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EDİTÖRE MEKTUP
LETTER TO EDITOR

Homozygous methylene tetrahydro folate reductase-677TT gene mutation: Case of pulmonary thromboembolism

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Pulmonary embolism is a life-threatening condition that needs prompt diagnosis and treatment in order to avoid adverse outcomes. While the mortality rate of PE reaches up to 30% in untreated patients, this rate is reduced to 3% in treated patients (1). Thus, early diagnosis and treatment is crucial. Despite treatment recurrence can be seen in 5-23% of the patients with venous thromboembolism (VTE) (2). However, recurrence is higher in cases with inherited thrombophilia (3). Genetic risk factors should be investigated in the following conditions; unexplained recurrent VTE before 40 years of age, presence of familial history according to VTE, patients with thrombosis in unusual areas, history of skin necrosis due to warfarin, and presence the history of neonatal (4). The use of anticoagulants for longlife would be life saving in patients with PE who have genetic risk factors. Herein, we aimed to present a young male PE patient with homozygous methylenetetrahydrofolate reductase (MTHFR) 677TT mutation who presented with PE in the light of literature.

A twenty two-year-old male patient who was operated for ureteropelvic stenosis before 3 weeks, admitted to our clinic with the complaint of right flank pain. Physical examination other than the decreasing of the respiratory sound in the right lower lung fields were unremarkable. Chest X-ray revealed elevated right diaphragm and closed right costodiaphragmatic sinus (Figure 1). The level of d-dimer was 3.85 ug/mL in this patient with moderate clinical probability. Thoracic CT angiography was taken in order to rule out the PE. Thoracic CT showed filling defects in the bilateral lower, middle lobar and interlobar arteries consistent with thrombus, and minimal right pleural effusion (Figure 2). The anticoagulant therapy was started the patient with the absence of self and familial history. After the one month of the cessation of the anticoagulant therapy that was continued for 6 months, genetic screening of the patient according to possible causes of genetic factors homozygous MTHFR 677TT mutation was detected. Factor 5 Leiden and prothrombin 20210A mutations did not determined. The anti-thrombin activity was 99 (75-125), protein C activity was 119 (70-140), protein S activity was 74.8 (60-130). After the patient informed, coumadin prophylaxis was started.

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Figure 1. Chest X-ray.

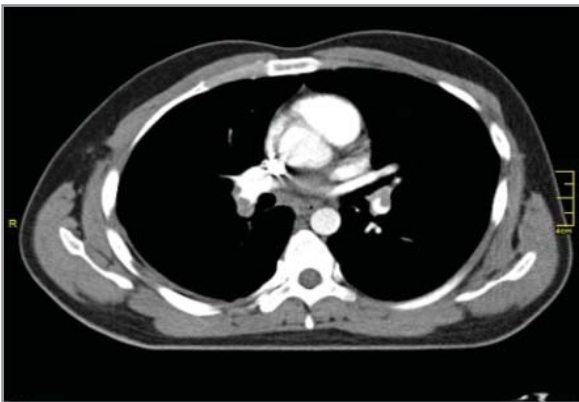


Figure 2. Thoracic CT angiography.

Under forty years of age in patients with a history of venous thromboembolism genetic risk factors must be investigated. Although regional differences in prevalence, the most common hereditary risk factors are Factor 5 Leiden mutation, prothrombin 20210A mutation, the presence of antiphospholipid antibodies, anti-thrombin 3, protein C and protein S deficiency and hyperhomocysteinemia. Mutations in the MTHFR gene lead to reduces the MTHFR enzyme activity and this condition is resulted increasing in the plasma homocystein levels. High plasma homocystein levels are associated with the tendency to various cardiovascular adverbs outcomes (5). The most common mutations in the MTHFR gene are C677T ve A1298C.

Particularly, in the presence of homozygot 677TT mutation the enzyme activity is much lower, and this condition is associated with higher plasm homocystein

and lower folate levels. The risk of venous and arterial thrombosis increases in these cases and lead to cardiovascular and cerebrovascular events at an early age, neural tube defects in pregnancy, and also lead to recurrent abortion and stillbirths.

Although, the previous studies and guidelines reported that hyperhomocysteinemia is commonly seen among the healthy subjects, and also was not a significant risk factor for PE. In recent years, studies have supported that homozygot MTHFR 677TT mutation is an important risk factor for venous thrombosis (6,7). Currently, there is a intense interest in studies related to the MTHFR mutations. In addition to VTE, MTHFR mutations are also investigated in neurological disorders, cardiovascular diseases, breast-lung and colorectal malignancies, in the presence of the recurrent abortions and neural tube defects.

In conclusion, patients who presented with PE at younger age should be evaluated genetic risk factors

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