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THE FIRST CASE OF SURGICAL MYOCARDIAL REVASCULARIZATION AND ENDARTERECTOMY OF THE RIGHT CAROTID ARTERY IN THE SAME PROCEDURE IN A PATIENT WITH HAEMOPHILIA A

PRVI SLUČAJ HIRURŠKE REVASKULARIZACIJE MIOKARDA I ENDARTEREKTOMIJE DESNE KAROTIDNE ARTERIJE U ISTOM AKTU KOD PACIJENATA SA HEMOFILIJOM A

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All authors were involved in the treatment of patient. All authors participated in the design, conception of work and critical revision of the text. All authors have read and approved the final version of the paper.

Kratak naslov rada: Myocardial revascularization and haemophilia A
Abstract

**Introduction.** Hemophilia A is the most common hereditary coagulation disturbances occurring due to the lack of coagulation factor VIII. It is widely accepted that people with haemophilia have a reduced incidence of coronary artery disease, potentially because of the protective effect of the impaired coagulation against the pathogenic mechanisms of acute coronary syndrome. **Case report.** A 53-year-old man with a mild haemophilia (FVIII 22%) was hospitalized because of a frequent anginal pain at rest. Selective coronary angiography revealed a severe three-vessel coronary disease. A need for urgent surgical revascularization was indicated. Color duplex scan showed the existence of hemodynamically significant stenosis on the right internal carotid artery.

**Conclusion.** Patients with haemophilia are not protected against development of atherosclerosis. Cardiac surgery in these patients presents a unique challenge to medical teams in securing haemostasis. Adequate substitution with factor VIII concentrate provides adequate haemostasis and possibility for treatment with antiplatelet therapy.

**Key words:** coronary disease, hemophilia, coronary artery bypass grafting, carotid artery endarterectomy.

Apstrakt

**Uvod.** Hemofilija A je najčešći nasledni poremećaj koagulacije koji nastaje zbog deficita faktora VIII. Uopšteno je prihvaćeno da ljudi sa hemofilijom imaju smanjenu incidencu koronarne bolesti, uglavnom zbog protektivnog efekta narušenog sistema koagulacije nasuprot patogenetskim mehanizma za razvoj akutnog koronarnog sindroma. **Prikaz slučaja.** Pedeset-trogodišnji muškarac sa blagom hemofilijom A ((FVIII 22%) hospitalizovan je zbog učestalih anginoznih bolova u miru. Selektivna koronarografija je pokazala tešku trosudovnu koronarnu bolest koja je zahtevala hitnu hiruršku revaskularizaciju miokarda. Kolor dopler krvnih sudova vrata je pokazao hemodinamski značajnu stenozu na desnoj karotidnoj arteriji. Nakon konsultacije sa kardiohirurgom, hematologom i vaskularnim hirurgom, a zbog povećanog rizika od krvarenja, odlučeno je da se hirurška revaskularizacija miokarda i endarterektomija desne karotidne arterije rade u istom aktu. Operacije su urađene uz supstituciju koncentratom faktora VIII. Najpre je urađena endarterektomija desne karotidne arterije, a zatim je iskoriscena leva arterija mamarija kao graft na LAD ,kao i dva venska grafa na OM1 i PD grane. Tokom intervencije nije bilo hemoragijskih komplikacija, nije bilo potrebe za transfuzijom krvi. Pacijent je otpušten kući sa antitrombocitnom terapijom, ASA 50mg. **Zaključak.** Pacijenti sa hemofilijom nisu zaštićeni od razvoja ateroskleroze. Kardiohirurške operacije kod ovih pacijenata predstavljaju pravi izazov za ceo medicinski tim kako bi se obezbedila zadovoljavajuća
hemostaza. Adekvatna supstitucija koncentratom FVIII osigurava adekvatnu hemostazu i daje mogućnost za primenu antitrombocitne terapije.

**Ključne reči:** koronarna boest, hemofilija, hirurška revaskularizacija miokarda, endarterektomija.

**Introduction**

Haemophilia A is the most common hereditary coagulation disorder occurring due to the lack of coagulation factor VIII (FVIII). The life expectancy of persons born with haemophilia, who have access to adequate treatment, should approach normal with currently available treatment [1].

It is widely accepted that people with haemophilia have a reduced incidence of coronary artery disease, potentially because of the protective effect of the impaired coagulation against the pathogenic mechanisms of acute coronary syndrome [2,3]. Also, data have demonstrated that mortality due to ischaemic heart disease is lower in haemophilia patients than in the general male population [4]. Advances in the management of haemophilia increase the life expectancy and development of age-related and lifestyle-associated disorders such as atherosclerosis and ischemic heart disease [2].

Cardiac surgery in these patients presents a unique challenge to medical teams in securing haemostasis.

**Case report**

A 53-year-old male patient was hospitalized because of a frequent chest pain at rest. The patient had history of hypertension, hyperlipidemia, long-term smoking experience. The personal history reads haemophilia A with FVIII activity around 20%.

Laboratory examination verified decreased activity of factor VIII (FVIII 22%), normal activity of von Willebrand factor (vWF 112%) and prolonged partial thromboplastin time (aPTT 37.5 s). He did not have FVIII inhibitors. The patient was treated with cryoprecipitate in case of joint haemorrhage or dental intervention since childhood. Since 1980 he was treated with factor VIII concentrate from human plasma in preparation for tonsillectomy and cholecystectomy.

Following the advice of haematologist, the patient received 3000 IU of human FVIII concentrate prior to coronary angiography (Figure 1). After substitution the level of FVIII was 104%. Catheterization was performed via the right radial artery and revealed a severe three-vessel coronary disease with high degree left main stenosis (Figure 2). It indicated a need for urgent surgical revascularization. There were no haemorrhagic complications after the procedure.

In preparation for surgery according to existing guidelines and the history of transient ischemic attack less than six months prior to surgery, color duplex scan of carotid arteries was performed [5]. It showed the existence of ulcerated plaque on the right internal carotid artery, that gives stenosis of 85%, hemodynamically significant. The CT scan of carotid arteries and aorta was performed and the ultrasound findings were confirmed. There was no significant plaques or calcifications in the ascending aorta. Due to medical record of transient ischemic
attack and the characteristic of the plaque and degree of stenosis, endarterectomy was indicated [6].

In patient with haemophilia surgical treatment is raising costs due to need for factor VIII administration, more complex perioperative period and multidisciplinary approach is need, as well as increased bleeding risk, thus the simultaneous interventions are advisable when possible. In addition to this it is known that haemophilic patients can develop anti factor VIII antibodies after 20-50 repeated factor VIII administration speaks in favour of joint operation. After consultation with a haematologist, cardiologist, cardiac surgeon and a vascular surgeon, we concluded that patient should undergo endarterectomy and a triple aortocoronary bypass in the same procedure.

Due to unsuitable radial artery diameter and quality on preoperative ultrasound screening and the fact that patient was obese (higher risk of deep sternal wound infection if both mammary arteries were harvested) surgeon's decision was to chose left mammary artery in addition with great saphenous vein as the grafts of choice for this procedure. After analysis of the coronary anatomy and the fact that there were no significant calcifications in the ascending aorta (no significant risk of cross clamp injury) on pump approach was selected over off-pump.

Before, during and after surgery, the patient was under constant monitoring of a haematologist. During surgery every 30 minutes the level of factor VIII and activated partial prothrombin time was measured. The administration of factor VIII was given according to given values. During the total heparinisation activated clotting time (ACT) was used to measure the heparinisation level. The entire perioperative period factor VIII level was kept in normal range.

Just before the surgery, the patient received bolus of 3500 IU of FVIII. After fifteen minutes the level of FVIII was 101%, and after one hour 90%. During that time, endarterectomy was performed on the right carotid artery and the great saphenous vein from right leg was harvested for the use as a venous graft. After that, median sternotomy was done, the left mammary artery was harvested. Systemic heparin was given in 30,000 units and the extracorporeal circulation started (ECC). Anticoagulation activity of heparin was monitored by activated clotting time (ACT) and protamine sulphate was given twice to maintain ACT around 400s. During the procedure, FVIII was added several times (Figure 3). The patient underwent implantation of left mammary artery to the LAD and two vein grafts to the OM1 and PD. There was no need for blood transfusion and antifibrinolytics were not prescribed. ECC lasted for 91 min, and total revascularization time was 4 hours. At the end of procedure, the level of FVIII was 60%.

On the first postoperative day aspirin in low-dose of 50mg and low-molecular-weight heparin were introduced to the therapy. The level of factor VIII was between 83% and 104% (Figure 4).

From the second to the sixth postoperative day 2x2000 units of FVIII were prescribed. In the coming days, the dose was reduced (Figure 4). There was no excessive bleeding in the postoperative period.

At discharge the level of FVIII was 55%. The patient was discharged with aspirin 50mg, statin and beta blocker. The haematologist decided as long as the FVIII levels stay above 30%, the patient did not receive FVIII.

Fourteen months after the surgery, the level of FVIII was 37% and during that period there were no hemorrhagic complications.
Discussion

As the haemophilia population is getting older, studies have established that cardiovascular mortality is three times more common as a cause of death [7], but that mortality is 60% lower than in general population [8-11]. There are several potential reasons that may explain the low incidence of coronary artery disease in patients with haemophilia. They have hipocoagulable status and are significantly less likely to form a thrombotic mass, and they also have less established atheroma in blood vessels [12]. However, patients with haemophilia might not be protected against atherosclerosis, as demonstrated by clinical studies [13] and autopsy reports on haemophiliacs with fatal myocardial infarction showing extensive atherosclerotic lesions, but only rarely fresh thrombi [14].

In patients with haemophilia a tendency to bleed is increased, and therefore any invasive procedure is associated with an increased risk of hemorrhagic complications. Artery incision is confined with a high risk of local complications, but it can be effectively reduced by the substitution of a coagulation factor or by choosing access via radial artery for catheterization [15], as was case in our patient. Considering that during invasive procedures different complications are possible and sometimes urgent surgery is necessary, we decided to give higher doses of FVIII.

However, application of missing coagulation growth factor may increase the risk of acute thrombosis in patients with unstable atherosclerotic plaques. Girolami et al studied 36 cases of acute coronary syndrome in patients with haemophilia A. In most cases, the event occurred during or after the infusion of recombinant FVIII, desmopressin and prothrombin complex concentrates [14].

Also, one of the complications of treatment occurring mainly in haemophilia A patients is the development of an inhibitor, usually an IgG antibody, which is directed against the specific deficient factor and may occur shortly after replacement therapy has been initiated [16].

Cardiac surgery constitutes a major haemostatic challenge because of sternotomy, the need of total heparinization, ECC, mild hypothermia and cardiac arrest. However, there is no uniform protocol for the substitution of FVIII that can be applied in a bolus or an infusion [17]. According to the World Federation of Haemophilia recommendations, patients with haemophilia A that are going to undergo a major surgery should be supplemented with factor VIII before the procedure to achieve the level of 80-100% of FVIII activity [1].

In many patients with haemophilia described in the literature, procedures using cardiopulmonary bypass incorporated standard heparinization protocols [18-24], after 100% correction of factor levels by bolus or continuous administration of factor concentrates [25-31].

During surgery, the level of FVIII was monitored and the concentrate was added according to values gathered. On heparin induction, the level of FVIII decreased to 10% and after that to 1%. Then patient received protamine-sulphate and more 500 IU. After that, the level of FVIII increased to 60%. The level of FVIII increased due to substitution and due to neutralization of heparin with protamine-sulphate.

Antiplatelet therapies are important for the prevention of thrombosis after a cardiac surgery [32]. Haemophilia is not associated with abnormalities of platelet number or platelet function. However, antiplatelet therapy can increase the hemorrhagic tendency [19]. To minimize these risks, the clotting factor deficiency has to be corrected. As CABG and patients with coronary disease are required to be on single or dual antiplatelet therapy, for haemophilic patients use of aspirin in 50 mg dosage is recommended as long as factor VIII is above 30% with
regular measurements of factor VIII level, dual antiplatelet therapy is discouraged in these patients. [33]

LITERATURA

Fig. 1 – Substitution with FVIII concentrate before and after coronary angiography.
Fig. 2 – Coronary angiography (severe three-vessel coronary disease: LM stenosis 50%, LAD mid 70-90%, Cx prox 90-99%, Cx mid 90-99%, Cx dist 90-99%, OM2 70-90%, RCA prox 70-90%, RCA mid 100%).
Fig. 3 – Supstitution with FVIII concentrate before and during the surgery.
Fig. 4 – Supstitution with FVIII concentrate after surgery.