Moderna (N = 11,689) or the Oxford-AstraZeneca (N = 16,509) COVID-19 vaccine. Due to the very rare but severe clinical entity of VITT, the use of the AstraZeneca vaccine in Denmark was put on hold on March 11, 2021, and later suspended. Therefore, individuals who were vaccinated with this vaccine in our study only had one injection. Of 2130 individuals with post-vaccination platelet measurements available, 50 (40 women and 10 men) had thrombocytopenia (platelet count $<145 \times 10^9$/L in men and $<165 \times 10^9$/L in women). Among 1873 women, 24/813 (3.0 %) vaccinated with the Oxford-AstraZeneca COVID-19 vaccine versus 16/1060 (1.5 %) vaccinated with PfizerBioNTech/Moderna COVID-19 vaccines had thrombocytopenia, odds ratio [95 % confidence interval] for thrombocytopenia of 1.99 [1.05–3.76] for Oxford-AstraZeneca versus PfizerBioNTech/Moderna. Among 257 men, the corresponding odds ratio [95 % confidence interval] was 0.49 [0.14–1.79].

Severe thrombocytopenia (platelet count $<50 \times 10^9$/L) was seen in three patients vaccinated with Oxford-AstraZeneca (all women between 50 and 60 years of age) versus none among the PfizerBioNTech/Moderna vaccines. One fatal event occurred following adrenal gland bleeding seven days after vaccination, thrombocytopenia (lowest platelet count of 5 × 109/L), massively elevated D-dimer (>100mcg/mL), and ischemic stroke nine days after vaccination [6]. This patient was strongly positive for platelet factor 4 (PF-4) reactive antibodies, imitating what is seen in HITT. The two other cases were evaluated in the emergency department on day 20 and 35 post-vaccination without subsequent hospitalization but referral to outpatient diagnostic work-up. FP4-antibodies were not proven in one of the remaining two cases with severe thrombocytopenia and not tested in the other. None of the three cases had previously received heparin.

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