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Proper diagnosis of antithrombin III deficiency

To the Editor,

We read the article written by Hayiroğlu et al. (1) entitled "Antithrombin III deficiency concomitant with atrial fibrillation causes thrombi in all chambers: 2-D and 3-D echocardiographic evaluation." published *Anatol J Cardiol* 2016; 7456: 21-2. in which they reported the case of a 62-year-old man who had antithrombin III (AT) deficiency concomitant with atrial fibrillation that caused thrombi in all chambers of the heart. The authors claimed that thrombosis in all chambers of the heart in a patient with atrial fibrillation was associated with AT deficiency. In diagnosis of AT deficiency, it should be considered that the disease is very rare. The estimated prevalence in the general population is thought to be in the range of 0.02% to 0.2% (2).

A study that re-evaluated 59 patients with pre-existing diagnosis of AT deficiency revealed AT deficiency in only 3, none of whom had a personal or family history of thrombosis (3). Above all, in patients with a thromboembolic event, testing is indicated; however, AT levels should not be measured at the time of the acute event because thrombosis may cause a transient reduction in all natural anticoagulants, including AT level, which could be misread to suggest an underlying deficiency. If the level of AT is found to be low during acute thrombosis, measurement should be repeated once the patient has recovered. A variety of commercial assays are available to measure AT level. Functional assays using the chromogenic substrate method are preferable, in order to detect both type I and type II deficiency. The test results should be evaluated according to the lower limit of the method used by the relevant laboratory and abnormal test results should lead to repeat testing with new blood sample (2).

Another subject we would like to point out is that AT deficiency is manifested primarily by recurrent venous thromboembolism. Although almost all vein sites have been reported to be involved with thrombosis in AT deficiency, isolated cardiac thrombosis in both arterial and venous chambers is not an expected clinical picture. The association of natural anticoagulant deficiencies with arterial thrombosis still remains unclear. It has been demonstrated that AT deficiency was not related to a significantly increased risk of arterial thromboembolic events (4).

If someone has inherited a natural anticoagulant deficiency, the clinical problem often occurs at an earlier age. In family studies, venous thrombosis occurred in 85% of AT deficient relatives before 55 years of age. Large patient series with natural anticoagulant deficiency, including AT deficiency, revealed no increased risk of arterial cardiovascular disease in affected family members older than age 55 (5).

In conclusion, it is not proven that AT deficiency is related to an increased risk of arterial thrombosis. Its diagnostic testing should be discouraged in the clinical evaluation of either arterial or venous thrombosis in elderly patients, particularly those with facilitating factors such as atrial fibrillation.

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Author's Reply

To the Editor,

We are pleased to see the valuable comments and contribution of our colleagues in response to our article entitled "Antithrombin III deficiency concomitant with atrial fibrillation causes thrombi in all chambers: 2-D and 3-D echocardiographic evaluation" published in the December 2016 issue of the *Anatolian Journal of Cardiology* (1). We have some points to explain further.

In our report, there were many precipitating factors contributing to the thrombi in all chambers. Antithrombin III (AT) deficiency was proposed as a precipitating factor in addition to coronary artery disease and atrial fibrillation. We are aware of the rarity of arterial thrombosis secondary to AT deficiency; it was for this reason that we reported our case. There are case reports in the literature concerning arterial thrombosis due to AT deficiency (2). Other procoagulant precipitating factors accompanying AT deficiency have a role in the time of clinical incidence, as reported by