□ LETTERS TO THE EDITOR □

The Timing of Thrombophilia Testing is Important: Comment on “Left Main Coronary Artery Thrombus Resulting from Combined Protein C and S Deficiency”

Key words: thrombophilia, protein C deficiency, protein S deficiency

(Intern Med 52: 695, 2013)

(DOI: 10.2169/internalmedicine.52.9298)

To the Editor I read with particular interest the manuscript of Sayin MR et al. (1). In this paper, the authors stated that the left main coronary artery thrombus resulted from combined protein C and S deficiencies. The authors neither mentioned when the thrombophilia tests were performed nor the reference ranges for the protein C and S levels. It appears that the thrombophilia tests were performed during the acute thrombotic process. At my institution, the reference range for functional protein S activity is 76-135%, while that of functional protein C activity is 70-130%. Therefore, I would consider that this patient's protein C level of 49% and protein S level of 37% to be mildly low. There was no mention of repeat testing of these levels a few months later.

I will not argue whether this patient merits thrombophilia testing, as there is no general consensus in the medical profession on this topic (2). However, before ordering clot-based thrombophilia assays, a few things should be kept in mind in order to obtain accurate results (3).

(a) True hereditary protein C and S deficiencies are very rare, with a prevalence of 0.2% to 0.5 % for hereditary protein C deficiency and 0.03% to 0.13 % for type I protein S deficiency in the Caucasian population (4). True cases of combined hereditary protein C and protein S deficiency are extremely rare.

(b) Antithrombin, protein C and S are natural anticoagulants and acute phase reactants. The plasma levels of these compounds may transiently decrease during acute thrombosis.

(c) Vitamin K antagonists such as warfarin can decrease

vitamin K-dependent factors such as the protein C and S levels. Heparin can also decrease antithrombin activity.

(d) For these reasons, testing for the protein C and S and antithrombin levels should be delayed for at least six weeks after the acute thrombosis and for at least several weeks after the discontinuation of warfarin. The plasma antithrombin level should not be tested while on heparin.

(e) Any abnormal results in the protein C and S and antithrombin activities should be confirmed with repeat tests, and, if feasible, testing in symptomatic relatives is also recommended.

As a consultant hematologist, I frequently receive consultation requests to evaluate patients with thrombophilia. Many patients diagnosed as having a deficiency of protein C, protein S and antithrombin are actually misdiagnosed, as the tests were performed during an acute thrombotic process, while on anticoagulant therapy or immediately following the discontinuation of anticoagulant therapy. Tests are not repeated in the majority of cases. In summary, requests for thrombophilia testing should be judiciously made, and tests should be conducted at the appropriate time. In my opinion, this patient does not have true combined hereditary protein C and protein S deficiency. His low protein S and protein C levels were most likely due to an acute thrombotic process. It would therefore be interesting to see repeat testing of the protein C and S levels in this patient.

The author states that he has no Conflict of Interest (COI).

Thein H. Oo

References

1. Sayin MR, Akpınar I, Karabag T, Aydın M, Dogan SM, Cil C. Left main coronary artery thrombus resulting from combined protein C and S deficiency. *Intern Med* 51: 3041-3044, 2012.
2. Moll S. Who should be tested for thrombophilia? *Genet Med* 13: 19-20, 2011.
3. Heit JA. Thrombophilia: common questions on laboratory assessment and management. *Hematology Am Soc Hematol Educ Program*. 2007: 127-135.
4. Khan S, Dickerman JD. Hereditary thrombophilia. *Thromb J* 4: 15, 2006.