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Letter to the Editors-in-Chief

Cerebral venous thrombosis and thrombocytopenia post-COVID-19 vaccination

We report the case of a 50-year-old white man who had always been in good health. He was a voluntary periodic blood donor (his last whole blood donation was on December 1, 2020) and all laboratory checks performed before donations, including blood cell count, were always within the normal range. His personal and family history was negative for thrombotic or hemorrhagic disorders. He had never suffered from COVID-19 and all molecular screens for SARS-CoV-2 (performed routinely every month as he worked in the public administration) were always negative. On March 4, 2021, he received the first dose of the anti-COVID-19 vaccine produced by AstraZeneca without any immediate adverse reaction. Seven day later (11 March 2021) he suffered from a worsening headache but, despite this symptom, he continued to work under analgesic medications. On March 15, 2021 the patient was referred unconscious to the emergency room of the city hospital of Mantua (Italy). Computed tomography (CT) scans of the brain showed intra-parenchymal hemorrhage in the left cerebral hemisphere while CT angiography of intracranial circle vessels showed multiple small bleeding spots in the context of the left parenchymal hemorrhage and lack of opacification of the left transverse and sigmoid sinuses, compatible with cerebral venous sinus thrombosis (CVST). The patient was immediately transferred to the Intensive Care Unit and underwent urgent neurosurgery in a desperate attempt to stop and remove the intracerebral hemorrhage, but 18 h after the intervention he died. Overall, the patient was transfused with 9 red blood cell units and 4 platelet apheresis units. Thromboelastogram (TEG6S, Haemonetics) studies performed before and during the operation showed a prolonged reaction time, decreased platelet function and the absence of fibrinogen, measured with a functional fibrinogen assay, with a consequent markedly reduced maximum amplitude of the clot (8.4 mm, normal range 52–69 mm) only partially and temporarily restored by an infusion of fibrinogen concentrate (10 g total). The most relevant abnormal laboratory results (Table 1), performed on admission to hospital, were severe thrombocytopenia and hypofibrinogenemia associated with factor XIII deficiency. In addition, heterozygous *MTHFR* C677T together with increased levels of homocysteine, which have been associated with an increased CVST risk [1,2], and concomitant folate deficiency were observed. Notably, like previous observations by other investigators [3,4], anti-PF4 antibodies were detected. Further studies are needed to assess the pathogenesis of thrombocytopenia (i.e., immune-mediated or protein spike-mediated) [5] and its relationship with the development of CVST following anti-COVID vaccination.

CRediT authorship contribution statement

M.F.: study design and concept, writing a draft of the manuscript; S.T.: coagulation assays, writing a draft of the manuscript; M.P.: study design and concept, interpretation of the data; C.G.: coagulation assays; B.C.: coagulation assays; I.T.: coagulation assays; C.P.: interpretation of the data from clinical point of view; S.A.B.: revising the manuscript; G.C.: interpretation of the data from clinical point of view, revising the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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