References

1. Nicolaes GA, Dahlback B. Activated protein C resistance (Factor V Leiden) and thrombosis: factor V mutations causing hypercoagulable states. Hematol Oncol Clin North Am 2003;17: 37-61.
2. Price DT, Ridker PM. Factor V Leiden mutation and the risk for thromboembolic disease: a clinical perspective. Ann Intern Med 1997; 127: 895-903.
3. Lensen RP, Rosendaal FR, Koster T, Allaart CF, de Ronde H, Bertina RM. Apparent different thrombotic tendency in patients with factor V Leiden and protein C deficiency due to selection of patients. Blood 1996; 88: 4205-8.
4. Koeleman BPC, Reitsma PH, Allaart CF, Bertina RM. Activated protein C resistance as an additional risk factor for thrombosis in protein C-deficient families. Blood 1994; 84: 1031-5.
5. Koeleman BPC, van Rumpt D, Hamulyak K, Reitsma PH, Bertina RM. Factor V Leiden: an additional risk factor for thrombosis in protein S deficient families? Thromb Haemost 1995; 74: 580-3.
6. Lensen RPM, Bertina RM, de Ronde H, Vandenbroucke JP, Rosendaal FR. Venous thrombotic risk in family members of unselected individuals with factor V Leiden. Thromb Haemost 2000; 83: 817-21.
7. Lopez FF, Sweeney JD, Blair AJ, Sikov WM. Spontaneous venous thrombosis in a young patient with combined factor V Leiden and lupus anticoagulant. Am J Hematol 1999; 62: 58-60.
8. Wahl DG, Guillemin F, de Maistre E, Perret-Guillaume C, Lecompte T, Thibaut G. Meta-analysis of the risk of venous thrombosis in individuals with antiphospholipid antibodies without underlying autoimmune disease or previous thrombosis. Lupus 1998; 7: 15-22.
9. Bili A, Moss AJ, Francis CW, Zareba W, Watelet LF, Sanz I. Anticardiolipin antibodies and recurrent coronary events: a prospective study of 1150 patients. Thrombogenic Factors, and Recurrent Coronary Events Investigators. Circulation 2000; 102: 1258-63.
10. Rosendaal FR, Siscovick DS, Schwartz SM, Beverly RK, Psaty BM. Factor V Leiden (resistance to activated protein C) increases the risk of myocardial infarction in young women. Blood 1997; 89: 2817-21.

Early postoperative left atrial thrombosis in a biatrial orthotopic heart transplant recipient successfully treated by intravenous heparin

Biatriyal ortotopik kalp nakil alıcısında intravenöz heparin ile başarılı tedavi edilmiş erken postoperatif sol atriyal trombus

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Introduction

Thrombus formation and spontaneous echocontrast (SEC) within the left atrium (LA) are harmful intermediate to long term complications of the standard orthotopic heart transplantation (OHT) (1). We present an OHT recipient with extremely mobile multiple LA thrombi diagnosed early after the operation by transthoracic echocardiography (TTE) and treated successfully without thrombectomy.

Case report

A 24-year-old man, with a history of idiopathic dilated cardiomyopathy, underwent OHT by the biatrial anastomosis approach. During the operation, the patient was given 800 mg protamine and 3 units of whole blood. After that, he had no hemorrhagic complication and no need for any other coagulation factor. A large pericardial effusion developed immediately after the operation for which close clinical and TTE follow-up on a daily basis was undertaken while we avoided anticoagulant and antiplatelet agents. On the 10th postoperative day a mobile mass within the LA was noted on TTE. Transesophageal echocardiography (TEE) confirmed the presence of multiple, homogeneous, dense, extremely mobile masses suggestive of thrombi along the LA suture line together with SEC (Fig. 1). Left atrial size was 4.0x7.0 cm. Left ventricular (LV) ejection fraction was 42% and mitral valve was normal. These LA masses were not apparent on the TTE examination the day before. On the same day, the patient suffered from severe abdominal pain that subsided quickly after vomiting. On physical examination his blood pressure was 140/90mmHg, pulse rate was 88bpm and regular, he had no fever. Abdominal examination was unremarkable. The 12-lead electrocardiogram showed normal sinus rhythm. Abdominal X-ray and computerized tomography revealed no pathology. No clinical evidence of peripheral embolization or neurological deficit was detected. Due to the unstable immediate postoperative course and relatively low LV ejection fraction, we were reluctant for surgical removal of thrombi and decided to put the patient on systemic anticoagulation with intravenous heparin upon detection of LA thrombi. A bolus heparin dose of 5000U followed by 1000U/hour was started as intravenous infusion. Subsequent heparin dose was adjusted by activated clotting time with a target of 200-250ms. LA masses dramatically reduced in size as depicted on serial echocardiographic studies. Control TEE on the 5th day of active heparinization showed a completely clear LA (Fig. 2) without any increase in the pericardial effusion and the patient did not suffer any embolic complication. Meanwhile repeat biopsies did reveal no rejection.

Discussion

Stasis within the atria due to enlarged cavities and prominent sutures, electrical discordance (2), atrial arrhythmias, LV dysfunction, increased platelet aggregation (3), acute rejection (4) and the surgical technique itself (1) are considered as predisposing factors for thrombus formation. The

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prevalence is reported to be higher in standard OHT recipients. In a series of 95 patients, SEC was present in 57% and 5%, and LA thrombus was present in 27% and 0% of standard and bicaval OHT recipients respectively (1). As thrombi have a tendency to be localized on the LA suture line (1), good approximation of donor and recipient atrial cuffs for complete coaptation of the endothelial surface is crucial to avoid nonendothelized nidus that can promote thrombus formation. Inverted and protruding nonendothelized margins from where subendothelial collagen is exposed to blood can activate platelets and the intrinsic coagulation pathway.

Our case is important in two aspects: 1) LA thrombi can complicate not only the intermediate to late postoperative course but also the early postoperative course and 2) early detection is important to achieve a successful dissolution with intravenous heparin. There is no consensus as to when these patients should be screened by TEE and which strategy should be adopted to prevent thromboembolic complications (1, 5). Riberi at al. (6) reported 15.2% rate of systemic embolism 21 days to 12 years after standard OHT and 5% after bicaval OHT with an increasing incidence over time. Patients with intracardiac thrombus are usually asymptomatic and diagnosed incidentally during routine echocardiographic examination late after the surgery (1, 2). In contrast to the data from the literature, our case points out that intracardiac thrombi may complicate the course from the earliest days after the OHT.

The use of thrombolytic agents despite providing rapid resolution of thrombi may be harmful with potential embolic and hemorrhagic complications in the postoperative period. Warfarin on the other hand leads to stabilization and gradual dissolution of thrombi over the weeks and months. Nevertheless, its use is challenging considering the urgent need for biopsy in allograft recipients. Also low dose aspirin therapy is not sufficient to inhibit platelet activation in transplant recipients (3). On the other hand, although surgical removal of the fresh LA thrombi seems to be the most widely adopted approach, it is associated with an increased risk of intraoperative embolization. Therefore, intravenous heparin, as in this case, appears as a safe and effective alternative therapy for intracardiac fresh thrombi detected early after OHT.

Conclusion

Although unexpected, prominent LA thrombi may occur in the early postoperative period of cardiac transplantation. We suggest that intravenous heparin therapy may be the best option in the early postoperative period and antiplatelet agents more potent than aspirin can be administered thereafter, if there are special concerns about increased risk for thrombus formation and no risk for hemorrhage. Recommendations on routine anticoagulation during the post operative period cannot be rationally based on observation of one patient but close TTE follow-up, as a non-invasive and reliable tool, is useful to detect intracardiac thrombi in the immature state when intravenous heparin can be effective for treatment.

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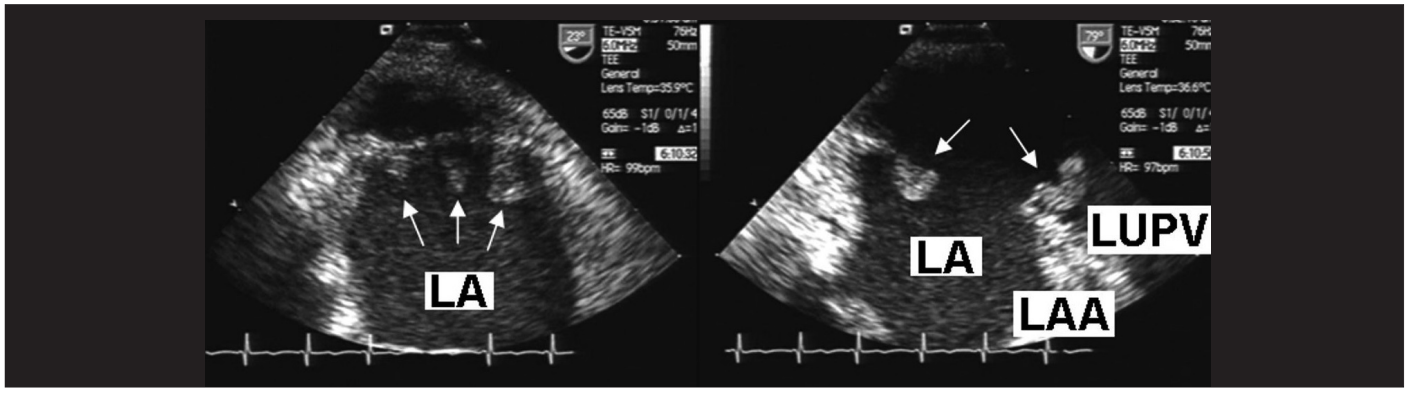

Figure 1. Transesophageal echocardiography: views from the long- axis showing mobile pedinculated left atrial masses attached by narrow necks to the suture line. (Arrows)

LA- left atrium, LAA- left atrial appendage, LUPV- left upper pulmonary vein

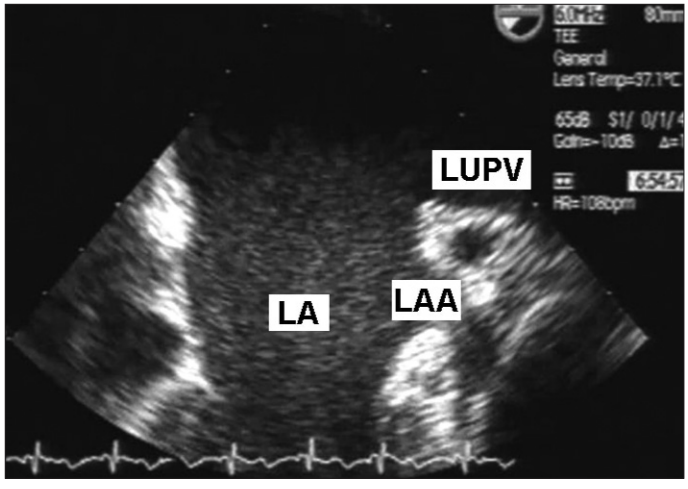

Figure 2. Transesophageal echocardiography after treatment with intravenous heparin showing complete resolution of left atrial thrombi

LA- left atrium, LAA- left atrial appendage, LUPV- left upper pulmonary vein

References

1. Derumeaux G, Habib G, Schleifer DM, Ambrosi P, Bessou JP, Metras D et al. Standard orthotopic heart transplantation versus total orthotopic heart transplantation. A transesophageal echocardiography study of the incidence of left atrial thrombosis. Circulation 1995; 92 (9 Suppl): II196-201.
2. Polanco G, Jafri SM, Alam M, Levine TB. Transesophageal echocardiographic findings in patients with orthotopic heart transplantation. Chest 1992; 101: 599-602.
3. de Lorgeril M, Dureau G, Boissonnat P, Ovize M, Monnez C, Monjaud I et al. Increased platelet aggregation after heart transplantation: influence of aspirin. J Heart Lung Transplant 1991; 10: 600-3.
4. Labarrere CA, Pitts D, Halbrook H, Faulk WP. Natural anticoagulant pathways in normal and transplanted human hearts. J Heart Lung Transplant 1992; 11: 342-7.
5. Forrat R, Ferrera R, Boissonnat P, Adeleine P, Dureau G, Ninet J et al. High prevalence of thromboembolic complications in heart transplant recipients. Which preventive strategy? Transplantation 1996; 61: 757-62.
6. Riberi A, Ambrosi P, Habib G, Kreitmann B, Yao JG, Gaudart J, et al. Systemic embolism: a serious complication after cardiac transplantation avoidable by bicaval technique. Eur J Cardiothorac Surg 2001; 19: 307-12.