

# Paradoxical embolism after splenectomy in a patient with hyperhomocysteinemia. A case report

Hiperhomosisteinemi olan hastada splenektomi sonrası paradoksal emboli.

Ahmet Seyda Yılmaz<sup>1</sup>, Ömer Faruk Çirakoğlu<sup>2</sup>

1 Recep Tayyip Erdogan University,  
Department of Cardiology, Rize, Turkey

2 Sağlık Bilimleri Üniversitesi Ahi Evren  
Göğüs Kalp Damar Cerrahisi Eğitim ve  
Araştırma Hastanesi Kardiyoloji Anabilim Dalı

**Anahtar Kelimeler:** Splenektomi,  
Paradoksal emboli, Hiperhomosisteinemi

**Keywords:** Splenectomy, Paradoxical  
embolism, Hyperhomocysteinemia

**Sorumlu Yazar:** Ahmet Seyda Yılmaz, MD  
Recep Tayyip Erdogan University, Faculty of  
Medicine, Department of Cardiology  
53020, Rize, Turkey

Phone: +90 464 2130491

E-mail: ahmetseydayilmaz@gmail.com

**Başvuru Tarihi:** 14 Şubat 2021

**Kabul Tarihi :** 4 Mart 2021

## Abstract

Spontaneous venous thrombosis is rare clinical condition without the presence of additional risk factors. Spontaneous arterial thrombosis is even rarer than venous thrombosis. Splenectomy is known to be risk factor for venous thromboembolism, postoperative deep venous thrombosis, and pulmonary thromboembolism. Paradoxical embolism defines the thrombus originating from venous circulatory system transverses to arterial bed through interatrial, interventricular, or arterio-pulmonary shunt. Systemic embolism in the absence of known intracardiac or carotid disease raises the suspicion of right-sided source.

## Introduction

Spontaneous venous thrombosis is rare without the presence of additional risk factors. Spontaneous arterial thrombosis is even rarer than venous thrombosis. Splenectomy is known to be related to high risk for venous thromboembolism (VTE), postoperative deep venous thrombosis (DVT), and pulmonary thromboembolism (PTE) which independent of reactive thrombocytosis 1,2. Paradoxical embolism defines the venous thrombus passes to the arterial system through interatrial, interventricular, or arterio-pulmonary shunt. Systemic embolism in the absence of known intracardiac or carotid disease raises the suspicion of right-sided source and diagnosis requires to exclude other possible causes of arterial occlusion.

## Case Report

A 64-year-old woman admitted to the emergency room with accelerating pain, weakness, and swelling of left arm, and shortness of breath. Heart rate was 105 beat per minute and blood pressure was 155/85 mmHg.

Peripheral oxyhemoglobin saturation was 91% in room air. Respiratory rate was 20 breaths per minute. On physical examination, it was found that left arm was white and insensate below the shoulder with complete loss of brachial and radial pulse. Urgent thorax computed tomography (CT) angiography demonstrated the acute obstruction at the left subclavian artery and massive bilateral pulmonary embolism (PE) (Figure 1A, 1B). The coincidence of venous and arterial thromboembolism raised suspicion for paradoxical embolism. Transthoracic echocardiography (TTE) demonstrated enlarged right ventricle and atrium with increased pulmonary artery pressure. After the treatment of the patient, detailed TTE was repeated and patent foramen ovale (PFO) was suspected. Due to the patient's clinical condition was not available, transesophageal echocardiography could not perform. Eventually, diagnoses were acute left subclavian arterial occlusion and massive PTE. The patient was taken to the operation room and subclavian

embolectomy was performed, immediately. The patient made a spectacular recovery and left arm pulse regained postoperatively. Sensation and motor function came back, and the pain was released. After the procedure, the patient was observed for 24 hours for compartment syndrome which did not occur. Anticoagulant therapy with heparin and warfarin was initiated due to the PTE. Thrombolytic therapy was not administered due to the vital parameters of the patient was stable and shortness of breath was released. Patient hospitalized for 5 days until international normalized ratio level of 2.5 was reached. Due to this embolus was second and secondary to the venous system, warfarin therapy was planned for long-life.

Past medical history of the patients revealed that she had cerebral infarct without sequelae, one-month ago. Brain diffusion magnetic resonance imaging showed the ischemic area of an antero-parietal region of the brain (Figure 2). After this ischemic stroke, she was under the treatment of clopidogrel 75 milligram per day. It was also noted that she had splenectomy due to the spleen enlargement, two years ago. Serum thrombocyte level was in normal range.

Because of multiple embolisms, we examined hypercoagulative factors that could be related with repeated thromboembolic events. Factor V Leiden mutation and methylene tetra hydro folate reductase 677 and 1298 (MTHFR) mutations did not exist. Protein C and S activities, antithrombin 3 activity, and each coagulation cascade factors (Factor 2-13) were at normal levels. Homocysteine level was 20,6 micromole per liter (reference interval: 0,0-12,0 micromole per liter) that means the patient had HHC.

### **Discussion**

Real incidence of paradoxical embolism is unknown. Depending on the site of embolization, clinical manifestations may vary neurological deficit secondary of ischemic stroke, acute kidney failure due to renal artery occlusion, abdominal pain secondary to acute bowel ischemia, and acute pain and pulseless of extremities as a result of peripheral arterial occlusion. PTE was not foreground and found incidentally despite it was bilateral and massive. It was thought that PTE made flow reverse from right atrium to left atrium across a PFO by increasing right

side pressure<sup>3,4</sup>. As reported previously, 25 to 30% of patients who experienced cryptogenic ischemic stroke, had also PFO<sup>5</sup>.

Factor V Leiden mutation is notified which is the most commonly known hereditary risk factor for thrombosis. Multiple embolisms require to explore other hereditary risk factors. In our patient Methylene tetra hydro folate reductase 677 and 1298 (MTHFR) mutations, protein C and S activities, and antithrombin 3 activity were shown to be in normal range. Homocysteine was 20,6 mmol/l (reference interval 0,0-12,0 mmol/l). It was shown that HHC damages endothelial cells, reduces the flexibility of vessels, and adversely affects the process of hemostasis. Thus, enhances the adverse effects of risk factors such as hypertension, smoking, and impaired glucose, lipid, and lipoprotein metabolism<sup>6,7</sup>. We think, arterial and venous multiple embolism occurred owing to coincidence of splenectomy, HHC, and PFO; despite the patient was under the treatment of clopidogrel 75 mg per day. Therefore, we should examine patients for PFO and hypercoagulative status including hematological and organically, who have repeated embolism.

### **Conclusion**

HHC and splenectomy are hypercoagulative conditions. Patients candidate for splenectomy can be observed for hypercoagulable status and PFO with other risk factors. Some studies did not show a significant benefit of PFO closure for the secondary prevention of ischemic stroke against medical therapy in recurrent events. Therefore, antiplatelet drugs or systemic anticoagulants are recommended for this patient populations<sup>7</sup>. In our patient, we planned warfarin therapy for long-life.

## References

1. Windecker S, Stortecky S, Meier B. Paradoxical embolism. *J Am Coll Cardiol*. 2014 Jul 29;64(4):403-15.
2. Bedeir K. Thrombus in Transit with Isolated Paradoxical Embolism to the Subclavian Artery. *J Stroke Cerebrovasc Dis*. 2015 Jul;24(7):e173-5.
3. Ha LP, Arrendondo M. Fatal venous thromboembolism after splenectomy: pathogenesis and management. *J. Am. Osteopath. Assoc.* 2012;112:291-300.
4. Rottenstreich A, Kleinstern G, Spectre G, Da'as N, Ziv E, Kalish Y. Thromboembolic Events Following Splenectomy: Risk Factors, Prevention, Management and Outcomes. *World J Surg*. 2018 Mar;42(3):675-681.
5. Lee DH, Barmparas G, Fierro N, Sun BJ, Ashrafian S, Li T, Ley EJ. Splenectomy is associated with a higher risk for venous thromboembolism: a prospective cohort study. *Int J Surg* 24:27-32.
6. Baszczuk A, Kopczyński Z. Hyperhomocysteinemia in patients with cardiovascular disease. *Postepy Hig Med Dosw (Online)*. 2014 Jan 2;68:579-89.
7. Naylor M, Maron BA. Contemporary approach to paradoxical embolism. *Circulation*. 2014 May 6;129(18):1892-7.

## Özet

Spontan venöz tromboembolizm ek risk faktörü olmadığı durumlarda nadir görülen bir durumdur. Spontan arteriyel tromboembolizm ise venöz tromboembolizme göre daha da ender görülür. Splenektomi operasyonunun venöz tromboemboli, postoperatif derin ven trombozu ve pulmoner emboliye yatkınlık oluşturduğu bilinmektedir. Paradoksal emboli venöz sistemden kaynaklanan trombüsün interatriyal, interventriküler veya arteriopulmoner şant vasıtasıyla arteriyel sisteme geçmesi olarak tanımlanır. İntrakardiyak ve karotis arteriyel sistem kaynaklı olmadığı sürece sistemik emboli durumunda kaynak olarak venöz sistem araştırılmalıdır.

64 yaşında kadın hasta acil servise sol kolda ilerleyici karakterde ağrı, güçsüzlük ve şişmenin yanısıra nefes darlığı yakınmalarıyla başvurdu. Yapılan fizik muayenesinde sol kolda omuzdan itibaren soğukluk, solukluk ile beraber periferik nabızların olmadığı görüldü. Çekilen acil toraks bilgisayarlı tomografide sol subklavian arter seviyesinde arteriyel trombus ve masif bilateral pulmoner emboli olduğu izlendi. Hasta acilen operasyon odasına alındı ve subklavian embolektomi gerçekleştirildi. Hastanın tedavisi tamamlandıktan sonra yapılan ayrıntılı transtorasik ekokardiografide sağ atriumdan sol atriuma doğru patent foramen ovale (PFO) kaynaklı olduğu düşünülen minimal geçiş olduğu izlendi. Hastanın 1 ay önce sekel bırakmayan trans-iskemik atak geçirdiği öğrenildi. Beyin görüntülemelerinde anteroparyetal bölgede iskemik alan olduğu görüldü. Aynı zamanda iki yıl önce dalak büyümesi nedeniyle splenektomi operasyonu geçirdiği öğrenildi. Serum homosistein düzeyi 20,6 micromol/litre olup normalin üzerindedir. Hastaya ömür boyu warfarin tedavisi başlandı. Hiperhomosisteinemi ve splenektomi başlıbaşına koagülasyon için risk faktörü olmakla beraber bir arada olmaları riski daha da artırmaktadır. Splenektomi için aday olan bireyler, koagülasyon artırıcı sebepler ve PFO açısından ayrıntılı değerlendirilebilir.