Guidelines: Diagnosis and Management of Thrombosis with Thrombocytopenia Syndrome (TTS) following Adenovirus Vectored COVID-19 Vaccinations

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Introduction

Rare cases of blood clots with low platelets after receipt of adenovirus vector COVID-19 vaccines (AstraZeneca (AZ) and Johnson & Johnson (J&J) COVID-19 vaccines) have been reported and are referred to as Thrombosis with Thrombocytopenia Syndrome (TTS).

Although initial media reports described older females to be at higher risk of developing this condition, at present there is no clear signal of risk factors that would predispose an individual to TTS. This document provides guidance to UN medical staff globally on the diagnosis, management and reporting of TTS. **UN medical staff need to be alert for this syndrome and arrange for early referral to local hospitals or consultation with hematologists and/or consider early medical evacuation for further confirmation (lab, imaging) and treatment of this condition if capacity does not exist at their local duty station.**

Note that this is a living document which will be updated as more information emerges. For any questions, contact DHMOSH Public Health at dos-dhmosh-public-health@un.org More information from the WHO is available here.

Current Situation Update

At the time of writing, the AZ vaccine is currently authorized for use in several other countries globally though some have restricted or limited it's use despite evidence that this is a rare event. The J&J vaccine is also given in some countries around the world. Based on a multinational Phase 3 trial, the AZ vaccine has around 70% efficacy in preventing symptomatic COVID-19 at/after 14 days post second dose. Although there is some concern about vaccine efficacy against certain COVID-19 variants, the WHO continues to recommend use of this vaccine even in countries where variants are circulating[1,2].

TTS is a condition of blood clots associated with low platelet counts, that occurs following receipt of the vaccine. The likely mechanism is antibodies that induce massive platelet activation against platelet factor 4 (PF4), reducing platelet count and causing thrombosis although the full mechanism remains to be elucidated. This syndrome is thought to clinically mimic "heparin-induced thrombocytopenia" (HIT) but does not require heparin itself as a trigger. Most cases occurred 3 to 30 days[3,4,5] after receipt of

[1] https://www.who.int/news-room/feature-stories/detail/the-effects-of-virus-variants-on-covid-19-vaccines
[2] AstraZeneca ChAdOx1-S/nCoV-19 [recombinant]. COVID-19 vaccine (who.int)
[3] https://b-s-h.org.uk/media/19530/guidance-version-13-on-mngmt-of-thrombosis-with-thrombocytopenia-occurring-after-c-19-

the AZ vaccine, and in women[6] under 60 years old[7].

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most occurred in women and within 4 days of vaccination. The WHO has not yet released guidance on this matter.

References

- UK: Guidance Produced from the Expert Haematology Panel (EHP) focused on Covid-19 Vaccine induced Thrombosis and Thrombocytopenia (VITT)
- Ontario: Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) Following AstraZeneca COVID-19 Vaccination
- Interim statement of the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety on AstraZeneca COVID-19 vaccine
- https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood
- https://www.uptodate.com/contents/covid-19-vaccine-induced-immune-thrombotic-thrombocytopenia-vitt?topicRef=129849&source=see_link
- NEJM: Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination (9 April 2021)
- WHO: Guidance for clinical case management of thrombosis with thrombocytopenia syndrome(TTS) following vaccination to prevent coronavirus disease (COVID-19) (who.int)

Annex 1: Summary of Algorithm for TTS