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Reviews

Thrombosis with thrombocytopenia syndrome associated with COVID-19 vaccines

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ABSTRACT

Background: Current vaccines for the Coronavirus Disease of 2019 (COVID-19) have demonstrated efficacy with low risk of adverse events. However, recent reports of thrombosis with thrombocytopenia syndrome (TTS) associated with adenovirus vector vaccines have raised concern.
Objective: This narrative review summarizes the current background, evaluation, and management of TTS for emergency clinicians.
Discussion: TTS, also known as vaccine-induced immune thrombotic thrombocytopenia, is a reaction associated with exposure to the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) and AD26.COV2·S (Johnson & Johnson) vaccine, which may result in thrombocytopenia and thrombotic events. There are several case series of patients diagnosed with TTS, but the overall incidence is rare. TTS is characterized by exposure to one of the aforementioned vaccines 4–30 days prior to presentation, followed by thrombosis, mild-to-severe thrombocytopenia, and a positive platelet factor-4 (PF4)-heparin enzyme-linked immunosorbent assay (ELISA). Thrombosis typically involves atypical locations, including cerebral venous thrombosis and splanchnic vein thrombosis. Evaluation should include complete blood count, peripheral smear, D-dimer, fibrinogen, coagulation panel, renal and liver function, and electrolytes, as well as PF4-heparin ELISA if available. Consultation with hematology is recommended if suspected or confirmed. Treatment may include intravenous immunoglobulin and anticoagulation, while avoiding heparin-based agents and platelet transfusion.
Conclusions: With increasing vaccine distribution, it is essential for emergency clinicians to be aware of the evaluation and management of this condition.

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1. Introduction

In response to the Coronavirus Disease of 2019 (COVID-19) pandemic, multiple vaccines have been developed and distributed worldwide [1-3]. Initial trials reported rare cases of anaphylaxis and low rates of serious adverse effects [4]. More recent reports describe cases of thrombosis with thrombocytopenia syndrome (TTS), previously known as vaccine-induced immune thrombotic thrombocytopenia (VITT), associated with venous and arterial thromboembolism [5-12].

The two primary vaccines associated with TTS currently include the ChAdOx1 nCoV-19 (Oxford-AstraZeneca [AZ]; also known as Vaxzevria) and AD26.COV2·S (Johnson & Johnson [JJ]) vaccines [7-21]. The ChAdOx1 nCoV-19 and AD26.COV2·S vaccines consist of recombinant adenovirus vectors from a chimpanzee adenovirus or human adenovirus, respectively, which encode a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein [11,12,14]. On March 14, 2021, several European countries halted administration of the ChAdOx1 nCoV-19 vaccine due to potential safety concerns, including thrombocytopenia and thrombosis [7,11,15]. As of April 4, 2021, 169 cases of cerebral venous thrombosis (CVT) and 53 cases of splanchnic vein thrombosis associated with TTS were found from approximately 34 million ChAdOx1 nCoV-19 vaccine administrations in the European Union [11,15]. On April 13, 2021, the United States Food and Drug Administration and the Centers for Disease Control and Prevention (CDC) recommended pausing administrations of the AD26.COV2·S vaccine due to concern of TTS [7,11,16-18]. There were 15 reported cases of thrombosis from over 6.8 million doses of the AD26.COV2·S vaccine administered at that time [11,16-18]. In the United Kingdom as of April 14, there were 77 cases of TTS associated with CVT and 91 cases of TTS associated with thrombosis in other veins with 32 deaths, from over 21.2 million doses administered of the ChAdOx1 nCoV-19 vaccine [7,11,15,19]. As of May 16, 2021, there have been no cases of TTS associated with the mRNA-based vaccines from Moderna or Pfizer-BioNTech [11,12,15,18]. Importantly, the CDC and European Medicines Agency state the overall benefits of the ChAdOx1 nCoV-19 and AD26.COV2·S vaccines outweigh

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