Cerebral Venous Thrombosis after BNT162b2 mRNA SARS-CoV-2 vaccine

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The development of SARS-CoV-2 vaccines has raised several concerns regarding venous thromboembolism, namely cerebral venous thrombosis. Although cerebral venous thrombosis has been reported after administration of a viral vector vaccine, due to a possible auto-immune mechanism inducing thrombocytopenia, the same has not happened in mRNA vaccines. We report two cases of cerebral venous thrombosis, shortly after administration of mRNA vaccine. In both patients, there was no evidence of thrombocytopenia or antiplatelet antibodies, and alternative causes for cerebral venous thrombosis were found. As such, despite the temporal relation of both cases to vaccine administration, these types of cerebral venous thrombosis do not seem to be pathophysiological different from cerebral venous thrombosis not associated to SARS-CoV-2 vaccination. Continuous pharmacovigilance is necessary to monitor possible new events and clarify this association.

Keywords: Cerebral Venous Thrombosis—COVID-19—SARS-CoV-2—Thromboembolism

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SARS-CoV-2 vaccine development raised several concerns regarding adverse events, particularly venous thromboembolism.[1,2] Cerebral venous thrombosis (CVT) was recently reported in patients vaccinated with AstraZeneca's vaccine and Janssen's vaccine.[3–6] This side effect has not been previously reported in mRNA vaccines. We hereby report two CVT cases in patients who took an mRNA vaccine (BNT162b2, Comirnaty®, Pfizer/BioNTech).

Case 1: A 47-year-old female, who had iron-deficiency anemia due to adenomyosis and used combined oral contraceptives, developed persistent headache, nausea and photophobia six days after the first vaccine dose. Three days later, she presented a sudden left motor deficit. Papilledema, left visual extinction, right gaze deviation, and left hemiparesis were documented. Brain MRI with venography revealed thrombosis of superior sagittal, right lateral, transverse, sigmoid sinuses and jugular vein and left sigmoid sinus, together with right frontal subarachnoid hemorrhage and a cortical venous infarct. Admission PCR test for SARS-CoV-2 was negative. Complete blood count revealed microcytic hypochromic anemia (9.3 g/dL) and normal platelet count (343.000/μL). Coagulation tests-aPTT, Quick test, fibrinogen-were normal. Prothrombotic screening-lupus anticoagulant, anticardiolipin antibodies, protein C, RAPC, antithrombin III, and prothrombin mutation-was negative except for low protein S (0.40, N>0.54). Autoimmune screening-immunoglobulins, complement, antinuclear antibodies-was negative. A chest-abdomen-pelvis CT excluded occult neoplasms. She started acetazolamide and enoxaparin 60 mg bid, later switched to warfarin. At two-month follow-up, slight gait instability was the only deficit. Antiplatelet-PF4-antibodies, measured 2 months after the event with ELISA technique, were negative. Anti-SARS-CoV-2 IgG was positive at low titers [anti-RBD IgG 17 U/mL (N<10), anti-S1 IgG 11 U/mL (N<10), anti-S2 and anti-N negative]. The second dose of the vaccine was never administered.

Case 2: A 67-year-old female had a history of multiple cerebral cavernous malformations, hypertension, diabetes, dyslipidemia, viral myocarditis, and depression. Three days after the second vaccine dose, she presented

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