Acute thrombus formation on an Amplatzer device during transcatheter closure of an atrial septal defect in a patient with homozygous factor V Leiden mutation

Homozigot faktör V Leiden mutasyonu olan bir hastada transkateter atriyal septal defekt kapatılması sırasında Amplatzer cihazı üzerinde gelişen akut trombüs

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Summary – A 32-year-old woman underwent transcatheter closure of a secundum type atrial septal defect with the Amplatzer device. The procedure was started under premedication with aspirin, clopidogrel, and heparin. During the procedure, a highly mobile thrombus attached to the left atrial disc of the device was detected by transesophageal echocardiography (TEE). The device and the associated thrombus were successfully withdrawn and the patient was started on a combination of heparin and tirofiban infusion. The procedure was successfully completed without any recurrent thrombus formation or residual shunt. Further investigation for thrombophilia revealed homozygous factor V Leiden mutation and the patient was started on a life-long warfarin therapy. Follow-up TEE showed proper device position with no recurrent thrombus and the follow-up was uneventful.

Özet – Otuz iki yaşında kadın hasta, transkateter yolla Amplatzer cihazı ile sekundum tip atriyal septal defekt kapatma işlemine alındı. İşlem öncesinde aspirin ve klopidogrel verilen hastaya işlem sırasında heparin uygulandı. İşlem sırasında transözofageal ekokardiyografide (TEE), Amplatzer cihazının sol atriyal diski üzerine tutunmuş aşırı derecede hareketli bir pıhtı görüntüsü izlendi. Cihaz ve üzerinde tutunmuş olan pıhtı sistemden dışarı başarıyla alındı ve hastaya heparin ile birlikte tirofiban infüzyonu uygulandı. Daha sonra, işleme devam edilerek defekt başarıyla kapatıldı ve yeni pıhtı oluşumu veya şant görülmedi. İşlem sonrasında trombofili açısından yapılan araştırmada, hastada homozigot tipte faktör V Leiden mutasyonu saptandı ve ömür boyu varfarin tedavisine başlandı. Kontrol TEE incelemesinde cihazın uygun pozisyonda yerleştiği ve üzerinde pıhtı bulunmadığı görüldü. Hastanın izleminde de bir soruna rastlanmadı.

Abbreviations:

ASD *Atrial septal defect*
TEE *Transesophageal echocardiography*

Transcatheter device closure is the currently accepted gold standard therapy for secundum type atrial septal defects.[1] Although it is generally a safe procedure, several complications associated with device implantation have been reported.[2] Thrombus formation on the occluder device is a relatively rare, but serious complication leading to embolic events both in the early and late follow-up.[3,4] Of several closure devices, the Amplatzer device has been associated with significantly lower rates of thrombosis.[3,4] We report a case of acute thrombus formation on the left atrial disc of Amplatzer ASD occluder in a patient with factor V Leiden mutation in spite of appropriate antithrombotic medication during the procedure.

CASE REPORT

A 32-year-old female with complaints of palpitations and exertional dyspnea of 6 six-month history was referred to our echocardiography laboratory. She was diagnosed as having a secundum

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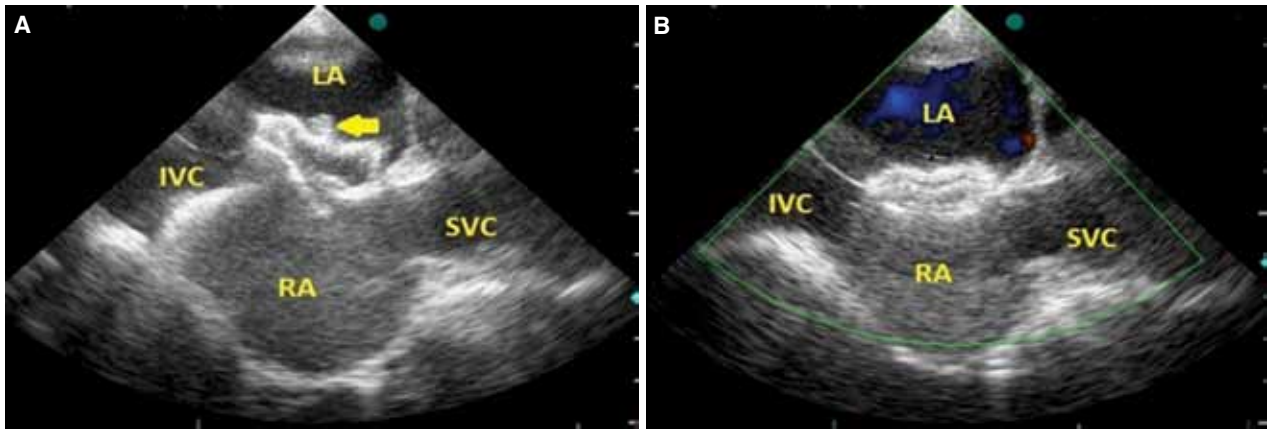

Figure 1. Bicaval transesophageal echocardiographic views: **(A)** Appearance of a mobile thrombus (arrow) attached centrally to the left atrial disc of the Amplatzer device. **(B)** After removal of the thrombus, color Doppler image shows complete closure of the atrial septum without thrombus on the device. LA: Left atrium; RA: Right atrium; IVC: Inferior vena cava; SVC: Superior vena cava.

type ASD with enlargement of the right ventricle and significantly increased pulmonary flow (Qp/Qs 2.1). Estimated pulmonary artery systolic pressure was 45 mmHg with mild-to-moderate tricuspid regurgitation. Transesophageal echocardiography revealed an 18-mm defect in the secundum interatrial septum without any other abnormality. Atrial septal anatomy was favorable for device closure with adequate rims (>10 mm) around the defect. The patient was started on a daily medication of 300 mg aspirin and 75 mg clopidogrel before the procedure and was given 100 IU/kg heparin at the start of the procedure.

Under general anesthesia and with TEE guidance, a 20-mm Amplatzer septal occluder (AGA Medical Corporation, Golden Valley, MN, USA) was advanced within the delivery sheath and the distal disc was deployed on the left side of the atrial septum. Upon withdrawal of the sheath, the proximal disc was opened properly on the right side of the atrial septum. Just before releasing the device, a highly mobile thrombus-like structure was detected on TEE, attached centrally to the left atrial disc of the Amplatzer device (Fig. 1a). Negative pressure was applied with an injector to suck the thrombus into the lumen of the delivery sheath while removing the whole device out of the vascular system. It turned out to be a pistol-shaped thrombus, 45 x 30 mm in size (Fig. 2). The patient was on adequate antiplatelet therapy and heparin infusion during the procedure. To overcome this highly thrombotic situation, an intravenous bolus of 25 mcg/kg tirofiban followed by 0.15 mcg/kg/min infusion was started and continued for 12 hours. Antithrombotic status was monitored with the activated coagulation time both during and after the procedure. Successful closure of the ASD with the 20-mm Amplatzer device was achieved with proper positioning of the device and without any recurrent thrombosis or residual shunt (Fig. 1b). The patient woke up from anesthesia without any neurological deficit and TEE performed on the following day confirmed the absence of thrombosis.

Figure 2. Macroscopic appearance of the pistol-shaped thrombus after withdrawal from the circulation and separated from the Amplatzer device.

There were no clinical predictors of thrombus formation (atrial fibrillation, enlarged left atrium, immobility, oral contraceptive use, pregnancy, or malignancy) and the patient had no history of previous embolic events. Screening for hypercoagulability with polymerase chain reaction revealed a positive result for homozygous factor V Leiden G1691A

gene mutation. The patient was discharged home on a regimen of low-dose aspirin and clopidogrel for six months and life-long warfarin therapy with a targeted international normalised ratio between 2 and 3. Follow-up clinical visits and TEE examinations were uneventful.

DISCUSSION

Currently, surgical closure of isolated secundum type ASDs has been replaced by transcatheter device closure due to high success and low complication rates.[1,2] The Amplatzer septal occluder has been associated with favorably lower rates of device-related thrombus ranging from 0% to 6% in different series.[3,4] Early thrombus formation is extremely rare with the current combination of aspirin, clopidogrel, and heparin use during the procedure.[4] Due to limited data, there is no consensus on the best management strategy in case of device thrombosis detected during transcatheter ASD closure.

Vanderheyden et al.[5] used a combination of thrombolytics and glycoprotein IIb/IIIa inhibitor as an alternative to surgery in case of biatrial thrombus associated with the closure device. Eren et al.[6] reported early thrombus formation on the delivery system during transcatheter closure of an ASD with the Amplatzer device. They removed the device and the whole system with negative aspiration and continued the procedure under additional heparin bolus without any complications. Willcoxson et al.[7] reported a 12-year-old boy in whom acute Amplatzer-related thrombosis was successfully treated with heparin and abciximab without any neurological event. Acar et al.[8] achieved complete resolution of a device-related thrombus with only heparin infusion. In our case, we followed a strategy of withdrawing the device and associated thrombus out of the circulation and continued the procedure under the infusion of tirofiban, a glycoprotein IIb/IIIa inhibitor. We completed the procedure without any recurrent thrombus formation and the patient had an uneventful recovery.

In the coagulation cascade, factor V stands as a cornerstone since both intrinsic and extrinsic pathways are incorporated into the common pathway by activation of factor Xa with factor Va, leading to subsequent thrombin formation. More importantly, factor V also serves as an endogenous anticoagulant system when inactivated by protein C. A genetic mutation in the factor V gene results in a change in the factor V protein rendering it resistant to inactivation by protein C. This phenomenon is called activated protein C resistance leading to a thrombophilic state by increased activity of factor V in the blood.

As a common inherited hypercoagulable condition, factor V Leiden mutation, especially in homozygous patients, is well-known to increase the risk for thrombus formation in percutaneous coronary interventions.[9] However, to our knowledge, our case represents the first case of acute thrombus formation associated with the Amplatzer septal occluder in a patient with homozygous factor V Leiden mutation treated with a combination of heparin and glycoprotein IIb/IIIa inhibitor. Specific guidelines for management and screening for this high-risk population are needed to avoid serious life-threatening embolic complications. This case also draws attention to the importance of TEE guidance during transcatheter septal closure for immediate detection of complications.

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Key words: Anticoagulants/therapeutic use; coronary thrombosis; echocardiography, transesophageal; factor V; heart catheterization; heart septal defects, atrial/therapy; mutation.

Anahtar sözcükler: Pıhtıönler/terapötik kullanım; koroner trombüs; ekokardiyografi, transözofageal; faktör V; kalp kateterizasyonu; kalp septal defekti, atriyal/tedavi; mutasyon.