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Letter to the Editor



Relapse of thrombotic thrombocytopenic purpura after COVID-19 vaccine

We report a case of a 48-year-old white female patient with a history of relapsing thrombotic thrombocytopenic purpura (TTP). The patient has been known to our department since 2015 when she was diagnosed for the first time with TTP with a high antibody titer (99 U/mL) against ADAMTS13 (A Disintegrin And Metalloproteinase with a Thrombospondin type 1 motif, member 13) and very low ADAMTS13 activity (Fluorescent Resonance Energy Transfer [FRET] assay: <3 %, normal range 45–138 %). She was treated with ten plasma-exchange (PEX) procedures and corticosteroids and obtained a complete remission. Her first relapse, in February 2019, presented as ecchymoses and severe thrombocytopenia; she was successfully treated again with seven PEX procedures and steroids. Afterwards, the patient was well and periodic blood cell counts (every 6 months, last check performed in October 2020) were normal. On March 12, 2021 the patient was referred to the emergency room of the city hospital of Mantua for a new onset of ecchymoses on both arms and forearms without any other symptoms or signs. The complete blood count demonstrated mild normocytic anemia (hemoglobin 11.5 g/dL, normal range 12.3–14.5 g/dL), moderate thrombocytopenia (platelet count $94 \times 10^9/L$, normal range $150\text{--}400 \times 10^9/L$), a coagulation profile and renal function within the normal range, and moderately increased lactate dehydrogenase (LDH, 637 UI/L, normal range 150–450 UI/L). On a peripheral blood smear, there were about 10 % schistocytes. ADAMTS13 activity was markedly reduced (FRET assay: <3 %) with a high titer of anti-ADAMTS13 antibodies (88 U/mL). Six days before the TTP relapse (March 6, 2021), the patient had received the second dose of the anti-COVID-19 vaccine produced by Pfizer-BioNTech (the first dose had been administered on February 11, 2021). At hospital admission the molecular search of SARS-COV-2 on nasopharyngeal swab was negative while anti-SARS-COV-2 IgG antibodies were 105 UA/mL (chemiluminescent immunoassay DiaSorin, positive >15 UA/mL). The patient was promptly treated with seven PEX procedures and steroids, with a rapid and excellent response (normalization of platelet count and LDH after the third PEX). This is the first case reported in literature of a TTP relapse following anti-COVID-19 vaccination. Other cases of vaccine-related thrombotic microangiopathies have been described, possibly related to the immune dysregulation and/or complement activation triggered by vaccination, particularly against influenza [1–4]. Further studies are needed to verify the possible association between microangiopathic thrombotic disorders with an autoimmune pathogenesis and the administration of vaccines against COVID-19.

Contribution

C.S. and A.A. designed research, F.F., R.G., P.M., E.M., M.A. and B.M. performed research; F.P. contributed analytical tools; C.S., A.A. and M.F. wrote the paper; F.P. revised the manuscript.

Declaration of Competing Interest

The authors report no declarations of interest.

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References

- [1] Sobolev O, Binda E, O'Farrell S, Lorenc A, Pradines J, Huang Y, et al. Adjuvanted influenza-H1N1 vaccination reveals lymphoid signatures of age-dependent early responses and of clinical adverse events. *Nat Immunol* 2016;17(2):204–13.
- [2] Bitzan M, Zieg J. Influenza-associated thrombotic microangiopathies. *Pediatr Nephrol* 2018;33(11):2009–25.
- [3] Yavaşoğlu İ. Vaccination and thrombotic thrombocytopenic purpura. *Turk J Haematol* 2020;37(3):218–9.
- [4] Dias PJ, Gopal S. Refractory thrombotic thrombocytopenic purpura following influenza vaccination. *Anaesthesia* 2009;64(4):444–6.

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