Alert: Vaccination Induced Immune Thrombocytopenia with Thrombosis (VITT)
University of Vermont Health Network.
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Prepared by: Mary Cushman, MD, MSc and Beth Kirkpatrick, MD

The FDA and CDC paused administration of the Johnson & Johnson (J&J) adenovirus vaccine for SARS-CoV2 on 4/13/21 due to six occurrences of clinical presentations consistent with VITT, a recently reported illness noted first in Europe and linked to the AstraZeneca (AZ) adenovirus vaccine for SARS-CoV2. Formal federal guidelines for use of J&J and clinical guidance are expected in the next days.

Please note the Vermont Department of Health Advisory and the CDC Health Alerts on this topic, both released April 13, 2021.
https://www.healthvermont.gov/sites/default/files/documents/pdf/COVID-HAN-JJ-Janssen-COVID-vaccine.pdf

https://emergency.cdc.gov/han/2021/pdf/CDC-HAN-00442.pdf

The cases that have occurred in the US have presented mostly as cerebral vein thrombosis, with thrombocytopenia, in six people out of over 6.8 million who received this vaccine. Including cases in the US and Europe (including from the AZ vaccine) patients also experienced splanchnic vein thrombosis (ie., portal, mesenteric vein) and lower extremity deep vein thrombosis or pulmonary embolus.

Some AZ vaccine related cases in Europe were reported in the NEJM in two articles on 4/9/21[1, 2]. These cases resemble autoimmune heparin induced thrombocytopenia, an extremely rare illness that has also been called "spontaneous heparin-induced thrombocytopenia." We do not have all details of the US cases, but the findings raise caution, and **we should be aware of this syndrome so it can be recognized**. The syndrome appears to occur starting about day 5 after the vaccine (a median of 9 days), and there are not cases with onset after about 16 days post vaccine (i/e., it is similar to classical heparin-induced thrombocytopenia (HIT) in terms of timing). Importantly, flulike symptoms such as joint and muscle pain or headache that persist for 1 to 4 days after J&J vaccination are a common side effect and not a cause for concern. Most patients reported with VITT are women under age 50. Unlike HIT, the thrombocytopenia can be severe and accompanied by disseminated intravascular coagulation.

Symptoms of concern that might suggest VITT include severe headache (with or without vomiting) and/or back pain, neurologic symptoms consistent with stroke (aphasia, weakness, visual disturbance), abdominal pain with or without vomiting, symptoms of DVT/PE, easy bruising or petechial rash.

Important points at this time:

- If a patient presents with the above VITT symptoms 4-21 days after the J&J vaccine (or outside of this range with high clinical suspicion), urgent evaluation for thrombosis should be undertaken and a complete blood count should be obtained.
- If there is thrombosis with any level of thrombocytopenia, we recommend urgent hematology consultation. In cases of VITT, heparin / low molecular weight heparin is contraindicated, an alternative anticoagulant is recommended, and intravenous immunoglobulin is indicated.

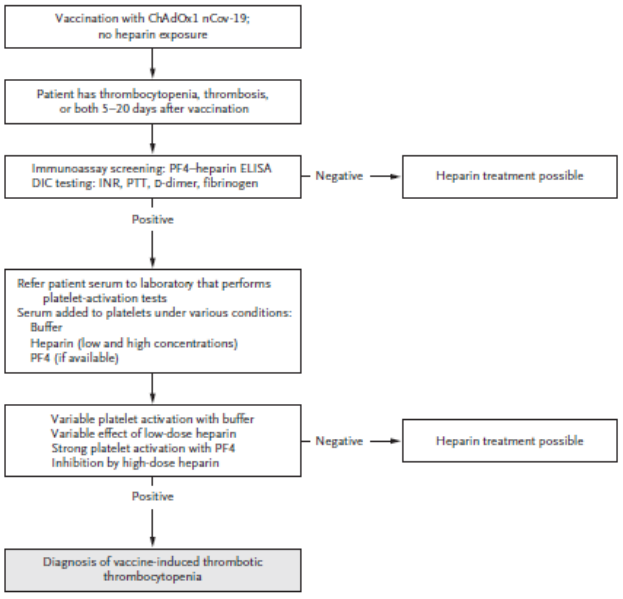
- If there is new thrombocytopenia without thrombosis, appropriate clinical evaluation should be done, careful monitoring of symptoms undertaken over time, and hematology consult considered.
- The table below suggests a proposed clinical approach, based upon the European experience with cases after the AZ vaccine[1].
- Consider at least a brief admission for initiation of treatment for patients with venous thrombosis (other than superficial vein thrombosis) that occurs up to 20 days after the J&J vaccine.

In Vermont, about 40,000 doses of the J&J vaccine have been administered and it is unlikely we will see a case of VITT. However, due to possible reporting bias to date nationally, it is certainly possible more cases or milder cases might be recognized as awareness increases.

It is important to note that this syndrome has not been reported after mRNA vaccines (ie., Pfizer and Moderna). We suspect that any thrombosis occurring after these vaccines are related to typical other causes and are occurring at baseline population rates. These don't require special treatment, but as always, all patients with venous thrombosis should have labs including a complete blood count before starting treatment.

Those with further interest may watch the 4/13/2021 Facebook Live interview with Alexandra Tursi of UVM Medical Center here: https://fb.watch/4SPXrf83r9/. This can also be shared with patients who want more information about vaccination.

Last, we remind you that reporting of certain vaccine side effects is required of healthcare workers, and we recommend all thrombosis cases after SARS-CoV2 vaccines (as well as any suspected adverse events) should be reported to the Vermont Department of Health and also to: https://vaers.hhs.gov/reportevent.html



Treatment Options	Comment
High-dose intravenous immune globulin (1 g per kg for 2 days)	Raises platelet count and decreases hypercoagulability (by analogy with autoimmune HIT); inhibits platelet activation by platelet-activating anti-PF4 antibodies (platelet Fcγ receptors)
Anticoagulants often used to treat heparin-induced thrombocytopenia	Direct oral Xa inhibitors (apixaban, rivaroxaban) Direct thrombin inhibitors (argatroban, bivalirudin) Indirect (antithrombin-dependent) Xa inhibitors: danaparoid (not available in U.S.), fondaparinux
Platelet transfusions	Avoid unless presence of bleeding (theoretical prothrombotic risk)
Vitamin K antagonist	Contraindicated during acute thrombocytopenia and disseminated intravascular coagulation (microthrombosis associated with protein C depletion)

Figure 2. Potential Diagnostic and Therapeutic Strategies for Management of Suspected Vaccine-Induced Immune Thrombotic Thrombocytopenia.

Shown is a decision tree for the evaluation and treatment of patients who have symptoms of thrombocytopenia or thrombosis within 20 days after receiving the ChAdOx1 nCov-19 vaccine and who have had no heparin exposure. The diagnostic and therapeutic strategies in such patients differ from those in patients with autoimmune heparin-induced thrombocytopenia (HIT).[13] DIC denotes disseminated intravascular coagulation, INR international normalized ratio, PF4 platelet factor 4, and PTT partial thromboplastin time.

References

1. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA and Eichinger S. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. *N Engl J Med*. 2021.
2. Schultz NH, Sorvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, Ahlen MT, Wiedmann M, Aamodt AH, Skattor TH, Tjonnfjord GE and Holme PA. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. *N Engl J Med*. 2021.