Treatment and detection of vaccine-induced thrombotic thrombocytopenia (VITT)

What is this research about?

Vaccination with an adenoviral vector vaccine against COVID-19 (i.e., ChAdOx1 nCoV-19, AstraZeneca) has been associated with a rare clotting disorder that has become known as vaccine-induced immune thrombotic thrombocytopenia (VITT). The clotting disorder develops when IgG antibodies recognize a platelet protein (PF4), forming a PF4-polyanion complex, which strongly activates platelets. This leads to a decrease in the number of platelets (platelet consumption) and promotes clot formation.

Little is known about treating patients with VITT. The recommendation to use high-dose intravenous immune globulin (IVIG) to reduce platelet activation is based on the observation that VITT strongly mimics autoimmune heparin-induced thrombocytopenia (HIT) (even though patients with VITT usually have not received the anticoagulant heparin). For HIT, IVIG can be an important adjunct treatment.

This report describes three Canadian patients who developed VITT after receiving the AstraZeneca vaccine. Using a newly developed diagnostic test for VITT, researchers documented the inhibition of platelet activation after treatment with IVIG in these three patients.

IN BRIEF: Early administration high-dose IVIG may be an important adjunct therapy for the management of VITT, a newly described, rare prothrombotic disorder.

What did the researchers do?

Researchers described the response to IVIG in three patients, the first in Canada to be diagnosed with VITT. The patients were between the ages of 63 and 72; one was female. Two had clotting in their legs and the third had clots blocking arteries and veins inside their brain.

- Serum was taken before and after administration of IVIG to identify any changes in platelet-activating reactivity.
- A commercial enzyme immunoassay test was used to detect antibodies against PF4-polyanion complexes
- A platelet activation test called the serotonin-release assay (SRA) was also performed. The test is used to diagnose HIT by measuring platelet activation with various levels of heparin in patient serum (antibody bound to PF4-polyanion complexes release serotonin, so higher levels of serotonin release indicates greater platelet activation).

- To detect VITT-specific antibodies, the HIT SRA test was modified by adding increasing doses of PF4 to serum rather than heparin.

What did the researchers find?

All three patients tested strongly positive for antibodies against PF4-polyanion complexes. Test results also showed that IVIG did not inhibit VITT antibody binding to PF4. However, in the three patients with VITT, administration of IVIG was associated with increased platelet counts. This is probably the result of IVIG inhibiting platelet activation (caused when antibodies bind to PF4) and reducing formation of clots.

Researchers showed testing for HIT and VITT antibodies can be achieved by performing the standard platelet-activation assay at the usual conditions, with the addition of PF4 instead of heparin.

How can you use this research?

This study developed an effective test and treatment for VITT by uncovering the mechanism that leads to platelet activation and vaccine-related blood clots. Since patients with VITT can have severe thrombocytopenia that potentially lasts for several weeks, early administration of IVIG may be an important adjunct therapy to anticoagulation for the management of VITT.

This Research Unit is derived from the following publication(s):
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About the research team: This research was led by Dr. Ishac Nazy, scientific director of the McMaster Platelet Immunology Laboratory at McMaster University and Dr. Donald Arnold, director of the McMaster Centre for Transfusion Research.

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