EDITÖRE MEKTUP / LETTER TO THE EDITOR

Methylenetetrahydrofolate reductase gene polymorphisms and venous thrombosis

Metylenetetrahidrofolat redüktaz gen polimorfizmleri ve venöz tromboz

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Dear Editor,

We read with a great interest the research article of Kılıcaslan et al about the risk factors of pediatric patients with thrombosis¹. We would like to comment on this paper because of the discrepancies of current literature.

Firstly, the arterial and venous thromboses (VTE) were evaluated together, whereas the etiological causes were different. It was stated that 31 patients were diagnosed with central nervous system thrombosis, but they did not describe as ischemic stroke or cerebral venous sinus thrombosis. It is a very important issue because testing for inherited thrombophilia disorders is not justified in patients presenting with arterial thrombosis, since hereditary thrombophilia is principally a risk factor only for VTE².

Secondly, methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms 677CT and 1298AC were identified as inherited genetic risk factors in this study. Bezemer et al performed the Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis (MEGA) study to evaluate the effect of the MTHFR genotype on the risk of VTE and showed no association between the MTHFR 677CT polymorphism and VTE³. Simone et al investigated the risk of VTE associated with single and combined effects of factor V Leiden, prothrombin 20210GA and MTHFR 677CT with a meta-analysis involving over 11,000 cases and 21,000 controls⁴. In this meta-analysis, which were included the data from Turkey, there was no significant association with VTE for homozygous MTHFR 677TT. In this large pooled analysis, other large studies, like MEGA no effect were found for MTHFR 677CT on VTE⁵,⁶. On the other hand, MTHFR 1298AC polymorphism either the homozygous or heterozygous states do not associate with a higher homocysteine or a lowered plasma folate concentration⁷. It is not surprising that the investigators found MTHFR polymorphisms were very common in patients with thrombosis, because the rate of MTHFR polymorphisms was much higher in Turkey than other countries. Sazci et al reported the genotype frequencies 47.4% for MTHFR 677CT, 9.6% for 677TT, 46.3% for 1298AC and 10.0% for 1298CC in Turkish population, respectively⁸.

The authors observed that 31.3% low protein C activity, 18% low protein S activity, low antithrombin activity in one patient, and presence of lupus anticoagulant in two patients at the time of acute thrombosis. Acute thrombosis and anticoagulants affect the functional activity of anticoagulant factors that are typically measured in hypercoagulable panels². It might be explained with continued anticoagulant therapy in some patients had still low activities for natural anticoagulants in follow-up period in this research. It should be preferred that all tests except genetic based have...
performed a minimum of two weeks following discontinuation of anticoagulation if it is feasible\textsuperscript{2}. The authors reported significantly higher levels of lipoprotein (a) in patients with thrombosis. It is a risk factor for the development of atherosclerotic events. Also, VTE has been associated with elevated plasma lipoprotein (a) levels. Von Depka et al found that serum lipoprotein (a) was higher in 20\% of patients with VTE but in only 7\% of healthy controls\textsuperscript{9}. Sofi et al showed a significant association between high lipoprotein (a) levels and the occurrence of VTE with a meta-analysis\textsuperscript{9}. Actually, there are needed the new prospective studies to evaluate the role of the lipoprotein (a) levels as a thrombophilic risk factor in patients with VTE as mentioned by the authors.

In conclusion, MTHFR gene polymorphisms should not be evaluated as thrombophilic risk factors in patients with VTE according to current literature.

REFERENCES