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Synopsis

Understanding mechanisms of thrombosis and thrombocytopenia with adenoviral SARS-CoV-2 vaccines: a comprehensive synopsis

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Plain language summary

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Plain language summary

Thrombosis with thrombocytopenia syndrome is rare: it is characterised by thrombosis and lowered platelet counts together with the development of an antibody against a protein called platelet factor 4. This syndrome has been linked to heparin use or can occur spontaneously. With COVID-19 vaccines, a new form called vaccine-induced immune thrombosis and thrombocytopenia appeared. The thrombosis with thrombocytopenia syndrome consortium formed to better understand this syndrome.

The consortium used various methods, like studying the data of the entire English population and analysing local data in real time. They tested patient and healthy control samples for antiplatelet factor 4 antibodies and sequenced genes from patients who got vaccine-induced immune thrombosis and thrombocytopenia after the AZD1222 COVID-19 vaccine. They also studied how these antibodies form and their effects, including changes in cytokines and platelet involvement.

Our studies showed a higher thrombosis risk after COVID-19 infection compared to vaccination. The first dose of the AZD1222 vaccine had higher risks of thrombosis and lowered platelets (occurring separately), but subsequent doses or mRNA vaccines were safer. Identifying vaccine-induced immune thrombosis and thrombocytopenia patients directly was difficult due to poor records. Real-time tracking of diseases across hospitals was not yet possible at scale. The prevalence of antiplatelet factor 4 antibodies was low in healthy, vaccinated and COVID-19-infected individuals. Genetic sequencing didn't find significant variants causing vaccine-induced immune thrombosis and thrombocytopenia, but there are ongoing ribonucleic acid studies.

Our studies found a possible mechanism for antiplatelet factor 4 antibody development involving the AZD1222 vaccine. The immune response caused generalised inflammation and clotting in distant organs. Platelet activation was influenced by certain factors. T-cell reactivity against the AZD1222 vaccine hinted at potential cross-reactivity with common human viruses.

The consortium's work has uncovered new insights into vaccine-induced immune thrombosis and thrombocytopenia, suggesting potential new diagnostic and treatment strategies. This is crucial, as thrombosis with thrombocytopenia syndrome can occur without exposure to heparin or adenovirus vaccines.