Early graft thrombosis following CABG due to antithrombin-III deficiency

Trombóza graftov po by-passovej operácií v skorom pooperačnom období v dôsledku deficiencie antitrombínu III

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Abstract. Early graft failure after coronary bypass grafting is a serious complication which may result in acute myocardial ischemia. In this report we present the case of a 79-year-old female patient with repeated multiple graft thrombosis of initially unclear origin which, after further investigation, was most likely caused by acquired antithrombin III deficiency. Although antithrombin III deficiency is a rare complication, in the case of simultaneous acute grafts thrombosis after cardiac revascularization surgery, it should be considered as a probable cause. Fig. 2, Ref. 6, online full text (Free, PDF), www.cardiologyletters.sk

Key words: multiple early graft thrombosis – coronary artery bypass grafting – acquired AT III deficiency

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Abstrakt. Zlyhanie graftov v skorom pooperačnom období po koronárnej by-passovej operácii je závažná komplikácia, ktorá môže spôsobiť akútnu myokardiálnu ischémiu. V tomto článku uvádzame kazuistiku 79-ročnej pacientky s opakovanou trombózou graftov spočiatku nejasnej etiológie. Po podrobnej analýze sa ako najpravdepodobnejšia príčina ukázala získaná deficiencia antitrombínu III. Obr. 2, Lit. 6, online full text (Free, PDF), www.cardiologyletters.sk

Kľúčové slová: opakovaná trombóza graftov – koronárna by-passová operácia – získaná deficiencia antitrombínu III

Early graft failure after coronary bypass grafting is a serious complication which may result in acute myocardial ischemia. The incidence is around 3% (1). Causes can be divided into graft and non-graft-related (2, 3) and the most common causes described were graft thrombosis or severe stenosis, anastomotic stenosis, extrinsic compression or graft kink, insufficient distal runoff, incomplete revascularization and subclavian artery thrombosis (4).

Graft failure usually affects only a number of the grafts, and simultaneous failure of multiple grafts is very rare (4).

In this case report we present a patient with repeated multiple graft thrombosis of initially unclear origin. Blood tests revealed antithrombin III deficiency as a probable cause. This is a rare cause and in the literature there are insufficient data concerning this complication.

Antithrombin III (ATIII) is a nonvitamin K-dependent protease that inhibits coagulation by neutralizing the enzymatic activity of thrombin (factors IIa, IXa, Xa). Antithrombin III activity is markedly potentiated by heparin, and deficiency of this factor may cause thrombosis (5).

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Case

A 79-year-old female was admitted to our hospital for elective coronary artery bypass grafting (CABG) due to left main and three vessel coronary artery disease. Coronarography showed 60-70% stenosis of the distal left main, 80% stenosis of the middle left anterior descending artery (LAD) and total occlusion of the first diagonal branch and the right coronary artery (RCA). She presented with a history of ischemic heart disease with recent myocardial infarction (4 months prior to operation), heart failure, type two diabetes mellitus, hypertension, dislipidemia, and subarachnoidal bleeding without ongoing neurological symptomatology. The patient also experienced thrombosis of the left jugular vein as a complication of acute renal failure of combined contrast-induced and infectious etiology, three months prior to surgery. Family history was positive for vascular stroke.

Preoperative echocardiography showed reduced ejection fraction of 35%, apical akinesis, anterior and posterior wall hypokinesis, and severe mitral regurgitation due to posterior leaflet restriction. Preoperatively, all the coagulation parameters including prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen level, thrombin time (TT) and AT III were normal.

The patient underwent a double coronary artery bypass graft with the use of cardiopulmonary bypass (CPB) and cardioplegic arrest. A saphenous vein graft was performed to the marginal branch of the circumflex artery and a left internal mammary artery (LIMA) graft to the left anterior descending artery. Right coronary artery and diagonal branch were not suitable for grafting due to the diameter and heavy calcification. The patient was also administered 18 ml of stem cells into akinetic and hypokinetic areas on the anterior and posterior wall, harvested from the iliac crest prior to operation. Initial ACT was 411 s and at the end of the procedure, the heparin was neutralized with protamin in a ratio 1:1 and an ACT of 81 s was reached, which was lower than expected. The procedure was uneventful and the duration of the CPB was 60 minutes. In the immediate postoperative period the patient was heamodynamically unstable with the need of increasing inotropic support and electrocardiographic changes (new left bundle branch block). Echocardiography showed heavily reduced ejection fraction of 15% and global hypokinesis and akinesis.

Based on these facts urgent surgical revision was indicated. The operation was performed with the use of CPB on a beating heart. Revision of both grafts showed unmeasurable flow velocity. The saphenous vein graft to the marginal branch was completely thrombosed and a new venous graft was

AT III levels-1

Date	Day	ATIII [75 - 125]	Comment
1.8.2017	1	88,4	
7.8.2017	7	66,8	Operation, 1st revision - reanastomoses + new venous graft
8.8.2017	8	45,4	2nd revision - Fogarty catheter embolectomy
9.8.2017	9	82,4	3rd revision - bypasses pink, patent, velocity on venous graft stem 81 ml/min, LAD 29 ml/min, OM 40 ml/min
10.8.2017	10	74,6	
20.8.2017	20	86,3	
25.8.2017	25	62,8	
30.8.2017	30	90,7	

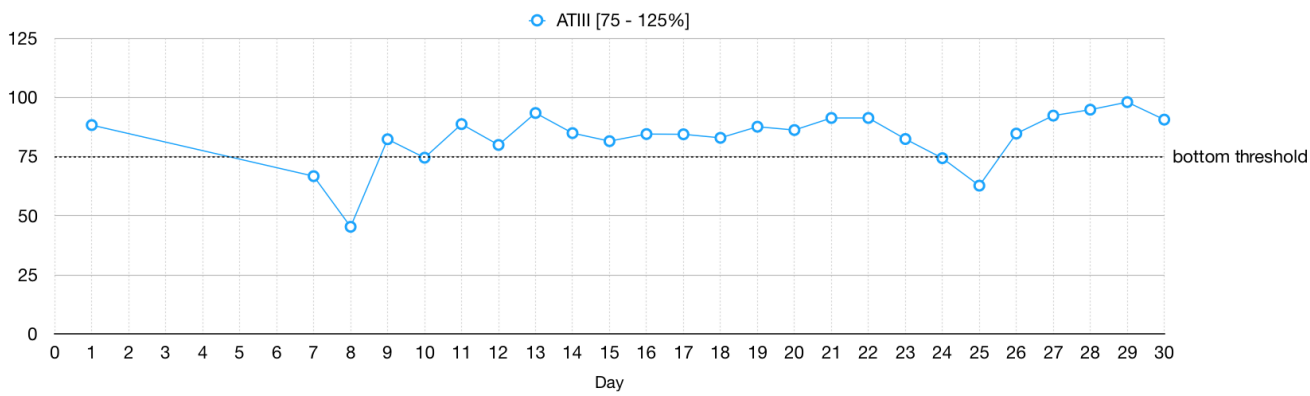

Figure 1 Daily measurements of antithrombin-III blood levels
LAD – left anterior descending artery, OM – obtuse marginal branch

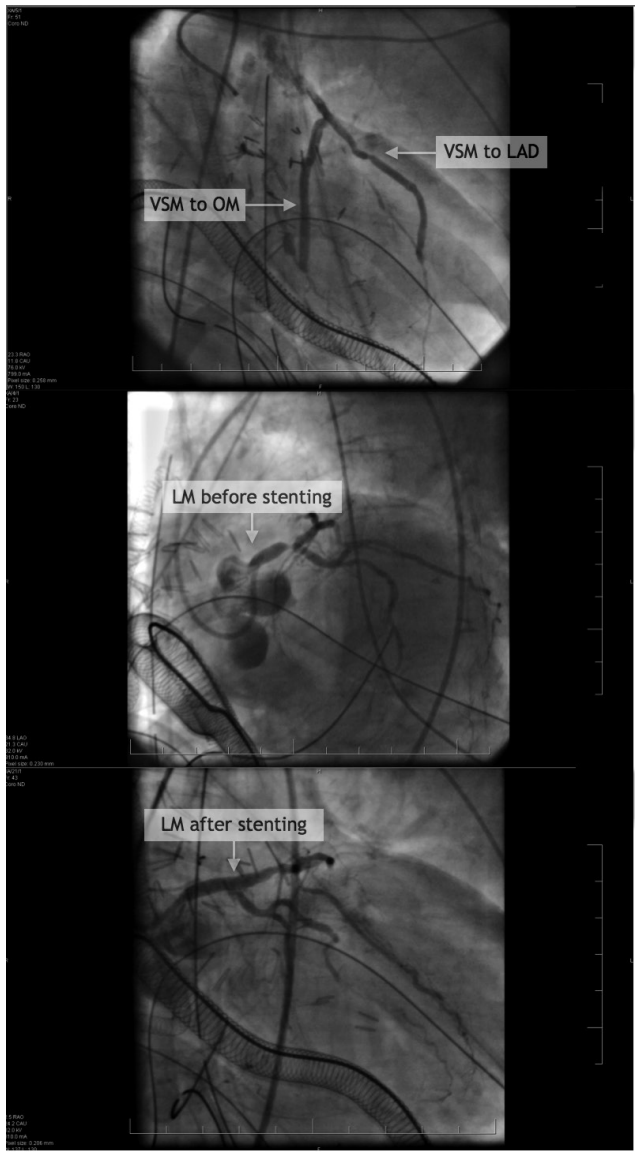

Figure 2 Coronary angiogram showing the Y-saphenous vein grafts to LAD and OM, and the LM stem before and after stenting
VSM – saphenous vein graft, LAD – left anterior descending artery, OM – obtuse marginal branch, LM – left main artery

anastomosed distally to the previous anastomosis. Similarly, the distal part of the LIMA graft to the LAD was completely thrombosed. After removing the thrombosed part the LIMA--graft was re-anastomosed to the same site. In addition a new venous graft was anastomosed distally to the previous LIMA anastomosis. The initial ACT was 599 s and this level was maintained during the CPB.

After unsuccessful attempts to wean the patient from the CPB, a central veno-arterial extracorporeal membrane oxygenator (ECMO) was established with cannulation of the right atrium and the ascending aorta. Total duration of CPB was 190 min, and the patient was transferred to the intensive care unit with an open chest.

Blood tests revealed reduced antithrombin levels (57,9%) presumably due to consumption during CPB. Congenital AT deficiency was very unlikely because the entry value of antithrombin was in physiological range **(Figure 1)**. Significantly elevated D-Dimer levels (3.26 mg/l) confirmed activation of the haemostatic and fibrinolytic systems. Antifibrinolytic therapy was routinely used during the hospitalization.

The following day due to inadequate ECMO flow another surgical revision was indicated where all the grafts were again thrombosed. Due to adverse coronary anatomic situation an embolectomy was performed on both venous grafts, using a Fogarty catheter.

The following day another surgical revision was performed where all bypasses were patent with adequate flow velocity and the patient's chest was closed. Moreover, a percutaneous coronary intervention on the left main was performed and levosimendan was added to treatment. However daily echocardiographic controls showed little improvement in cardiac function with ejection fraction varying between 10 to 15% and extensive hypo- and akinetic zones **(Figure 2)**.

After two unsuccessful attempts to wean the patient from the ECMO later during hospitalization, on postoperative day 30 she died.

Informed consent and institutional review board permission were obtained to present this case

Discussion

Early graft failure after coronary bypass grafting is a serious complication which may result in acute myocardial ischemia. There are several causes for early graft thrombosis including anastomotic stenosis, extrinsic compression, overstretching or tension, significant spasm, incomplete revascularization, graft kinking, insufficient distal runoff and subclavian artery thrombosis (4).

In our patient we have excluded any other cause. During the surgical revisions we did not find any bypass kinking, overstretching or extrinsic compression of the grafts. Original grafts were either re-anastomosed or replaced by new grafts to rule out anastomotic stenosis, and their graft velocity flow was checked regularly intraoperatively to rule out any technical error. Subclavian artery thrombosis and arterial graft spasm were also excluded. All the grafts were thrombosed in a simultaneous repeated fashion in the immediate postoperative period (less than 24h) after each procedure while the ATIII levels were low. After the patient's haemocoagulation parameters were stabilized, and the AT III levels were normal after replacement therapy, no further graft thrombosis occurred. This fact is in favor of the AT III deficiency as probable

cause of the early graft thrombosis in our case report. A very similar clinical case is reported by Kovacevic et al. indicating ATIII deficiency also as a probable cause (6).

Learning points

Multiple early graft thrombosis after coronary artery bypass grafting is a very serious complication. Although antithrombin III deficiency is a rare complication, in case of simultaneous acute grafts thrombosis after cardiac revascularization surgery, it should be considered as a probable cause.

Declaration of conflict of interest

All the authors declare no conflict of interest.

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