




## Deep vein thrombosis (DVT) occurring shortly after the second dose of mRNA SARS-CoV-2 vaccine

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Dear Editor,

Currently, the SARS-CoV-19 pandemic represents the leading global health emergency, and vaccines are the primary health strategy to eradicate this global challenge. In Europe, three vaccines have been approved by the European Medicines Agency (EMA), two based on mRNA technology, and one with an adenovirus vector [1]. Published data show high protective efficacy rates in the face of mostly mild-to-moderate and short-lasting adverse effects, mainly after the second dose [2–4]. Venous thromboembolic (VTE) complications have been consistently reported to be increased in SARS-CoV-2 infection, most probably as the results of a thrombophilic state secondary to inflammation and immunethrombosis [5]. On the other hand, no reports are available regarding a possible association between VTE and SARS-CoV-2 post-vaccine acute-phase reaction. Here we describe a case of distal deep vein thrombosis occurring immediately days after the second dose of mRNA vaccine.

A 66-year-old woman received the first dose of mRNA Covid-19 vaccine (BNT162b2, Comirnaty, Pfizer/BioNTech) subcutaneously on January 4th, 2021, without any reported clinical problem; she was scheduled for the second dose on January 25th. Her medical history was unremarkable except for post-trauma left leg neuropathy. She never had previous thrombotic events; she had one successful delivery. Her body mass index was 23 kg/m<sup>2</sup>; she did not smoke or had no allergic problems; she intermittently took painkillers for the neuropathy. On January 26th, 24 h after

the second vaccine dose, she received acetaminophen for persistent fever with chills, fatigue, malaise, and muscle pain. On January 27th, 48 h after the second vaccine dose, persistent fever was still present, and acute right calf pain appeared in the absence of trauma. On January 28th, she was admitted for evaluation at the emergency room because of persistent pain and inability to walk. Physical examination was unremarkable except for mild edema in the right calf. Blood tests (Blood count, INR, PTT, fibrinogen, renal and hepatic function) were normal, as notably was the D-dimer measurement. A Color-Doppler ultrasound scan revealed the presence of deep vein thrombosis involving the right peroneal vein and extending up to the popliteal vein, without signs of venous insufficiency. Thrombophilia screening was otherwise negative except for the presence of heterozygous FV Leiden mutation. The patient started apixaban 10 mg bid for 1 week, followed by 5 mg bid, with rapid symptoms resolution.

To our knowledge, this is the first reported case of DVT presenting as an adverse event post-SARS-CoV-2 vaccination. Arguably, the intense immunological response evoked by the second dose of vaccine could be a trigger for the thrombotic event described, a mechanism recognized in many clinical conditions. No DVT cases have been reported on 21,720 persons receiving BNT162b2, suggesting that the DVT incidence may be lower than one case every 5889 (this figure representing the 95% upper boundary of confidence interval) [4]. No apparent correlation can be made with the presence of a mild thrombophilia mutation in this patient. In our district, the vaccination program started on January 2021 and involved only health workers, of whom 3010 received two doses on January 25th. This case notwithstanding, we may consider that DVT post-vaccination incidence may still be very low and within the expected incidence figure. A longer follow-up and a greater diffusion of SARS-CoV-2 vaccines in the population are needed

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to clarify the magnitude of this potential side effect—that, although extremely low, may not be negligible on a population-wide basis.

## Compliance with ethical standards

**Conflict of interest** The authors state that they have no relevant conflict of interest to disclose.

**Statement of human and animal rights** Ethical approval was waived by the local Ethics Committee in view of the observational nature of the study and all the procedures being performed were part of the routine care.

**Informed consent** The authors obtained informed consent from the patient involved in this report.

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