Vaccine-Induced Immune Thrombotic Thrombocytopenia: How It Happens and How to Spot It

Tuesday | April 20, 2021 | 5:00-6:00pm ET

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Narayan Nair, MD | Ishac Nazy, PhD | Menaka Pai, MD, MSc, FRCPC
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Agenda

1. Clinical presentation of VITT – D. Arnold

2. Report from the US FDA – N. Nair

3. Testing for VITT – I. Nazy

4. Lessons learned from heparin-induced thrombocytopenia – T. Warkentin

5. Practical approach to diagnosis and management – M. Pai
Clinical Presentation of VITT

Donald M. Arnold MD MSc
Professor, Department of Medicine
Medical Director, McMaster Platelet Immunology Laboratory
Conflicts of interest – D. Arnold

none
Vaccine-induced immune thrombotic thrombocytopenia

• Thrombocytopenia

• Thrombosis

• 5 – 24 days post vaccines for COVID-19
  
  - ChAdOx1 nCov-19 (AstraZeneca)
  
  - Ad26.COV2.S (Johnson & Johnson/Janssen)
Germany, Austria (N=11, AZ vaccine)

**Thrombosis in unusual locations:**
- Cerebral sinus vein thrombosis (n=9)
- Splanchnic vein thrombosis (n=2)
- Pulmonary embolism (n=3)
- Arterial (n=1)
- Disseminated intravascular coagulation (n=5)

**Demographics:**
- Median nadir platelet count: 20 x10⁹/L (range, 9 – 107 x10⁹/L)
- Median age 36 years (range 22 – 49); females: 9/ 11 (82%)
- 5 – 16 days post vaccine
- None received heparin
- 5/11 died

Greinacher et al, NEJM April 9 2021
Laboratory testing (4 + 24 samples)

• POSITIVE anti-PF4 (ELISA) – *quantitative test*
• POSITIVE platelet activation assay – *functional test*

*Greinacher et al, NEJM April 9 2021*
Norway (N= 5, AZ vaccine)

Clinical:
• Health care workers; 7 – 10 days post vaccine
• Ages 32 to 54 years; females: 4/5 (80%)
• Platelet nadir: 14 – 70 x10⁹/L
• CSVT, portal vein thrombosis
• 3/5 died

Laboratory:
• POSITIVE anti-PF4 antibody assay: 5/5
• POSITIVE functional assay: 4/5

Schultz et al, NEJM April 9 2021
United Kingdom (N= 23, AZ vaccine)

**Clinical:**
- 6 – 24 days post vaccine
- CSVT, arterial thrombosis, PE
- Median age: 46 years (range, 21 to 77); 14/23 (61%) female
- Platelets: 7 – 113 x10⁹/L; Low fibrinogen, high D-dimer
- 7/23 (30%) died

**Laboratory:**
- 9 /23 had a NEGATIVE rapid HIT screen test; 22/23 POSITIVE in the ELISA
- 5/7 were POSITIVE in the platelet activation assay

*Scully et al, NEJM April 16, 2021*
Proposed mechanism

- Brisk, pathological immune reaction
- Similar to heparin-induced thrombocytopenia
- VITT antibodies target platelet factor 4 (PF4)
- Bind Fc-receptors on platelets
- Intense platelet activation
- Thrombocytopenia and thrombosis
Frequency - ?

- 1 in 26,000 (Norway, NEJM)
- 1 in 100,000 (Cines and Bussel, NEJM)
- 1 in 250,000 (Canada)
- 1 in 1,000,000 (US, J&J vaccine)
Overall clinical picture

- Aggressive thrombosis (venous > arterial)
- CSVT, splanchnic, hepatic thrombosis
- Moderate – severe thrombocytopenia (PLT 20 – 50)
- 5 – 24 days post vaccination (AZ or J&J)
- Young females, no predisposing risk factors
- ~50% case fatality (includes delays in recognition)
- Early recognition: non-heparin anticoagulants, immune-modulating therapy

Thrombosis + low platelets = think of VITT
Summary of Reports of Cerebral Venous Sinus Thrombosis (CVST) and Thrombocytopenia in U.S. following vaccination with COVID-19 vaccines

Narayan Nair, MD
Division of Epidemiology
Office of Biostatistics and Epidemiology
Center for Biologics Evaluation and Research
Food and Drug Administration
Disclaimer

My comments are an informal communication and represent my own best judgment. These comments do not bind or obligate the US FDA.
Organization Chart

Department of Health and Human Services
Food and Drug Administration
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Office of Communication, Outreach & Development
Director
Lorne H. McNeill

June 2020
Vaccine Adverse Event Reporting System (VAERS)

• National passive safety surveillance program administered by FDA and CDC, established in 1990
• Collects data from reports of adverse events following vaccination
• Prior to 2021 received ~50,000 reports annually (10-15% of reports thought to be serious)
• Reports can be made online or on paper
• Data can be accessed through CDC Wonder
Reports of CVST to VAERS after COVID-19 vaccines as of April 12, 2021

- **Janssen COVID-19 vaccine**
  - 6 reports of CVST with thrombocytopenia (platelet counts <150K/mm3) following 6.86 million doses administered
    - Reporting rate of 0.87 cases per million doses administered

- **Pfizer-BioNTech COVID-19 vaccine**
  - 0 reports following 97.9 million doses administered

- **Moderna COVID-19 vaccine**
  - 3 reports following 84.7 million doses administered
  - All 4 with normal platelet counts

Source of doses administered: [https://covid.cdc.gov/covid-data-tracker/#vaccinations](https://covid.cdc.gov/covid-data-tracker/#vaccinations)
Characteristics of patients with CVST and thrombocytopenia after Janssen COVID-19 vaccine, N=6

- Median age 33 years (range 18–48)
- Median time to symptom onset 8 days (range 6–13 days)
- All cases occurred in white females
- Current estrogen/progesterone use (n=1)
- Pregnant or post-partum (n=0)
- Pre-existing conditions
  - Obesity (n=3)
  - Hypothyroidism (n=1)
  - Hypertension (n=1)
  - Asthma (n=1)
  - Coagulation disorders (none known)
### Initial and late signs and symptoms among CVST patients*, N=6 (patients listed in no particular order)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Initial features</th>
<th>Late features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Headaches, lethargy</td>
<td>Severe headache, left-sided weakness, vomiting</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Headaches</td>
<td>Severe headache, aphasia</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Headaches, vomiting, fever</td>
<td>Left arm weakness, right gaze deviation, left neglect</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Headaches, chills, myalgias</td>
<td>Severe abdominal pain and fever</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Headache, chills, dyspnea, fever</td>
<td>Bruising, unilateral leg swelling, loss of consciousness</td>
</tr>
<tr>
<td>Patient 6</td>
<td>Back pain, bruising</td>
<td>Headache, abdominal pain</td>
</tr>
</tbody>
</table>

*All were hospitalized and admitted to the intensive care unit*
### Locations of CVST, intracerebral hemorrhage, and other thromboses, N=6

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of CVST</td>
<td>Right transverse sinus and right sigmoid sinus</td>
<td>Left transverse sinus, left sigmoid sinus, confluence of sinuses, and straight sinus</td>
<td>Superior sagittal sinus, inferior sagittal sinus, and straight sinus</td>
<td>Right transverse sinus and right sigmoid sinus</td>
<td>Right transverse sinus and right sigmoid sinus</td>
<td>Right transverse sinus</td>
</tr>
<tr>
<td>Location of intracerebral hemorrhage</td>
<td>Right temporoparietal lobe</td>
<td>Left temporal lobe</td>
<td>Bilateral frontal lobes, intraventricular</td>
<td>None</td>
<td>None</td>
<td>Occipital lobe</td>
</tr>
<tr>
<td>Locations of other thromboses</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Portal vein and right pulmonary artery</td>
<td>Portal vein and right extremity VTE, right internal jugular vein</td>
<td>Portal vein</td>
</tr>
</tbody>
</table>
SARS-CoV-2 test results among CVST patients, N=6

<table>
<thead>
<tr>
<th>Patient</th>
<th>SARS-CoV-2 viral test</th>
<th>SARS-CoV-2 serology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Negative</td>
<td>Not documented</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Negative</td>
<td>Nucleocapsid Ab negative</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Negative</td>
<td>Not documented</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Negative</td>
<td>Not documented</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Negative</td>
<td>Unspecified COVID Ab negative</td>
</tr>
<tr>
<td>Patient 6</td>
<td>Negative</td>
<td>Unspecified COVID Ab negative</td>
</tr>
</tbody>
</table>
### Hematology test results among CVST patients, N=6

<table>
<thead>
<tr>
<th>Patient</th>
<th>Lowest platelet value (per mm³)</th>
<th>PF4 HIT* antibody test result(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>12,000</td>
<td>Not done</td>
</tr>
<tr>
<td>Patient 2</td>
<td>69,000</td>
<td>Positive</td>
</tr>
<tr>
<td>Patient 3</td>
<td>18,000</td>
<td>Positive</td>
</tr>
<tr>
<td>Patient 4</td>
<td>127,000</td>
<td>Positive</td>
</tr>
<tr>
<td>Patient 5</td>
<td>10,000</td>
<td>Positive</td>
</tr>
<tr>
<td>Patient 6</td>
<td>14,000</td>
<td>Positive (&quot;highly positive&quot;)</td>
</tr>
</tbody>
</table>

*Platelet factor 4 heparin induced thrombocytopenia
Treatment and outcomes among CVST patients, N=6

- **Treatment**
  - Heparin (n=4)
  - Nonheparin anticoagulants (n=5)
  - Platelets (n=3)
  - Intravenous immunoglobulin (n=3)

- **Outcomes**
  - Death (n=1)
  - Remain hospitalized (n=3)
    - Intensive care unit (n=2)
  - Discharged home (n=2)

* All 5 of these patients received Argatraban
Acknowledgments

FDA Division of Epidemiology

CDC Immunization Safety Office – Slides provided by Dr. Tom Shimabukuro
Laboratory Diagnosis of Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT)

Ishac Nazy, Ph.D.
Associate Professor, McMaster University
Scientific Director, McMaster Platelet Immunology Laboratory
Conflicts of Interest

I have no financial or non-financial conflicts of interest to declare
Immunological Assays

- Commercially available
- Rapid turnaround time
- Technically easy
- Sensitivity/Specificity??
- Excellent screening tool to rapidly exclude HIT (VITT??)
- VITT samples have high antibody titres
- **Test includes PF4 and PF4/heparin antigens (No Rapid Immunoassays)**

Warkentin TE., Transfus Med Rev. 2006
Functional Assays

- Not commercially available
- Performed in specialized laboratories
- Sensitivity/Specificity
- Positive predictive value
- VITT samples have strong platelet-activating antibodies
- **Test includes platelet activation with/without heparin or PF4**

Warkentin TE., Transfus Med Rev. 2006
VITT Testing Algorithm

Screening immunobinding test for VITT in 24 hours

- Sample received at MPIL
- Immunoassay testing for Abs against PF4 and PF4/H
  - Test is NEGATIVE for Abs. Report to physicians (Exclude VITT)
    - Report adverse effects to Public Health
  - Test is POSITIVE for Abs. (Further investigate VITT)
- Functional assays to detect platelet activating Abs

Confirmatory functional test for VITT in 48 hours

- Test is NEGATIVE for platelet activating Abs. Report to Physician (Exclude VITT)
  - Report adverse effects to Public Health
- Test is POSITIVE for platelet activating Abs. Report to Physician (VITT Suspected)
  - Report adverse effects to Public Health
Representative Case

**Immunobinding Assay (ELISA/EIA)**

<table>
<thead>
<tr>
<th>Assays</th>
<th>Antibody Titre (OD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immucor</td>
<td>3.347</td>
</tr>
<tr>
<td>Anti-PF4/hep EIA</td>
<td>1.362</td>
</tr>
<tr>
<td>Anti-PF4/hep EIA</td>
<td>1.633</td>
</tr>
</tbody>
</table>

*Avoid the use of Rapid Immunoassays (RIA)*

**Functional Assays (SRA)**

Samples drawn after the initiation of treatment, such as IVIg, could inhibit the reaction.
CONCLUSIONS

Vaccination with ChAdOx1 nCov-19 can result in the rare development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia.

VITT = Vaccine-induced Immune Thrombotic Thrombocytopenia
Outline

Explain:
- classic HIT
- autoimmune HIT
- spontaneous HIT syndrome
- VITT

*These are anti-PF4 platelet-activating disorders*

IVIG: why this is important treatment
VITT: mnemonic for diagnosis
Classic HIT

Timing: 5-10 days after immunizing heparin exposure

Timing: Rapid (<1d) upon heparin re-exposure (within 100d)

Heparin-dependent antibodies

Platelet factor 4 (PF4)
Heparin

"Classic" HIT
PF4/heparin complexes
IgG antibody
Fc receptor clustering
Platelet activation
Classic HIT
(anti-PF4/heparin)
(Heparin-triggered)
Typical-onset HIT
Rapid-onset HIT

Autoimmune HIT (aHIT)
(Heparin-triggered)
(anti-PF4/heparin + heparin-independent anti-PF4 antibodies)

0.1 UFH 0.3 UFH 100 UFH

Percent Serotonin Release

Heparin (U/mL)

0 10 20 30 40

50

60

70

80

90

100

typical cut-off

Feature of autoimmune HIT: strong release at 0 U/mL heparin
Autoimmune HIT

Platelet count (x10^-9/L)

Days after cardiac surgery

Discharged POD6
HIT test (SRA) strongly positive
Patient asked to return to hospital
Pleuritic chest pain: VQ lung scan → PE

Admitted

Rivaroxaban 15mg twice-daily per os × 12 weeks; then 20mg once-daily for >2 weeks (last follow-up, day 136)

Autoimmune HIT

Platelet count (x10^-9/L)

Discharged POD6
HIT test (SRA) strongly positive
Patient asked to return to hospital
Pleuritic chest pain: VQ lung scan → PE

Admitted
Patient discharged to home on rivaroxaban
Persisting HIT: platelet count recovery is inversely parallel to waning of HIT antibody-induced heparin-independent platelet activation

Rivaroxaban 15mg twice-daily per os×12 weeks; then 20mg once-daily for >2 weeks (last follow-up, day 136)

Serum-induced heparin-dependent platelet activation
Serum-induced heparin-independent platelet activation

UFH (mean of 0.1 and 0.3 U/mL)
0 U/ml UFH (“buffer control”)

Family doc
Patient “well”

Platelet factor 4 (PF4)

Heparin

IgG antibody HIGHLY PATHOGENIC SUPER Abs

“Classic” HIT

“Autoimmune” HIT (same without heparin!)

Fc receptor clustering

Platelet activation

X
Classic HIT (anti-PF4/heparin)  
- Heparin-triggered  
- Typical-onset HIT  
- Rapid-onset HIT

Autoimmune HIT (aHIT)  
- (Heparin-triggered)  
- (anti-PF4/heparin + heparin-independent anti-PF4 antibodies)

aHIT Disorders  
- Delayed-onset HIT  
- Persisting HIT  
- Heparin “flush” HIT  
- Fondaparinux-assoc. HIT

Warkentin et al. SUBMITTED
Autoimmune HIT (aHIT) (Heparin-triggered)

Autoimmune HIT (WITHOUT preceding heparin)
- Spontaneous HIT syndrome
  - Post-knee replacement
  - Medical variant (e.g., post-viral infection)

Classic HIT (anti-PF4/heparin)
- Typical-onset HIT
- Rapid-onset HIT

(WITHOUT) preceding heparin

Heparin-triggered
<table>
<thead>
<tr>
<th>Year</th>
<th>Setting</th>
<th>Plt nadir</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>Dental infection</td>
<td>11</td>
<td>Limb artery, MI</td>
</tr>
<tr>
<td>2008</td>
<td>Groin abscess</td>
<td>15</td>
<td>Limb artery, CVA</td>
</tr>
<tr>
<td>2008</td>
<td>URTI; pneumonia</td>
<td>62*</td>
<td>Anaphylactoid Rx*</td>
</tr>
<tr>
<td>2012</td>
<td>No precipitant</td>
<td>54*</td>
<td>PE, DVT</td>
</tr>
<tr>
<td>2012</td>
<td>MRSA infection</td>
<td>86*</td>
<td>Skin necrosis, VLG</td>
</tr>
<tr>
<td>2014</td>
<td>Viral illness</td>
<td>15</td>
<td>CVST</td>
</tr>
<tr>
<td>2015</td>
<td>No precipitant</td>
<td>91*</td>
<td>CVST, DVT</td>
</tr>
<tr>
<td>2017</td>
<td>MGUS</td>
<td>80</td>
<td>CVST</td>
</tr>
<tr>
<td>2018</td>
<td>No precipitant</td>
<td>41+</td>
<td>Limb artery, CVA</td>
</tr>
<tr>
<td>2020</td>
<td>Viral illness</td>
<td>24</td>
<td>CVST</td>
</tr>
</tbody>
</table>

40% with CVST (60% overall with “stroke”)

Warkentin et al. SUBMITTED
Autoimmune HIT (aHIT) (Heparin-triggered)

Classic HIT (anti-PF4/heparin) (Heparin-triggered)
- Typical-onset HIT
- Rapid-onset HIT

Autoimmune HIT (WITHOUT preceding heparin)
- Spontaneous HIT syndrome
  - Post-knee replacement
  - Medical variant (e.g., post-viral infection)

Vaccine-induced immune thrombotic thrombocytopenia (VITT)

Warkentin et al. SUBMITTED
High-dose intravenous immunoglobulin for the treatment and prevention of heparin-induced thrombocytopenia: a review

Theodore E. Warkentin\textsuperscript{a,b,c,d}

\textbf{ABSTRACT}

\textbf{Introduction:} Heparin-induced thrombocytopenia (HIT) is known for its strong association with thrombosis and distinct pathogenesis involving anti-PF4/polyanion antibodies that activate platelets strongly through clustering of platelet Fc\textgamma\textsubscript{y}lla receptors. Autoimmune HIT (aHIT) refers to a subgroup of patients whose HIT antibodies have both heparin-dependent and heparin-independent platelet-activating properties. aHIT patients have atypical clinical presentations including delayed-onset HIT, persisting (refractory) HIT, heparin ‘flush’ HIT, fondaparinux-associated HIT, severe thrombocytopenia (platelet count <20 x 10\textsuperscript{9}/L) with overt disseminated intravascular coagulation, and spontaneous HIT syndrome.

\textbf{Areas covered:} This article reviews all available literature describing the use of high-dose intravenous immunoglobulin (IVIG) as an adjunct treatment to anticoagulation in HIT patients. IVIG is usually effective in interrupting platelet activation by aHIT antibodies, manifesting as a rapid platelet count increase after starting IVIG (usual dose, 1g/kg x 2 days). Experience to date suggests IVIG de-escalates HIT and likely reduces thrombotic risk. A new case of aHIT successfully treated with IVIG is presented. Use of IVIG to prevent acute HIT with planned heparin reexposure in antibody-positive patients is also discussed.

\textbf{Expert opinion:} High-dose IVIG appears to rapidly inhibit HIT antibody-induced platelet activation and has the potential to become an important treatment adjunct for HIT, particularly in patients with aHIT.
1988
Kelton shows platelet FcγIIa receptors are implicated in HIT pathogenesis

1994
Warkentin & Kelton report response in HIT patient given IVIG to treat Guillain-Barré syndrome
Greinacher describes scientific rationale of IVIG to treat HIT

1989
First report of IVIG to treat HIT

2000
Greinacher & Warkentin recommend IVIG as “possible” adjunct treatment of HIT

2007
IVIG Expert Panel advises against IVIG to treat HIT

2014
First report of IVIG to treat aHIT

2017
Greinacher et al. recommend IVIG to treat aHIT
Padmanabhan reports IVIG effective for refractory HIT

2018
ASH HIT guidelines: IVIG is research priority
IVIG reported to treat heparin “flush” HIT

Spontaneous HIT (Post-Knee Replacement)

52F
TKR
Aspirin

POD12
Abd pain → Splanchnic vein thrombosis

RAPID ↓ heparin-independent platelet activation

Spontaneous HIT syndrome

Knee arthroplasty

UFH: 0.1 U mL^{-1} (McMaster)

UFH: (mean, 0.1, 0.2, 0.3 U mL^{-1})

No UFH

EIA-IgGAM (OD units)

Rapid ↓ heparin-independent platelet activation

IVIG: Plt 21 → 200 (3 days)

No new, progressive, or recurrent thrombosis; total parenteral nutrition (short gut syndrome) (last follow-up, 20-weeks)

Mnemonic for VITT Recognition

#1 V = Vaccine

#2 I = Interval (5-30 days)

#3 T = Thrombosis (presenting feature)

#4 T = Thrombocytopenia
If your jurisdiction uses the ChAdOx1 nCov-19 vaccine, be aware of VITT.

Diagnosis and Management of Vaccine-Related Thrombosis following AstraZeneca COVID-19 Vaccination: Guidance Statement from the GTH

Version 1.0
Published: March 30, 2021

Key Message
This Science Brief provides information for health care professionals about Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT), a rare adverse event following the AstraZeneca COVID-19 vaccine. This brief describes the pathophysiology, presentation, diagnostic work-up and treatment of VIPIT. Figure 1 presents a decision tree for diagnosing and ruling out VIPIT.

Guidance agreed with Expert Haematology Panel (EHP) April 10th 2021
Guidance agreed with British Society of Neuroradiologists (BSNR) and RCR April 11th 2021
The challenge: quickly rule VITT in (or out) and initiate life saving treatment

- **Suspected VITT**: symptoms + time frame + basic tests
- **Presumptive VITT**: advanced tests + imaging
- **Confirmed VITT**: specialized tests

Be aware of TYPICAL symptoms in a TYPICAL time frame after vaccination

- Typical symptoms of arterial or venous clots
  - Persistent and severe headache, focal neurological symptoms, seizures, blurred or double vision (suggesting cerebral vein thrombosis or arterial stroke)
  - Shortness of breath or chest pain (suggesting pulmonary embolism or acute coronary syndrome)
  - Abdominal pain (suggesting splanchnic thrombosis)
  - Limb swelling, redness, pallor, or coldness (suggesting deep vein thrombosis or acute limb ischemia)

- Typical time frame is 4 to 28 days post-vaccination

Suspected diagnosis?
Focus on basic testing with high NPV

Key questions:
- Symptoms?
- Date of the vaccine?

Key diagnostics:
- Complete blood count (CBC)

Symptoms of VITT:
Persistent and severe headache, focal neurological symptoms, seizures, blurred vision, shortness of breath, chest or abdominal pain, swelling and redness in a limb, pallor and coldness in a limb.

- Onset between 4 and 28 days after vaccination

- CBC shows platelets <150 x 10⁹/L

- Do not proceed to HIT testing

Suspected VITT
Presumptive diagnosis?
Focus on advanced tests and imaging

Key diagnostics:
- D-dimer (> 2000 mcg/mL FEU or DDU)
- Blood film should show only thrombocytopenia
  - Mimickers may have other abnormalities
- Imaging
  - CT venogram is rapid, accessible, and accurate
  - MR/MR venography may be a practical alternative

Presumptive VITT
Initial management: anticoagulation and managing the immune reaction

- NO heparin
- NO platelet transfusions
- First line anticoagulation:
  - Direct oral anti-Xa inhibitors
  - If patient unstable, or renal function is impaired, consider parenteral anticoagulants
- IVIG 1 g/kg daily for at least 2 days, especially for severe or life-threatening clots
- Report to Public Health Ontario and Health Canada

Hematology consultation + HIT ELISA

Many questions remain – for clinicians, regulators, and the public

- When do we use second line treatment (steroids, plasma exchange)?
- Do these antibodies persist?
- How do we monitor patients at discharge?
- What are the implications for the second dose of ChAdOx1 nCov-19 and other vaccinations?
- Is this the same as the adverse events reported after the J&J vaccine?

https://covid19-science-table.ca/

Evidence based scientific and lay summaries, and focused clinical guidance