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"UNMASKING COVISHIELD: THE TRUTH BEHIND VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA"

Immunohematology

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ABSTRACT

The Covishield vaccine, developed by AstraZeneca and the University of Oxford, has been crucial in the global fight against COVID-19. Its effectiveness in reducing severe disease and hospitalizations has significantly contributed to public health efforts. Concerns have arisen about vaccine-induced immune thrombotic thrombocytopenia (VITT) associated with Covishield and other adenoviral vector vaccines. The article delves into Covishield's development process, clinical trial challenges, and its importance in global vaccination campaigns. It explores the epidemiology of VITT, noting varying incidence rates across populations and age groups. The pathogenesis of VITT involves antibodies targeting platelet factor 4 (PF4), offering insights into this rare condition's mechanisms and clinical manifestations like thrombosis and thrombocytopenia. Controversies surrounding Covishield, particularly VITT cases, are discussed, with ongoing research aiming to understand and mitigate these risks. The article emphasizes the need to rebuild public trust and the critical role of robust pharmacovigilance systems in monitoring vaccine safety and efficacy.

KEYWORDS

Covishield, Astrazeneca, Thrombosis, Thrombocytopenia

INTRODUCTON

The Covishield vaccine, developed by AstraZeneca and the University of Oxford, was a significant tool in combating the COVID-19 pandemic.(1) However, concerns were raised about vaccine-induced immune thrombotic thrombocytopenia (VITT), a rare condition linked to Covishield and similar adenoviral vector vaccines. This article delves into the development of Covishield, its clinical trials, epidemiology, and the mechanisms underlying VITT's pathogenesis.(2) The controversies surrounding Covishield's safety, particularly the reported cases of VITT, have led to debates and raised doubts about the vaccine's safety. The article examines ongoing research to understand these risks and implement strategies, and emphasizes the importance of rebuilding public confidence in vaccines and the role of pharmacovigilance systems in clinical trial safety monitoring.(3)

BACKGROUND OF COVISHIELD VACCINE

Covishield, a COVID-19 vaccine developed by AstraZeneca and the University of Oxford, entered its third phase of trials in July 2020. With significant public funding, the vaccine was distributed to low-income or under-developed countries as part of the WHO's COVAX program.(4) Despite facing challenges, trials resumed in November 2020, showing 70% efficacy.

A new multi-country trial, including India, confirmed the vaccine's efficacy, with up to 81.3% efficacy rates when administered in a two-dose regimen.

The vaccine also proved effective in preventing severe disease and hospitalization.(5) In March 2021, interim results from the US phase III trial showed 79% efficacy at symptomatic COVID-19 and 100% efficacy at preventing severe disease and hospitalization.(6) Even a single dose of Covishield provides significant protection against COVID-19-related hospitalizations, with a vaccine effect of 94% observed in some populations.(7)

EPIDEMIOLOGY

The AstraZeneca-Oxford vaccine has been linked to vaccine-induced immune thrombotic thrombocytopenia (VITT), but the incidence varies significantly across countries and age groups. In Norway, there were five cases among 130,000 vaccinated individuals, indicating a one in 26,000 incidence.(8) In the UK, the rates were one per 67,302 vaccinations after the first dose and one per 518,181 after the second dose.

There is limited information on the characteristics of VITT in people with comorbidities and previous COVID-19 infection. A UK study found that younger individuals had a higher risk of VITT, while those over 50 years old had a lower risk.(9)

Decoding Vaccine Induced Thrombosis And Thrombocytopenia

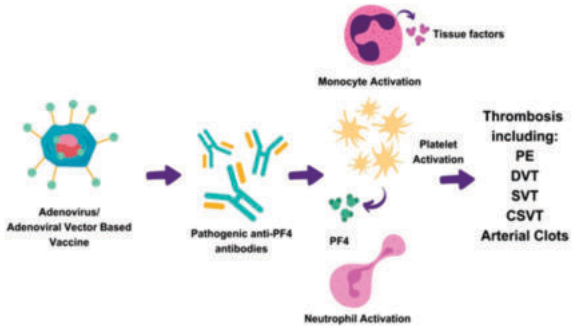

Fig 1: Diagrammatic representation of the general thrombosis pathology(39)

Thrombosis with thrombocytopenia syndrome (TTS) is an uncommon adverse event that has been reported in individuals who have been vaccinated with non-replicating adenovirus vector-based vaccines against coronavirus disease 2019 (COVID-19).(10)

These vaccines include the AstraZeneca COVID-19 ChAdOx-1 vaccine and the Johnson & Johnson (J&J) Janssen COVID-19 Ad26.COV2-S vaccine.(11) Vaccine-induced immune thrombotic thrombocytopenia (VITT) is the term that has been used to describe this condition in people who have antibodies that activate platelets against platelet-activating factor 4 (PF4).(12)

Pathogenesis Of VITT

Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a condition caused by certain adenoviral vector vaccines, causing antibodies to activate platelets, leading to blood clots in arteries and veins(13).

VITT is closely linked to heparin-induced thrombocytopenia (HIT),(14) as both involve antibodies targeting platelet factor 4. VITT may also result in consumptive coagulopathy, low platelet levels, and high D-dimer concentrations.(15) The detailed pathogenesis shown in the Fig 2.

Clinical Manifestations

The study reveals mild-to-moderate constitutional symptoms like fever, fatigue, headache, and muscle aches within 24 to 48 hours after vaccination, but these should not cause concern. Severe headaches, abdominal pain, back pain, nausea, vomiting, vision changes, altered mental state, and shortness of breath are common symptoms lasting 4 to 42 days.(16,17)

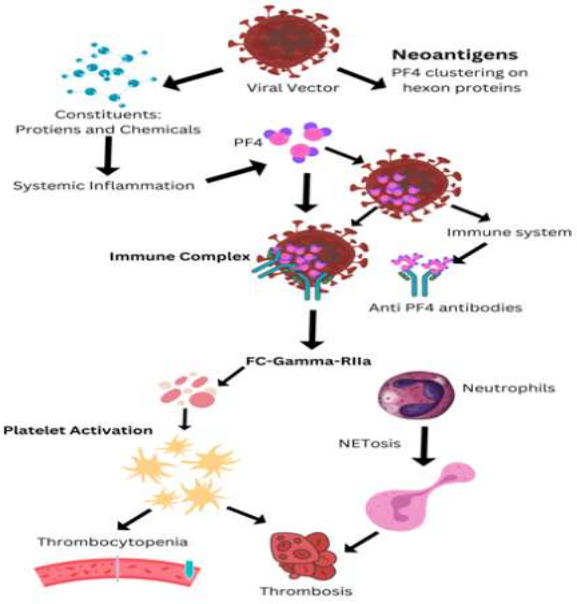

Fig 2: Schematic presentation of Pathogenesis of VITT.

Table 1: Symptoms of the Thrombosis

SYMPTOMS OF THROMBOSIS	
Fever	Back pain
Fatigue	Nausea and vomiting
Headache	Vision changes
Muscle aches	Altered mental state
Severe headache	Shortness of breath
Abdominal pain	Leg pain and swelling

Table 2: Differences between Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) and Thrombosis and Thrombocytopenia Syndrome (TTS)(18)

Criteria	VITT	TTS
Definition	Narrow group with high mortality, needs urgent diagnosis and treatment	Broader category encompassing various causes of thrombosis and thrombocytopenia post-vaccination
Label Implication	Implies vaccine causality and immune-mediation	Descriptive label without implying causality or mechanism
Diagnostic Criteria	Positive anti-PF4 testing, specific symptoms, thrombosis, thrombocytopenia	Positive anti-PF4 testing, thrombosis, thrombocytopenia, but may include cases without thrombosis or thrombocytopenia
Sensitivity and Specificity of Testing	Combined anti-PF4/heparin IgG EIA and PF4-dependent platelet activation testing: 96% sensitive, 77% specific	Combined anti-PF4/heparin IgG EIA and PF4-dependent platelet activation testing: 96% sensitive, 77% specific
Missed Cases	Overreliance on thrombosis may miss cases	Can pick up cases outside Brighton Collaboration Definition, including those without thrombosis or thrombocytopenia
Management	Urgent treatment required for VITT	Early treatment may benefit cases without thrombosis or thrombocytopenia

Unveiling Covishield's Controversy

Covishield which is a COVID 19 vaccine had faced both ups and downs. Even it was well effective,there have been some controversies. Recently AstraZeneca has itself admitted that TTS may be induced in very rare condition by the Covishield vaccine(19) This was happened as AstraZeneca has faced legal issue in UK court by a Covishield recipient who experienced symptoms of TTS within 10 days of vaccine administration led to a year long Coma(20). This made people worried about Vaccine's safety. This controversy has been leading to discussions about whether people should trust the vaccine . With the false information online, people were unsure about getting vaccinated. More over it is worth noting that the TTS symptoms usually found within 4 to 42 days of vaccine's administration,(21) and there are very low chances of TTS occurrence if recipient doesn't show symptoms.(22)Many studies are being performed on Vaccine's properties to ensure and safeguard public health.

Protecting Vaccine Safety: Rebuilding Future Confidence

The European Medicines Agency (EMA) has reported an increase in reporting of heavy menstrual bleeding (HMB) in COVID-19 vaccine recipients. The agency has reassured the public that there is no evidence that menstrual abnormalities impact fertility or reproduction.(23) An EU network evaluation found that mRNA COVID-19 vaccinations reduce hospitalization and death risks in both pregnant and non-pregnant women. To ensure global vaccination safety, the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) is responsible for assessing the safety of human pharmaceuticals. (24)

CONCLUSION

The Covishield vaccine has been instrumental in combating the COVID-19 pandemic, despite safety concerns related to VITT. Emphasizing the rarity of VITT is essential while underscoring the vaccine's effectiveness in averting severe COVID-19 cases. Research endeavors and robust pharmacovigilance systems are pivotal in addressing safety apprehensions, restoring public trust, and aiding informed vaccination choices. Transparency, continual assessment, and effective communication are key in overcoming obstacles and leveraging vaccines to safeguard public health.

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