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Kasuistika | Case report

Acute myocardial infarction, primary percutaneous coronary intervention and stent thrombosis in heart transplanted patient: Potential role of elevated coagulation factor VIII

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SOUHRN

Je prokázáno, že zvýšené koncentrace faktoru VIII představují rizikový faktor vzniku trombózy. V této kasuistice popisujeme případ 51letého pacienta po transplantaci srdce a akutním infarktu myokardu, řešeném implantací stentu, který byl dopraven na oddělení urgentního příjmu se subakutní trombózou stentu. Jako nejpravděpodobnější příčina této trombotické příhody byly uvedeny zvýšené hodnoty faktoru VIII. Článek uvádí i výsledky rešerše příslušné literatury.

ABSTRACT

Elevated factor VIII levels have been established as thrombotic risk factor. In this case report, we describe a 51-year-old patient with a history of heart transplantation and acute myocardial infarction, treated by stent implantation who presented with sub-acute stent thrombosis. Elevated factor VIII levels were detected as most plausible cause of this thrombotic event. A review of the literature is also performed.

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Introduction

The prevalence of heart failure is increasing, and the prognosis of end-stage heart failure remains dismal. At present time, heart transplantation (HTx) remains the gold-standard therapy in this pathology [1]. The median survival for the entire cohort of adult heart recipients who receives an allograft is approximately 11 years according to the Registry of the International Society for Heart and Lung Transplantation (ISHLT) [2].

Cardiac allograft vasculopathy (CAV) is the leading cause of late morbidity and death among heart transplant recipients. Angiographic studies indicate that CAV occurs in up to 42% of all transplanted hearts, although by the use of more sensitive techniques such as intravascular ultrasound (IVUS) or optical coherence tomography this percentage may increase up to 75% of patients at 3 years after HTx [1].

CAV usually progresses rapidly and causes graft failure. More uncommon is the occurrence of ST-segment elevation myocardial infarction (STEMI) as clinical manifestation of CAV [3]. Furthermore, little is known about the outcomes of percutaneous treatment of STEMI in patients with HTx [4].

In this case report, we present the case of an HTx patient with a recent history of STEMI, treated by primary percutaneous coronary intervention (PCI) who presented with sub-acute stent thrombosis. A discussion of this clinical scenario and a review of the potential etiology are also performed.

Clinical case

A 51-year-old male patient with a history of HTx at the age of 41 due to ischemic dilated cardiomyopathy was admitted due to an acute coronary syndrome. Prior history only included one episode of acute rejection that required intensive immunosuppressive therapy with cyclosporine followed by tacrolimus and micofenolatus. A coronary angiography, performed as control 17 months before, showed no significant lesions in the epicardial arteries, whereas left ventricular fraction ejection (LVFE) measured by echocardiogram was around 55–60%. No further events were reported during 10 years after HTx and the patient remained in good general condition.

He was admitted, in our division, for atypical pain in the left arm and dyspnea. The patient was in Killip-Kimball class II. Duration of such symptoms was 24 hours. The ECG (Fig. 1) showed a complete right bundle branch block, known since one year later HTx. Maximal troponin I was 110.5 ng/ml and creatine kinase-MB 4.6 IU/l. Coronary angiography revealed a three-vessel disease, with an acute thrombosis of proximal circumflex artery as culprit vessel, TIMI grade 0 (Fig. 2A**),** a 70% stenosis in a mid portion of left anterior descending artery (LAD) and chronic total occlusion of a non dominant right coronary artery. Primary PCI of the "culprit vessel" was then performed by the use of manual aspiration thrombectomy and bare metal stent implantation with good angiographic result and TIMI grade 3 (Fig. 2B). The patient received 300 mg aspirin and 600 mg clopidogrel as loading dose and 100 mg of aspirin

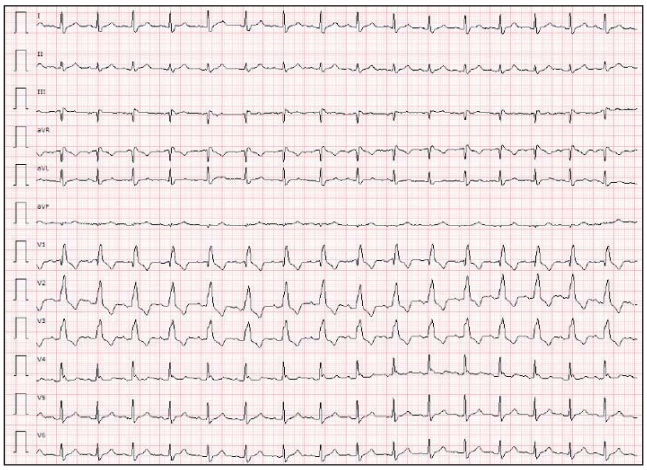

Fig. 1 – The ECG showed a complete right bundle branch block, known since HTx.

and 75 mg of clopidogrel daily as maintenance dose. Five days later, the patient experienced sudden cardiac arrest due to ventricular fibrillation, requiring cardiopulmonary resuscitation. A new angiography was immediately carried out revealing stent thrombosis of circumflex artery, with TIMI grade 3 (Fig. 3A and B). Manual aspiration of macroscopic thrombotic material was performed followed by balloon dilation with good angiographic result. Clopidogrel was changed for prasugrel 10 mg SID. The patient was recovered in the Coronary Care Unit and extubated 4 days later. Echocardiogram performed at 7 days showed LVEF of 38% with akinesia of infero-posterior and basal-lateral

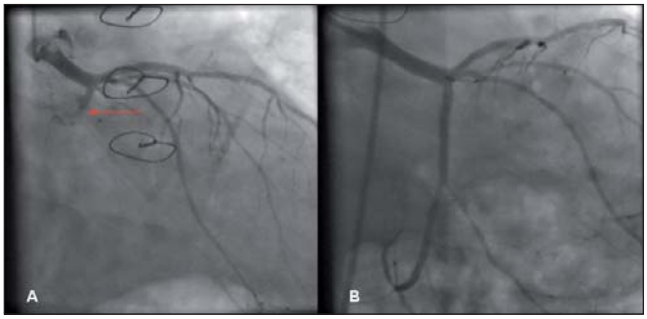

Fig. 2 – (A) Angiogram from right anterior oblique (RAO) caudal view prior to coronary intervention with an acute thrombosis of proximal circumflex artery "culprit vessel", TIMI grade 0. (B) Angiogram after aspiration thrombectomy and implanted bare metal stent with no residual stenosis and TIMI grade 3.

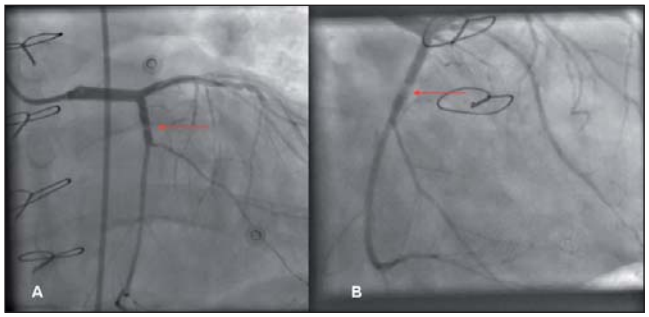

Fig. 3 – (A and B) Angiogram showing stent thrombosis of circumflex artery, with TIMI grade 3.

walls. Haematology study was performed six months later revealing a high level of coagulation factor VIII (216 U/dl; normal reference level of 65-135 U/dl) as the only blood abnormality. At 6 months, the patient remains in NYHA class II without new episodes of coronary events and new echocardiogram showed LVEF of 30%.

Discussion

CAV is the leading cause of late grafts failure following HTx [1]. According to ISHLT registry, incidence of CAV is around 10% at 1 year and reaches 50% at 5 years after HTx [3].

When acute myocardial infarction (AMI) occurs at a later stage after HTx, it is most often related to CAV. Gao et al. in 1989 published the only study to date that specifically addresses the incidence of late AMI following HTx. Among 329 heart transplant recipients at Stanford, 22 were found to develop MI at a mean time of 3.9 years after transplantation [5]. Besides, there are few case reports of ST elevation myocardial infarction following HTx as presentation of CAV [6–11].

Several factors may explain the apparently low incidence of MI following HTx. Under-reporting by patients due to lack of angina pectoris from the denervated heart may likely play a role. The sensation of angina during myocardial ischemia is generally thought to require functional sympathetic afferent fibers [12]. Although there exist some reports in human and animal models of spontaneous sympathetic re-innervation years after transplantation, heart transplant recipients usually do not present with typical anginal symptoms [13]. Dyspnea, fatigue, rate or rhythm changes or even sudden death may be the only early clinical symptoms and signs of AMI [14,15].

Therefore, it is not uncommon for HTx to present massive myocardial infarction similar to this case and yet not experience any chest pain. In our case the patient experienced AMI requiring late primary percutaneous coronary intervention (PCI) and bare metal stent implantation. Despite good initial angiographic result, the patient suffered from subacute stent thrombosis leading to ventricular fibrillation and subsequent cardiac arrest.

PCI in patients with HTx who develop CAV has been associated with greater restenosis rates compared to PCI in patients with native coronary artery disease [4,16]. Use of the first generation drug eluting stents (DES) appears to reduce the incidence of in-stent restenosis in CAV as compared with bare metal stents [17–20], but they do not appear to improve the clinical end points of death and major adverse cardiac events as stent thrombosis [21,22].

We herein report the first case of an HTx patient with documented elevation of factor VIII (FVIII) level who sequentially presented two thrombotic events: a STEMI, treated by stent implantation (PCI) followed by sub-acute stent thrombosis. High FVIII levels are common risk factor for deep venous thrombosis and may also be associated with risk of arterial thrombosis in coronary heart disease and stroke [23]. Apart from ABO blood group, no genetic components have been associated with plasma FVIII levels. The main determinant is an elevated von Willebrand factor (vWF) level [24]. However FVIII may have some effect independent of vWF. Few acquired factors such as active infections, specific treatments (micofenolatus) or acute-phase reaction may also increase FVIII levels [23,25]. Compared with tests for venous thrombophilia that must be performed a minimum of 6 weeks after the acute thrombotic event, tests for arterial thrombophilia are much less susceptible to the effects of acute thrombosis and could be performed soon after an acute thrombotic event [26]. Besides, some studies demonstrated that a high FVIII level may persist over time, beyond the acute phase state [27,28]. In any case, our blood analysis was performed well beyond the acute phase of MI and the theoretical window of acute inflammatory reaction.

Elevated FVIII levels have been established as thrombotic risk factor after endovascular intervention for peripheral arterial disease and also after lung transplantation [29,30]. In particular, elevated FVIII levels were encountered in 5 out of 6 patients suffering from thromboembolic events after lung transplantation [30]. But, up to date, no cases have been described in patients receiving HTx. In our clinical case, however, we cannot completely rule out the presence of resistance to aspirin or clopidogrel as no platelet function test was performed after stent thrombosis.

In conclusion, AMI in HTx patients may have misleading clinical manifestation. A high degree of clinical suspicion has to be maintained in the event of subtle ECG changes and atypical chest pain. Besides, stent thrombosis may also develop in such scenario where the prothrombotic milieu of the acute coronary syndrome, together with elevated FVIII levels converges. In the case of any thrombotic event after HTx, complete haematologic analysis that includes FVIII levels should be performed.

Conflict of interest

Salvatore Brugaletta has recived speaker fees from Abbott Vascular and St. Jude Medical. Manel Sabaté has received consultant and speaker fees from Abbott Vascular, Medtronic. Other authors have no conflict of interest.

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Ethical statement

We declare that the subjects' written consent was obtained according to the Declaration of Helsinki, and the study has been approved by a local ethics institutional review board or that it conforms to standards currently applied in the country of origin.

Informed consent

The patient was asked to consider allowing Dr. Omar Gómez to use his medical records to write a case report. The case report has been fully explained to the patient and all questions have been answered. We explained to the patient the objective of this manuscript, share new unique information experienced by one patient during his clinical care that may be useful for other physicians and members of a health care team, and may be published in *Cor et Vasa* Journal for others to read.

The patient authorized access to his personal health information and he has agreed to participate in this case report.

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