Therefore, warfarin was applied without discontinuing the dual antiplatelet therapy for 1 month.

Conclusion

Because carotid artery dissection generally has a nonspecific presentation, patients were closely evaluated after CAS, and even mild symptoms should be taken into consideration. Although the Mo.Ma device balloons have an atraumatic design, the balloon inflation can result in carotid artery dissection depending on high pressure and inflation that lasts for a long time. Thus, the application of the Mo.MA device balloons should be more gentle. Anticoagulant therapy can be convenient without stenting in the case of iatrogenic carotid artery dissection.

Informed consent: An informed consent was obtained from the patient.

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Mitral valve and right ventricular thrombi possibly caused by heparin-induced thrombocytopenia

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Introduction

Heparin-induced thrombocytopenia (HIT) is a devastating complication of heparin treatment that can be associated with arterial and venous thrombosis (1). The major clinical manifestations are presented in Table 1. Sachais et al. (2) reported that in patients receiving heparin, prevalence of HIT ranges up to 5.0%. Serological and platelet function tests have high sensitivity in diagnosis of HIT. The cessation of heparin and using direct thrombin inhibitors (e.g., argatroban, lepirudin, and danaparoid) as an anticoagulation therapy are the mainstays of treatment.

Case Report

A 36-year-old male patient was referred to the emergency department with signs and symptoms of deep vein thrombosis (DVT) and segmental pulmonary embolism (sPE). Target medical history was unremarkable. Electrocardiography indicated nothing unusual other than sinus tachycardia (105/min). The patient's laboratory tests except D-dimer levels were within normal limits. Bedside transthoracic echocardiography (TTE) showed mild enlargement in the right ventricle (RV); mild-moderate tricuspid regurgitation; with a normal left ventricle ejection fraction. The estimated pulmonary artery systolic pressure from the tricus-

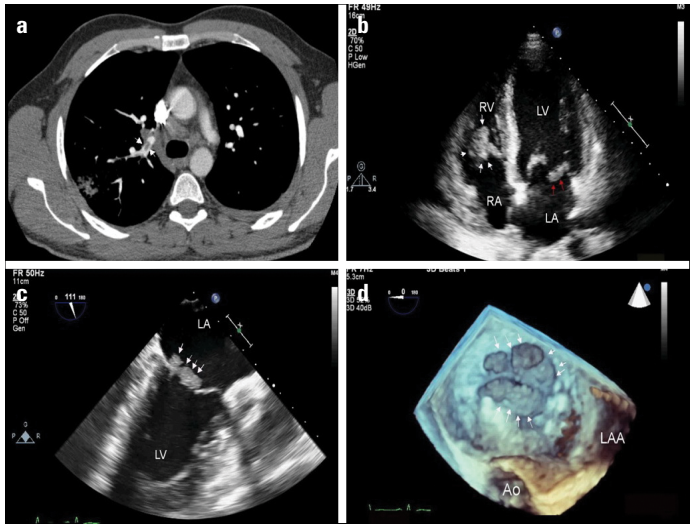

Figure 1. Contrast enhanced computed tomography indicates the right segmental pulmonary embolism (a) (white arrowheads). Transthoracic echocardiography shows a mobile thrombus in the right ventricle and a nonobstructive mitral valve thrombosis (b) (white and red arrowheads, respectively). Two- and three-dimensional transesophageal echocardiography demonstrate that a nonobstructive mitral valve thrombosis on the left atrial side (c, d) (white arrowheads)

pid regurgitant jet was 38 mm Hg. Duplex ultrasonography and contrast enhanced computed tomography (cCT) examination confirmed the diagnosis (Fig. 1a). Subsequently, intensive anticoagulation therapy with unfractioned heparin (UFH) was initiated with a target-activated partial thromboplastin time of between 50 and 70 s. At the third day of UFH treatment, the patient's hemodynamic parameters became unstable. In addition, physical examination included severe dyspnea, tachypnea, and rales in the right lower and middle zones of the lung. The laboratory results showed a significant decrease of platelet count (from 213×10^9/L to 30×10^9/L).TTE and transesophageal echocardiography demonstrated a large, mobile mass in the RV, which was suspected to be a thrombus in the RV and a nonobstructive mitral valve thrombosis on the left atrial side (Fig. 1b-1d and Video 1, 2). Furthermore, echocardiography excluded atrial septal defect, patent foramen ovale, and ventricular septal defect. Intravenous UFH treatment was immediately discontinued, and fondaparinux was subcutaneously administered (5 mg/daily). Fallowing days, the platelet count significantly increased (from 30×10^9/L to 150×10^9/L). The patient was suspected of HIT as he scored 7 on the 4Ts clinical score for the diagnosis of HIT (Table 2). To exclude other differ-

Table 1. The major clinical manifestations of heparin-induced thrombocytopenia

Arterial	Venous	Microvascular
Ischemic stroke	Deep vein thrombosis	Skin necrosis
Myocardial infarction	Pulmonary embolism	Venous limb gangrene
Ischemic limb necrosis	Upper extremity venous thrombosis	Anaphylactoid reaction
Acute kidney injury due to embolism	Cerebral sinus venous thrombosis	
Mesenteric ischemia	Splanchnic vein thrombosis	
Splenic infarct	Adrenal vein hemorrhagic necrosis	

Table 2. The 4Ts clinical scoring system of heparin-induced thrombocytopenia according to Warkentin (13)

	0 points	1 point	2 points
Thrombocytopenia	Platelet count falls <30% and platelet nadir $<10\times10^9$/L	Platelet count falls 30%–50% and platelet nadir $10–19\times10^9$/L	Platelet count falls >50% and platelet nadir 20×10^9/L
Timing of onset	Platelet count fall <4 days without recent heparin exposure	>10 days, or platelet fall within 24 h (prior heparin exposure 30–100 days ago)	5–10 days or platelet fall within 24 h (prior heparin exposure within 30 day)
Thrombosis or clinical sequelae	New thrombosis, or clinical sequelae (confirmed) after heparin therapy	Progressive or recurrent thrombosis, or skin lesions, or suspected thrombosis (not proven)	-
Different causes of thrombocytopenia	Clearly	Possible	Uncertain

Probability of heparin-induced thrombocytopenia: high, 6 to 8 points; intermediate, 4 or 5 points; low, 0 to 3 points

ential diagnosis, thoraco-abdominal CT was performed that displayed no significant pathology. In addition, sepsis, disseminated intravascular coagulation, rheumatologic diseases, infective or non-infective endocarditis, and malignancy markers were normal limits (except the heterozygote factor-V Leiden mutation). Although laboratory tests (including immunologic, platelet activation assays) were necessary for the definitive diagnosis for HIT, we could not perform these tests in our clinic. During the follow-up, a cerebrovascular event occurred, and cranial CT showed diffuse ischemic infarction. Subsequently, the patient died within 12 h due to respiratory failure and extensive cortical and brainstem infarction.

Discussion

UFH and low molecular weight heparin are the most commonly used anticoagulant agents for DVT and sPE worldwide (3). Although hemorrhagic events are the most common complications of heparin treatment, interestingly, thrombotic events predominate in patients with HIT. The pathophysiology of HIT is as follows. Heparin binding to platelet factor 4 (PF4) and forming an antigenic form of heparin-PF4 complex is an immune-mediated condition. PF4 is normally contained in alpha granules of platelets and is released into the circulation by platelet activation. It is a positively charged molecule, and some of it adheres to the platelet surface after it is released into the circulation. Because heparin and other glycosaminoglycans are negatively charged, they bind to PF4 molecules to form an antigenic structure. The antibody-antigen complex triggers activation and aggregation in platelets. This leads to further release of PF4 into the circulation. Because of the presence of molecules on the endothelial surface, such as heparan sulfate, it causes more accumulation of antigen-antibody complexes. Thrombin by activating tissue factor coagulation cascade released from platelets and endothelium in response to these immune complexes formation and eventually leads to thrombotic problems. There is up to 89% incidence of thrombosis if patients with HIT do not receive appropriate treatment. In addition, HIT-related mortality has been reported up to 30% (4).

Whenever a patient in the hospital or who has recently been in the hospital has a decrease in platelet count or occurs a new thrombi, HIT should be considered. Documented heparin exposure is helpful; however, the use is ubiquitous, so the exposure cannot be ignored if not charted (e.g., heparin flushes during catheter placement). Three major scoring systems were suggested to predict the likelihood of HIT by clinical characteristics. They include the HIT expert probability score, a post-CPB scoring system, and the commonly used 4Ts scoring system by Warkentin et al. (5). The negative predictive value of the 4Ts system is 99%. Because the probability of a definite diagnosis is low in low-score patients, its use should not be preferred for diagnosis (6). Recently, Salter et al. (7) reported that moderate or high scores generally mandate eliminating all heparin exposures and initiating alternative anticoagulation; and its positive predictive values of moderate and strong clinical scores are only 10%–20% and 40%–80%, respectively, emphasizing the need for serologic confirmation. There can be some subjectivity to awarding points for clinical features, and the 4Ts score is dependent on complete and accurate clinical data. It should be emphasized that to avoid contributing to harmful over diagnosis, serologic tests should not be ordered when the clinical probability score is low. The enzyme-linked immunosorbent assay and serotonin release assay are similar and highly sensitive (>90% and 95%, respectively) for the definitive diagnosis of HIT (8). Although the 4Ts score of this case report is high, we know that the positive predictive value is about 64%. Therefore, the most important limitation of this article is the lack of antigenic and platelet activation studies for definitive diagnosis.

Unlike other drug-induced thrombocytopenia, bleeding in HIT is rare, even in patients with severe thrombocytopenia. Indeed, the most dreaded and frequent complication of the disease is thrombosis, which may be life-threatening. Nand et al. (9) reported that lower extremity DVT and PE are the predominant thrombotic manifestations of HIT. Thrombosis of other venous beds is presented in Table 1. In addition, as a rare clinical entirety, Gündüz et al. (10) indicated that acute myocardial infarction during thrombolysis of prosthetic valve thrombosis associated with HIT. In this case report, we present an extremely rare thrombotic complication of HIT, involving both the mitral valve and the RV, it is the first case of its kind to be reported.

In patients with HIT, direct thrombin inhibitors (e.g., argatroban, lepirudin, danaparoid) have long been recommended as anticoagulation agents. However, in the most recent American College of Chest Physician guidelines, because fondaparinux can rarely cause HIT, it was not recommended as first-line treatment for HIT (11). Previously, Kang et al. (12) with the largest series to date indicated that fondaparinux has efficacy and safety equivalent to argatroban and danaparoid in patients with suspected HIT. In this case report, fondaparinux treatment was administered because of the absence of anticoagulation options such as argotroban, bivaluridine, and danaparoid. This is the major limitation of treatment management.

Conclusion

In conclusion, HIT is a complication that can take fatal course in patients receiving heparin treatment. Although, clinical scoring systems are helpful in the diagnosis, their sensitivity is low in definitive diagnosis. Physicians should keep in mind that thrombocytopenia can represent an early warning sign of HIT. Moreover, the use of fondaparinux as an anticoagulant agent in the treatment of HIT is controversial.

Informed consent: Written informed consent was obtained from the patient for the publication of this case report and the accompanying images and videos.

Video 1. Transthoracic echocardiography shows a mobile thrombus in the right ventricle and a nonobstructive mitral valve thrombosis.

Video 2. Two-dimensional transesophageal echocardiography demonstrates a nonobstructive mitral valve thrombosis on the left atrial side.

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