Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT)

Preliminary Recommendations

Summary:

As of April 12, 2021, approximately 6.85 million doses of the Johnson & Johnson (J&J) COVID-19 vaccine (Janssen) have been administered in the United States. The Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA) are reviewing data involving six U.S. cases of a rare type of blood clot in individuals after receiving the J&J COVID-19 vaccine that were reported to Vaccine Adverse Event Reporting System (VAERS). In these cases, a type of blood clot called cerebral venous sinus thrombosis (CVST) was seen in combination with low levels of blood platelets (thrombocytopenia). All six cases occurred among women aged 18–48 years. The interval from vaccine receipt to symptom onset ranged from 6–13 days. When these specific types of blood clots are observed following J&J COVID-19 vaccination, treatment is different from the standard treatment that might typically be administered for blood clots. The pathogenesis of these rare and unusual adverse events following vaccination may be associated with platelet-activating antibodies against platelet factor-4 (PF4). Usually, the anticoagulant drug heparin is used to treat blood clots. However in this setting, the use of heparin may be harmful, and alternative treatments must be given.

VITT Preliminary Recommendations are designed to provide considerations around the diagnosis and treatment of VITT, and will be updated as more information becomes available.

Assessment:

Maintain a high index of suspicion for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J COVID-19 vaccine, including:

1. Severe headache
2. Backache
3. New neurologic symptoms
4. Severe abdominal pain
5. Shortness of breath
6. Leg pain swelling
7. Petechiae (tiny red spots on the skin)
8. New or easy bruising

Evaluation:

Consultation with a hematologist is strongly recommended.

Draw blood prior to any therapeutic intervention such as IVIG, given potential interference with both the PF4 ELISA and platelet activation assays.

Initial work-up:

1. CBC with platelet count: Mean platelet count in published reports, 20,000; range, 9,000-107,000.
2. Imaging for thrombosis based on symptoms focused on detection of:
    a. CVST with non-contrast head CT followed by MRI brain with MR venogram

   b. Splanchnic thrombosis
   c. Pulmonary emboli.
3. D-dimers: The majority of VITT patients have shown markedly elevated values.
4. Fibrinogen: Some VITT patients are reported to have low values.
5. PF4/Heparin ELISA: All cases reported had positive assays, with optical density > 2.0 -3.0 in the majority. Non-ELISA HIT assays have not been validated as sensitive or specific for VITT and should not be used.
6. Blood draw for a confirmatory PF4 platelet activation assay (serotonin release assay, P-selectin expression assay, or HIPA): These assays can be obtained if locally available and the PF4 ELISA is low positive or if there is uncertainty regarding the diagnosis.

Initial Treatment:

In patients presenting with thrombocytopenia, documented or suspected thrombosis, and a positive or pending PF4 ELISA 4-20 days post-vaccination, recommended treatment is similar to severe HIT.

1. IVIG 1 gram/kg daily X 2 days
2. Non-heparin anticoagulation, chosen based on the clinical status and organ function of the patient:
   a. Parenteral direct thrombin inhibitors (argatroban or bivalrudin provided the baseline aPTT is normal),
   b. Direct oral anticoagulants without lead-in heparin phase,
   c. Fondaparinux
3. Low fibrinogen or bleeding are associated with VITT, and should not absolutely preclude anticoagulation, particularly if platelets are >20,000/uL or rising following IVIG initiation
4. Avoid platelet transfusion

Adverse Event Reporting:

Report adverse events to VAERS, including serious and life-threatening adverse events and deaths in patients following receipt of COVID-19 vaccines as required under the FDA Emergency Use Authorization for COVID-19 vaccines.

References:

1. CDC Health Alert, Cases of CVST with thrombocytopenia following receipt of the J&J vaccine. Available at: https://emergency.cdc.gov/han/2021/han00442.asp. Accessed April 17, 2021.

2. American Society of Hematology (ASH), Vaccine-Induced Thrombotic Thrombocytopenia: FAQ. Available at: https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia. Accessed April 17, 2021.