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## Case Report

# Anti-PF4 antibody negative cerebral venous sinus thrombosis without thrombocytopenia following immunization with COVID-19 vaccine in an elderly non-comorbid Indian male, managed with conventional heparin-warfarin based anticoagulation



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## Introduction

The most neoteric, mercendized disquietude has been promoted by sporadic cases of COVID-19 vaccine induced thromboses [1,2]. From perspective of neurologists, infrequent cases of post-vaccination cerebral venous sinus thrombosis (CVT) have been a matter of consternation [3] apart from sporadic reports of other (non-CVT) neurological manifestations [4]. Several cases of CVT following immunization with adenovirus-vector vaccines ChAdOx1 nCoV-19 (Oxford-AstraZeneca) and Ad26.COV2.S (Janssen/J&J) have been reported [5,6] which is promoting "vaccine hesitancy", endangering vaccine implementation, and summoning strict vaccine surveillance and monitoring [5,7]. These two vaccines, do not require ultra-cold chain maintenance for storage, are befitting for middle/low-income countries [8]. However, amidst two, only Oxford-AstraZeneca vaccine is available in India branded as COVISHIELD [8].

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CVT is a well-recognized form of stroke, especially affecting young women, resulting from partial or complete occlusion of cerebral venous sinus system or the small-caliber draining veins further leading to physiologic venous backflow, venous hypertension and reduced cerebrospinal fluid (CSF) absorption [9]. These will consequently result in localized parenchymal edema, infarction and rarely hemorrhage and raised intracranial pressure (ICP). It has kindred well-studied genetic and non-genetic risk factors [9]. COVID-19 itself has thrombogenic potential, which is managed by therapeutic/prophylactic anticoagulation [10]. Recently, COVID-19 vaccines too have been alleged to have similar potential [1–3,5,6,11]. Several patho-mechanistic models have been proposed to explain such vaccine induced immune-thrombosis [12]. Salient most amongst them is breach of immune tolerance and production of autoantibodies to platelet factor-4 (PF4) and has been termed as vaccine-induced thrombotic thrombocytopenia (VITT), having extraordinary resemblance to the well-known entity heparin-induced thrombocytopenia (HIT) [12]. A cascade of micro-events following intramuscular COVISHIELD inoculation includes microvascular injury, microhemorrhage and activation of platelets with release of PF4, adenovirus cargo-dispersement with DNA-PF4 engagement might breach immune tolerance resulting in anti-PF4 directed autoimmunity [12]. The alternative pathomechanisms deciphered have stressed upon molecular mimicry, contaminants in vaccine proteins, vector-viral proteins, buffers or immunity against SARS-CoV-2 spike proteins [12].

Herein, the authors, report a case of CVT following immunization with COVISHIELD vaccine in an elderly Indian male without any pre-existing comorbidities. This is arguably the first report of such kind from India, and case will add to the tally of cases of CVT following COVISHIELD vaccination; besides, the fact that this patient had neither anti-PF4 antibodies nor thrombocytopenia and responded remarkably with low-molecular weight heparin (LMWH) therapy, will provide insights regarding other elusive mechanisms of CVT following COVISHIELD vaccination; questions