Vaccine Induced Thrombotic Thrombocytopenia

Priyanka Kavdikar, Divya Honavar, The GTF Group
Mentor: Aditya Sathe

Abstract

- Vaccine-induced thrombotic thrombocytopenia (VITT) is a rare but devastating adverse event following adenoviral vector-based vaccinations for COVID-19 resulting in thrombosis, especially of the cerebral and splanchnic vasculature.

- The pathogenesis of this condition stems from unregulated, widespread activation and consumption of platelets causing thrombosis in all blood vessels

- Diagnosis of the condition is based on the presence of thrombotic symptoms in recently vaccinated patients along with confirmatory laboratory studies.
- Treatment involves immediate hospitalization, anticoagulation to prevent further thrombosis, and plasma exchange therapy to clear the antibodies from the blood.

Introduction

1. In early 2020, vaccines were developed to combat the COVID-19 pandemic and prevent serious infection, hospitalization, and death. However, it was discovered that the vaccine components might trigger an unwanted immune response by the body.

1. The scientific community proposed that these cases represent a vaccine-related variant of spontaneous heparin-induced thrombocytopenia and the condition be named VITT, to differentiate it from another similar condition called Heparin Induced Thrombocytopenia (HIT).

1. Preliminary evidence suggests that this condition is quite rare and exact risk factors are still unknown. Initial reports suggested that there may be a female and young age predominance but this has not been confirmed through large studies.

COVID-19 Vaccines

The European Medicines Agency approved five vaccines against COVID-19, and more than 600 million doses have been administered globally.
Within 10 days after receiving a first immunization with ChAdOx1 nCoV-19, five health care workers 32 to 54 years of age (four females and 1 male) presented with thrombosis in unusual sites and severe thrombocytopenia at the Oslo University Hospital.

Vaccine Induced Thrombotic Thrombocytopenia

Which vaccines are implicated?

- The Johnson&Johnson and AstraZeneca vaccines are the two adenoviral vaccines that have been administered to large numbers of individuals with reported cases of VITT.

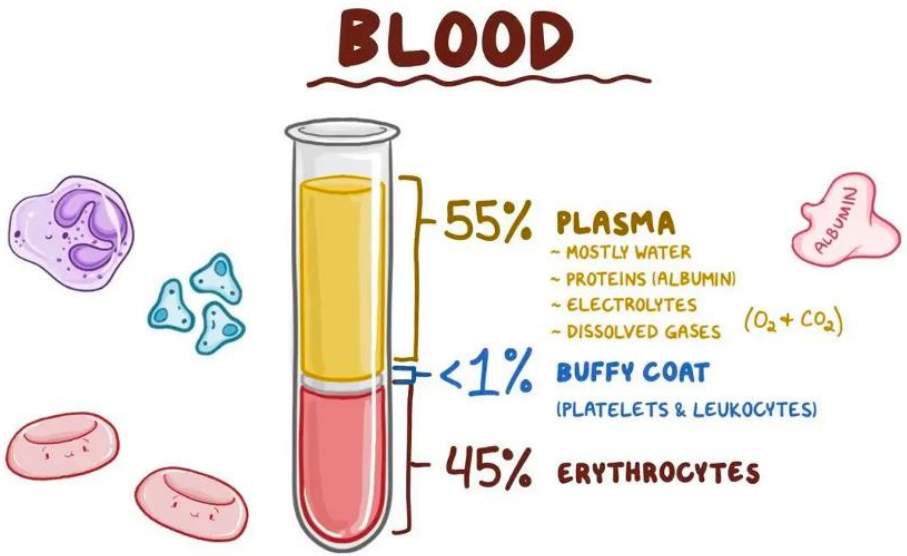
How many cases have been reported so far?

- The incidence of VITT is still exceedingly rare. A large-scale study in Norway was completed and it was found that there were 5 cases in approximately 130,000 individuals vaccinated with the AstraZeneca vaccine.

Are there specific populations at risk?

- It may be possible that people with a history of heparin induced thrombocytopenia (HIT) or cerebral sinus vein thrombosis (CSVT) with low platelets are at an increased risk of VITT. They should receive an mRNA vaccine such as Pfizer or Moderna.

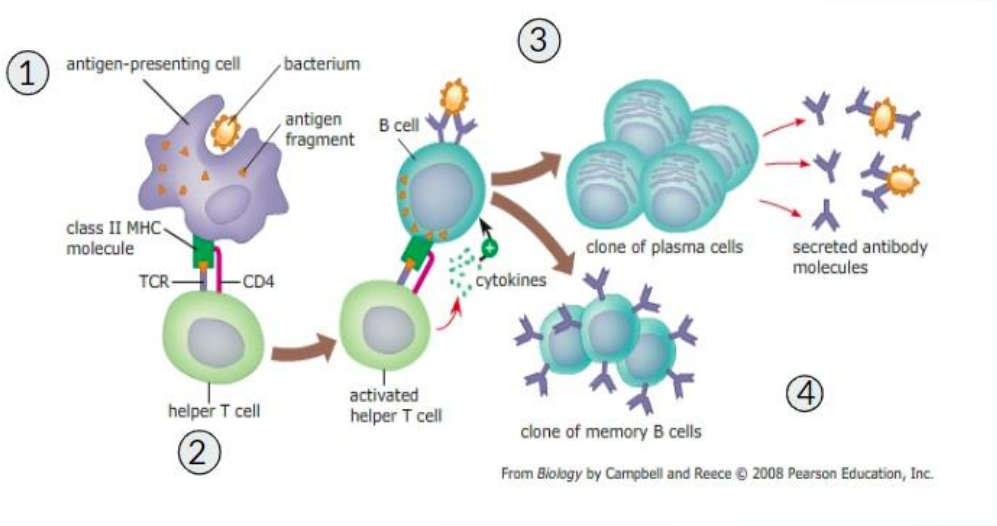
Role of Hematologic System



Blood is composed of 3 distinct layers that each serve a specific function in the body:

Plasma, which is 55% of the total volume, contains the solutes and nutrients that are delivered to the organs
Erythrocytes, which are 45% of the total volume, bind and deliver oxygen to the organs
The **buffy coat**, which is only 1% of the total volume, consists of platelets and white blood cells

Role of Immune System



The production of antibodies to fight infection requires a coordinated response by the immune system:

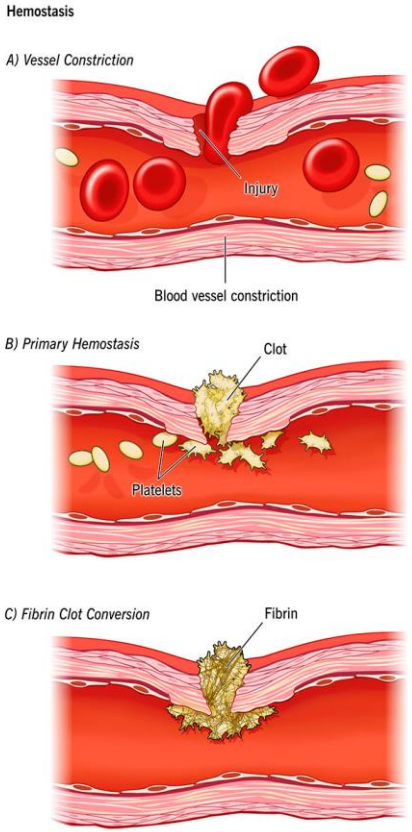
1. Antigen-presenting cell engulfs the pathogen and presents fragments to helper T cells
2. Helper T cells relay the response and activate B cells
3. B cells mature into either plasma cells or memory B cells
4. Plasma cells secrete antibodies specific for the pathogen that circulate throughout the bloodstream

Hemostasis

Platelets are essential for the repair of blood vessel injury such as a bruise or a cut.

Steps of Hemostasis:

1. Reflex vasoconstriction
2. Platelets arrive and bind to the collagen on the blood vessel surface and become sticky
3. More platelets arrive and form a platelet plug
4. Formation of fibrin meshwork
5. Further repair of vessel and formation of scar tissue



COVID-19

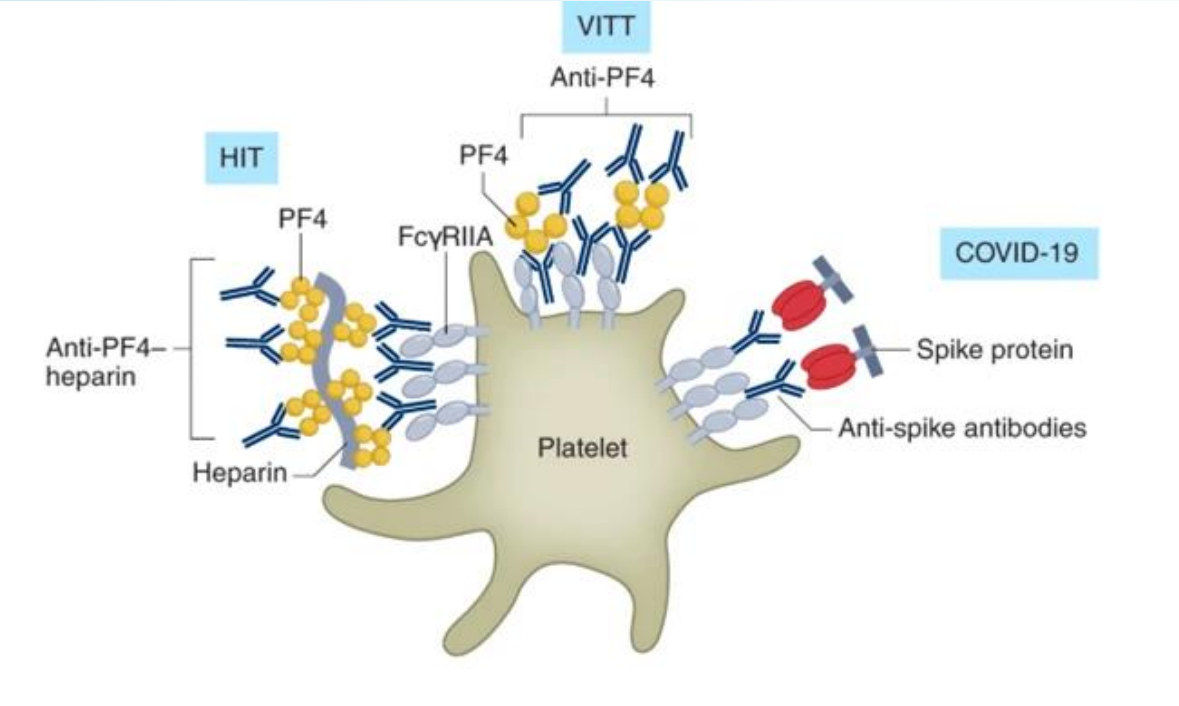
Origin: COVID-19 was first discovered in Wuhan, China after reports of a deadly pneumonia-like disease

Symptoms: cough, fever or chills, shortness of breath, fatigue and body ache, congestion or runny nose, nausea and vomiting, sore throat, and headache. New evidence has shown that COVID-19 symptoms may include a loss of taste and smell.

Complications: pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, septic shock, thrombosis, and death

Death Toll: As of May 29, 2022, 6,310,616 people have died Worldwide from COVID-19

Pathophysiology of VITT



Diagnosis and Treatment of VITT

Criteria for a definitive diagnosis of VITT include:

1. A COVID vaccine 4 to 42 days prior to symptom onset
2. Any venous or arterial thrombosis and subsequent thrombocytopenia
3. A positive PF4 ELISA.

Key considerations in the management of VITT to prevent additional thrombotic complications and reverse the effects of widespread platelet activation:

1. It is recommended that patients with confirmed VITT are treated in the hospital under strict monitoring
2. Therapeutic anticoagulation is one of the primary treatments for VITT and is used unless there is a contraindication such as expanding intracerebral hemorrhage.
3. It is unknown whether heparin is safe and effective or harmful in individuals with VITT. Early reports in which patients were treated with heparins described clinical worsening and early recommendations were to avoid heparin because of the resemblance of VITT to HIT.

Complications of VITT

Because VITT causes a systemic response in the body, it can affect multiple organs and lead to fatality.

Serious complications include:

1. Ischemic stroke
2. Myocardial infarction
3. Pulmonary embolism
4. Serious bleeding
5. Sudden death

Conclusions and Key Takeaways

#1: Vaccines have demonstrated remarkable **efficacy** and safety in the fight against the COVID-19 pandemic

#2: VITT is a rare complication of COVID-19-specific vaccinations characterized by widespread **platelet activation** and **thrombosis**

#3: Although the etiology is still unclear, possible mechanisms of platelet activation may include **nonspecific cross-reactivity** between the antibodies produced by the vaccine and surface proteins found on platelets

#4: The diagnosis is made largely by the clinical presentation along with laboratory studies that show evidence of thrombosis and platelet consumption. Treatment involves **therapeutic anticoagulation** and supportive care

Future Directions

- Further characterization of mechanism
- Duration of anticoagulation
- Treatment strategies to prevent platelet activation

Acknowledgements

We would like to extend our sincere gratitude to the GTF board, our parents, Dr. Atul Laddu, and our mentor, Aditya Sathe, for giving us the opportunity to learn and grow through the completion of this project.

References

1. Franchini M, Liumbruno GM, Pezzo M. COVID-19 vaccine-associated immune thrombosis and thrombocytopenia (VITT): Diagnostic and therapeutic recommendations for a new syndrome. *Eur J Haematol*. 2021;107(2):173-180. doi:10.1111/ejh.13665
2. John, C.V., Kumar, R., Sivan, A.K. *et al.* Vaccine-induced thrombotic thrombocytopenia (VITT): first report from India. *Thrombosis J* 20, 11 (2022). https://doi.org/10.1186/s12959-022-00370-6
3. McGonagle D, De Marco G, Bridgewood C. Mechanisms of Immunothrombosis in Vaccine-Induced Thrombotic Thrombocytopenia (VITT) Compared to Natural SARS-CoV-2 Infection. *J Autoimmun*. 2021;121:102662. doi:10.1016/j.jaut.2021.102662
4. Swan, D. et al. “Vaccine-induced thrombosis and thrombocytopenia (VITT) in Ireland: A review of cases and current practices.” *Thrombosis Update* vol. 5 (2021): 100086. doi:10.1016/j.tru.2021.100086