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Letter to the Editor

Cerebral Venous Thrombosis following COVID-19 Vaccination

Dear Editor,

We appreciate the literature review by Abdalkader et al.[1] to summarize the clinical epidemiology and features of cerebral venous thrombosis (CVT) in patients with coronavirus disease 2019 (COVID-19). Based on the meta-analysis performed by Baldini et al.,[2] the estimated proportion of CVT cases among hospitalized patients with COVID-19 was 0.08%; therefore, it is not surprising that COVID-19 associated CVT had not been given much attention compared to the more common deep vein thrombosis and pulmonary embolism events in this patient population. However, we were recently shocked by the occurrence of CVT following administration of ChAdOx1 nCoV-19 vaccine, which is also accompanied by thrombocytopenia and platelet activation, although we would stress that the direct causality had not been proven as of the time of writing.

While the development of CVT is more common in women than men, the 33 cases of COVID-19-associated CVT summarized by Abdalkader et al.[1] had a male preponderance (57.1%), which thus suggests that the male patients are more likely to develop CVT upon acquisition of COVID-19. Nevertheless, there had been a female preponderance thus far among the documented cases of CVT following administration of ChAdOx1 nCoV-19 vaccine.[3] Similar to the general population, COVID-19-associated CVT and CVT following COVID-19 vaccination generally occur in relatively young individuals.[1,3] Perhaps, young individuals, especially those with risk factors for CVT such as the use of oral contraceptives, should avoid the ChAdOx1 nCoV-19 vaccine, pending further investigations.

Anticoagulation is the mainstay of treatment for patients who develop CVT, where Abdalkader et al.[1] reported that more than half of the patients who developed COVID-19 associated CVT in the published cases received therapeutic anticoagulants. Traditionally, subcutaneous low-molecular-weight heparin or intravenous unfractionated heparin is an appropriate antithrombotic treatment for patients with acute symptomatic CVT[1]; but due to the resemblance of the prothrombotic thrombocytopenic disorder following administration of ChAdOx1 nCoV-19 vaccine to heparin-induced thrombocytopenia, it is best for heparin-based anticoagulants to be avoided in patients with CVT after COVID-19 vaccination. With non-heparin-based anticoagulants, we have few options, namely argatroban, bivalirudin, danaparoid, fondaparinux, and direct oral anticoagulants.

Clinicians may acknowledge that the definitive evidence of the effectiveness of non-heparin-based anticoagulants in acute CVT is lacking, but case reports and case series have demonstrated the successful use of these agents.[4-6] For example, there is a case report[4] of an adolescent boy with CVT and heparin-induced thrombocytopenia, who was initiated with fondaparinux and later with warfarin and achieved clinical remission. There was also a case report[5] of a woman in middle age with CVT due to heparin-induced thrombocytopenia who made a remarkable recovery upon treatment with systemic argatroban infusion. We were not aware of the use of bivalirudin in acute CVT in the literature, and the utility of direct oral anticoagulants such as dabigatran and rivaroxaban in CVT was mainly in the post-acute phase after administration of parenteral anticoagulants.

Yet, it should be noted that these non-heparin-based anticoagulants have been successfully used in patients with heparin-induced thrombocytopenia; cautious administration of these agents is still warranted considering the catastrophic consequences of CVT. High-dose intravenous immunoglobulin to block platelet activation may also hasten the recovery and prevent recurrent thrombosis and thus should also be considered.

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https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105866

References

1. Abdalkader M, Shaikh SP, Siegler JE, et al. Cerebral Venous Sinus Thrombosis in COVID-19 Patients: A

DOI of original article: http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2021.105733.
1052-3057/$ - see front matter

Multicenter Study and Review of Literature [published online ahead of print, 2021 Mar 4]. J Stroke Cerebrovasc Dis. 2021;30(6):105733.
2. Baldini T, Asioli GM, Romoli M, et al. Cerebral venous thrombosis and severe acute respiratory syndrome coronavirus-2 infection: A systematic review and meta-analysis [published online ahead of print, 2021 Jan 11]. Eur J Neurol. 2021. https://doi.org/10.1111/ene.14727.
3. Greinacher A, Thiele T, Warkentin TE, et al. A prothrombotic thrombocytopenic disorder resembling heparin-induced thrombocytopenia following coronavirus-19 vaccination. Research Square 29 March 2021 www.researchsquare.com/article/rs-362354/v1.
4. Thorsteinsson GS, Magnussson M, Hallberg LM, et al. Cerebral venous thrombosis and heparin-induced thrombocytopenia in an 18-year old male with severe ulcerative colitis. World J Gastroenterol. 2008;14(28):4576-4579.
5. Dean A, Zyck S, Gould G, Schmidt E, Latorre JG. Good Outcome Following Catastrophic Cerebral Sinus Thrombosis due to Heparin-Induced Thrombocytopenia: Case Report and Review of Literature. Ann Clin Case Rep. 2018;3:1517.
6. Meppiel E, Crassard I, Latour RP, et al. Cerebral venous thrombosis in paroxysmal nocturnal hemoglobinuria: a series of 15 cases and review of the literature. Medicine (Baltimore) 2015;94(1):e362.