Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elevated Lipoprotein(a) and Cerebral Venous Sinus Thrombosis in COVID-19

Letter to Editor

Elevated Lipoprotein(a) and Cerebral Venous Sinus Thrombosis in COVID-19 in response to "Cerebral Venous Sinus Thrombosis in COVID-19 Patients: Multicenter Study and Review of Literature" by Abdalkader et al.[1]

We found the recent paper by Abdalkaber et al.[1] comprehensive and very interesting. The study found that COVID-19 patients with the rare and unique cerebral venous sinus thrombosis (CVST) were mostly female and that their D-dimer levels and inflammatory markers were significantly elevated. The authors also found that estrogen-modulating medications, the antiphospholipid syndrome, and morbid obesity belong to the risk factors of CVST. Additionally, the authors speculate that endothelial dysfunction may be of importance in the pathogenesis of CVST, although its role is less well-defined when compared with arterial ischemic stroke.[2]

We wish to add elevated serum lipoprotein(a) [Lp(a)] to the list of risk factors. Thus, based on a study by Skuza and coworkers[3] in which 80 CVST patients were followed after CVST, recurrence of CVST was found in 12 patients (15%) during a median follow-up time of 26 months. Serum Lp(a) concentrations were higher in the patients with recurrent CVST than those without it, i.e., 28 (19-36) mg/dL vs. 14 (9 -25) mg/dL. The importance of elevated serum Lp(a) as a potential risk factor for CVST maybe even more significant in patients with SARS-CoV-2 infection. The reason for this assumption is the fact that Lp(a) inhibits endogenous fibrinolysis and enhances inflammation thereby causing a procoagulant state.[4] Also, in patients with COVID-19, the disease-associated increased interleukin-6 level induces an elevated serum Lp(a) level which again further increases the risk of thrombosis.

Even though the incidence of CVST is low (about 0.02%) among patients with COVID-19, the figure is still 30 to 60 times greater than that among CVST in patients without SARS-CoV-2 infection.[1] There might be also special groups of COVID-19 patients with a particularly elevated risk of CVST. As an example, it has been shown that about 30 - 50% of heterozygous familial hypercholesterolemia (HeFH) patients, an estimated number of 5 million patients worldwide, have an elevated Lp(a) level.[5] HeFH is the most common inherited condition affecting cardiovascular disease and occurs in about 1:250 in the general population worldwide. Patients with HeFH suffer from endothelial dysfunction already in childhood because of a strongly elevated serum low-density cholesterol (LDL-C) level which is often accompanied by an elevated serum Lp(a) level.[6, 7] Thus, we can assume that HeFH patients have an elevated CVST risk. Alarmingly, a few cases of CVST after AstraZeneca COVID-19 vaccination were reported just very recently, and, by now (March 19, 2021) The European Medicines Agency's Pharmacovigilance and Risk Assessment Committee has reviewed in total 18 cases of CVST out of more than 20 million vaccinations carried out with this vaccine in Europe.[8] However, the benefits of the vaccinations vastly override this potentially serious harm. Nevertheless, safety monitoring is important especially among patients having an elevated risk profile for CVST, not to forget the HeFH patients with an elevated level of Lp(a).[5]

Declaration of Competing Interest

AV, MK none. PTK has received lecture honoraria and/or travel fees from Amgen, Novartis, Raisio Group, and Sanofi.

Author contribution: AV, PTH: writing the first draft and editing to produce the final draft; MK reviewing the final draft.

Alpo Vuorio,[*,†]
Markku Kaste,[‡§]
Petri T. Kovanen,[¶]
[*]*University of Helsinki, Department of Forensic Medicine, 00014 Helsinki, Finland*
[†]*Mehiläinen Airport Health Centre, 01530 Vantaa, Finland*
[‡]*Department of Neurosciences, University of Helsinki, Helsinki, Finland*
[§]*Department of Neurology, Helsinki University Hospital, Helsinki, Finland*
[¶]*Wihuri Research Institute, Biomedicum Helsinki 1, 00290 Helsinki, Finland*

Correspondence: Alpo Vuorio, Lentäjäntie 1 E 01530 Vantaa, Finland.
E-mail address: alpo.vuorio@gmail.com

https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105865

References

1. Abdalkader M, Shaikh SP, Siegler JE, et al. Cerebral Venous Sinus Thrombosis in COVID-19 Patients: A Multicenter Study and Review of Literature [published online

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

ahead of print, 2021 Mar 4]. J Stroke Cerebrovasc Dis. 2021;30(6):105733. https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105733.
2. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020;395 (10234):1417-1418. https://doi.org/10.1016/S0140-6736 (20)30937-5.
3. Skuza AA, Polak M, Undas A. Elevated lipoprotein(a) as a new risk factor of cerebral venous sinus thrombosis: association with fibrin clot properties. J Thromb Thrombolysis 2019;47(1):8-15. https://doi.org/10.1007/s11239-018-1769-0.
4. Moriarty PM, Gorby LK, Stroes ES, Kastelein JP, Davidson M, Tsimikas S. Lipoprotein(a) and Its Potential Association with Thrombosis and Inflammation in COVID-19: a Testable Hypothesis. Curr Atheroscler Rep. 2020;22(9):48. https://doi.org/10.1007/s11883-020-00867-3.
5. Vuorio A, Watts GF, Schneider WJ, Tsimikas S, Kovanen PT. Familial hypercholesterolemia and elevated lipoprotein(a): double heritable risk and new therapeutic opportunities. J Intern Med. 2020;287(1):2-18. https://doi.org/10.1111/joim.12981.
6. Sorensen KE, Celermajer DS, Georgakopoulos D, Hatcher G, Betteridge DJ, Deanfield JE. Impairment of endothelium-dependent dilation is an early event in children with familial hypercholesterolemia and is related to the lipoprotein(a) level. J Clin Invest. 1994;93:50-55.
7. Vuorio A, Raal F, Kaste M, Kovanen PT. Familial hypercholesterolaemia and COVID-19: A two-hit scenario for endothelial dysfunction amenable to treatment. Atherosclerosis 2021;320:53-60. https://doi.org/10.1016/j.atherosclerosis.2021.01.021.
8. World Heath Organization 2021. Statement of the WHO Global Advisory Committee on Vaccine Safety (GACVS) COVID-19 subcommittee on safety signals related to the AstraZeneca COVID-19 vaccine. https://www.who.int/news/item/19-03-2021-statement-of-the-who-global-advisory-committee-on-vaccine-safety-(gacvs)-covid-19-subcommittee-on-safety-signals-related-to-the-astrazeneca-covid-19-vaccine