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Case report
Prikaz slučaja
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PROSTHETIC HEART VALVE THROMBOSIS – A HEADACHE FOR THE HEART TEAM – A CASE REPORT

TROMBOZA VEŠTAČKOG SRČANOG ZALISKA – GLAVOBOLJA ZA TIM ZA SRCE – PRIKAZ SLUČAJA

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Summary

Introduction. Prosthetic valve thrombosis is usually a subacute or chronic condition, although it may also present with a fresh thrombus. It occurs in two forms: obstructive and non-obstructive thrombosis. **Case Report.** We present a case of a female patient who underwent mitral valve replacement with mechanical prosthesis due to severe mitral stenosis. The postoperative course was uneventful and the patient was discharged on vitamin K antagonist therapy with international normalized ratio target 3.0. Five months later, the patient was admitted with severe shortness of breath and signs of acute heart failure. International normalized ratio at that moment was 2.3. Transthoracic echocardiography indicated severely raised gradient across the prosthetic valve and mechanical valve malfunction was suspected. Cinefluoroscopy showed that one of the prosthetic valve leaflets was completely immobile. Transesophageal echocardiography definitely confirmed thrombosis of the prosthetic valve with large multiple thrombi that completely fixed one leaflet in closed position, and partially limited the motion amplitude of the other leaflet. There were thrombi floating between the left ventricle and left atrium. Thrombectomy of the prosthetic valve was performed, which was sufficient for the complete restoration of the mechanical valve function. The vitamin K antagonist dosage was carefully up-titrated in order to reach and maintain the target international normalized ratio of 3.0. **Conclusion.** Prosthetic valve thrombosis is a serious and life-threatening condition that requires urgent management. Coordination and cooperation of the whole heart team is necessary for optimal choice of treatment, which primarily includes surgery or fibrinolysis.

Key words: Heart Valve Prosthesis; Thrombosis; Mitral Valve; Heart Valve Prosthesis Implantation; Anticoagulants; Vitamin K; Signs and Symptoms; Diagnosis; Reoperation

Sažetak

Uvod. Tromboza veštačkog zaliska obično predstavlja subakutno ili hronično stanje, mada može biti i akutno sa svežim trombom. Tromboza može da se javi se u dve forme - kao opstruktivna i neopstruktivna. **Prikaz slučaja.** Prikazujemo slučaj pacijentkinje kojoj je zamenjen mitralni zalistak mehaničkom protezom zbog teške stenoze. Postoperativni tok je protekao uredno i pacijentkinja je otpuštena sa terapijom antagonistom vitamina K sa ciljnim internacionalnim normalizovanim odnosom od 3,0. Pet meseci kasnije, pacijentkinja je primljena zbog gušenja i znakova akutne srčane slabosti. Vrednost protrombinskog vremena iznosila je 2,3. Transtorakalna ehokardiografija ukazala je na značajno povišene gradijente nad veštačkim zaliskom i postavljena je sumnja na malfunkciju mehaničke valvule. Sinevalvulografija je pokazala da je jedan listić veštačkog zaliska potpuno nepokretan. Transezofagealna ehokardiografija je definitivno potvrdila trombozu veštačkog zaliska sa multiplim velikim trombima koji su u potpunosti fiksirali jedan listić u zatvorenoj poziciji, a takođe delimično ograničili amplitudu pokreta drugog listića. Trombne mase su flotirale između leve komore i leve pretkomore. Načinjena je trombektomija veštačkog zaliska, što je bilo dovoljno za potpuni oporavak funkcije mehaničkog zaliska. Doza antagoniste vitamina K je pažljivo povećana kako bi se dostigla i održala ciljna vrednost protrombinskog vremena od 3,0. **Zaključak.** Tromboza veštačkog zaliska je ozbiljno i životnougrožavajuće stanje koje zahteva hitno zbrinjavanje. Za optimalan izbor lečenja, koji primarno obuhvata operaciju ili fibrinolizu, neophodna je koordinacija i saradnja celog tima za srce.

Ključne reči: veštački srčani zalistak; tromboza; mitralni zalistak; implantacija veštačkog zaliska; antikoagulanti; vitamin K; znaci i simptomi; dijagnoza; reoperacija

Introduction

More than 100 million people worldwide are affected by valvular heart disease and surgical aortic valve replacement is the treatment of choice (or repair of mitral valves). There are two different types of surgical prosthetic heart valves: mechanical heart valves and bioprosthetic heart valves. All implanted prosthetic valves are thrombogenic, especially mechanical, yet they are more durable than biological [1].

The pathogenesis of intracardiac thrombus formation is complex. According to Virchow's triad, the predisposing factors to thrombus formation can be divided into endothelial, hemodynamic, and hemostatic factors. Endothelial or surface factors include biocompatibility of the prosthesis and interactions between the prosthesis and the suture zone. Hemodynamic factors include the patient's cardiac hemodynamic status, as well as the intrinsic hemodynamic characteristics of the prosthetic valve. Last but not least, there are he-

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Abbreviations

NYHA – New York Heart Association
TTE – transthoracic echocardiography
MVA – mitral valve area
BSA – body surface area
VKA – vitamin K antagonist
INR – international normalized ratio
TEE – transesophageal echocardiography
CT – computed tomography

mostatic factors that involve the adequacy of anticoagulant treatment [1, 2]. The risk of thrombus formation, despite adequate oral anticoagulation, is estimated to be between 1 - 4% per year [3].

Prosthetic valve thrombosis is usually a subacute or chronic condition, although it may also present with a fresh thrombus [2]. It occurs in two forms: obstructive and non-obstructive thrombosis. The incidence of obstructive prosthetic valve thrombosis varies between 0.3 - 1.3% patient-years. On the contrary, the non-obstructive form is a relatively frequent finding in the postoperative period (as high as 10%), although thromboembolic complications are more frequent in the obstructive form, and occur at a rate of 0.7 - 6% patient-years [2].

Prosthetic valves in the tricuspid position have the greatest thrombogenic potential (up to 20%), followed by the mitral position (0.5 - 8%) [4]. According to a series of surgical interventions for prosthetic valve thrombosis, the first postoperative year is marked by 24% incidence of thrombosis, with a stable incidence between the second to fourth years of approximately 15%, with a subsequent decrease thereafter [2].

Case Report

A 60-year-old female patient was admitted for surgical treatment of mitral valve disease. She complained of fatigue, dyspnea on minimal exertion and occasional palpitations, while her New York Heart Association (NYHA) class was III. The symptoms started one year before and gradually increased over time. Her only comorbidity was hypothyroidism that was well controlled with substitution therapy. Physical examination showed a diastolic murmur of low-frequency over the mitral valve.

Transthoracic echocardiography (TTE) showed severe mitral stenosis with thickened, fibrous degenerative mitral cusps and mitral annular calcification **(Figure 1A)**. Maximal and mean transmitral gradients were 24 and 13 mmHg, respectively **(Figure 1B)**. Planimetry showed mitral valve area (MVA) of 0.8 cm^2 (0.4 cm^2/m^2 indexed for body surface area (BSA)). Mitral annulus was dilated at 3.9 cm and moderate mitral regurgitation was also registered. Left atrium was severely dilated with 5.9 cm in diameter and 182 ml volume (90.5 ml/m^2 indexed for BSA). Moderate tricuspid regurgitation was present as well. The systolic function of both ventricles was preserved (left ventricular ejection fraction 60%; tricuspid annular plane systolic excursion 22 mm).

Preoperative coronary angiography was without lesions, so coronary artery disease was excluded, and

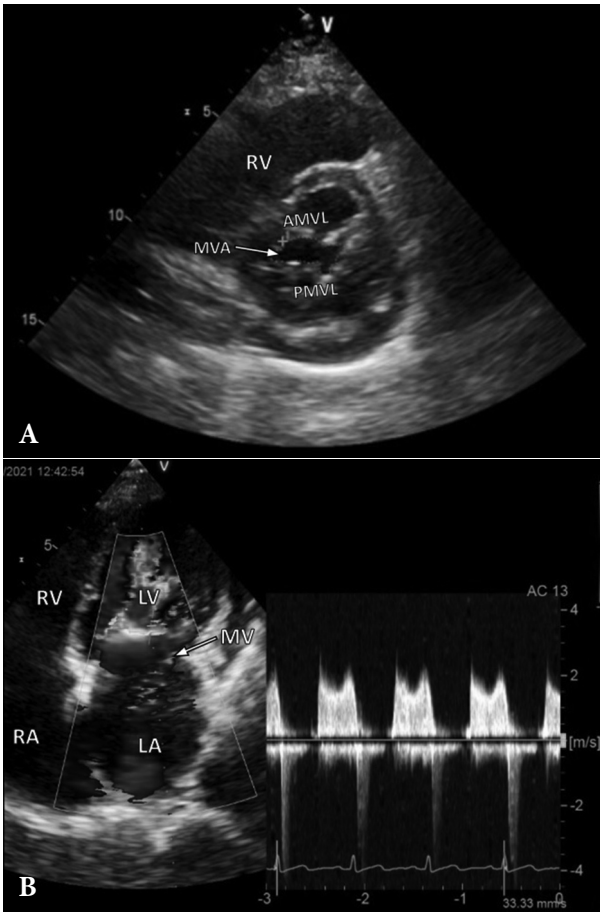

Figure 1. Transthoracic echocardiography on admission: A) mitral valve stenosis from parasternal short-axis view; B) transmitral flow with continuous wave Doppler, maximal gradient 24 mmHg, mean gradient 13 mmHg

Slika 1. *Transtorakalna ehokardiografija pri prijemu: A) stenoza mitralnog zaliska na parasternalnom poprečnom preseku; B) transmitralni protok kontinuiranim doplerom, maksimalni gradijent 24 mmHg, srednji gradijent 13 mmHg*

Legend: AMVL – anterior mitral valve leaflet; LA – left atrium; LV – left ventricle; MV – mitral valve; MVA – mitral valve area; PMVL – posterior mitral valve leaflet; RA – right atrium; RV – right ventricle

Legenda: AMVL – prednji mitralni kuspis; LA – leva pretkomora; LV – leva komora; MV – mitralni zalistak; MVA – površina mitralnog zaliska; PMVL – zadnji mitralni kuspis; RA – desna pretkomora; RV – desna komora

heart valve surgery was indicated by the heart team. The patient underwent surgery in general endotracheal anesthesia with extracorporeal circulation. Mitral valve replacement with a mechanical prosthesis (On-X No. 27/29) with preservation of P2 and P3 scallops, along with tricuspid valve repair were performed. Histopathological analysis of the removed mitral valve tissue showed fibromyxomatous degeneration of mitral leaflets. The postoperative course was uneventful and the patient was discharged on the 8th postoperative day in good general condition on vitamin K antagonist (VKA) therapy with international normalized ratio (INR) target 3.0.

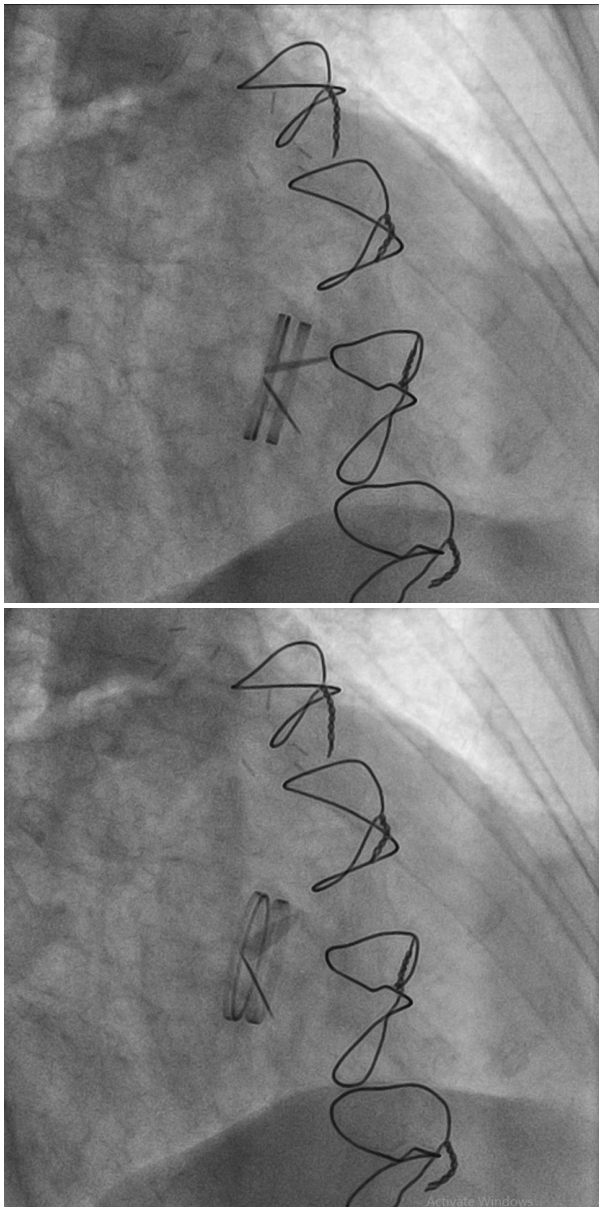

Figure 2. Cinefluoroscopy of the prosthetic valve shows complete immobility of one leaflet
Slika 2. *Sinefluoroskopija veštačke valvule: jedan listić je u potpunosti nepokretan*

One month later, the patient was admitted as an emergency due to dyspnea and palpitations. Echocardiography showed cardiac tamponade with large pericardial effusion, so an emergency subxiphoid pericardial drainage was performed and 500 ml of sero-hemorrhagic effusion was evacuated. The chest tubes were removed two days later so VKA was discontinued and bridge therapy with low-molecular weight heparin was administered. After chest tube removal, VKA was continued and the patient was discharged.

Five months after the heart valve surgery and mechanical valve implantation, the patient presented with severe shortness of breath and signs of acute heart failure, with NYHA class IV. A TTE was immediately performed and revealed severely elevated maximal and mean pressure gradients across prosthetic valve (43 and 24 mmHg, respectively) and mechanical valve malfunction was suspected. The INR value at that moment was 2.3, N-terminal pro-brain natriuretic peptide was elevated (13.583 pg/ml), while other blood laboratory test results were normal. Immediately after admission, continuous intravenous infusion of unfractionated heparin was initiated.

Cinefluoroscopy showed that one of the prosthetic valve leaflets was completely immobile, while the other was moving properly **(Figure 2)**. Transesophageal echocardiography (TEE) was also performed for confirmation. Thrombosis of the prosthetic valve was confirmed, with large multiple thrombi that have completely fixed one leaflet in closed position, and also partially limited the motion amplitude of the other leaflet. There were thrombi floating between the left ventricle and left atrium **(Figure 3)**.

After a detailed heart team evaluation, urgent surgical reoperation was indicated. Following a 72-hour clinical stabilization, the patient once again underwent

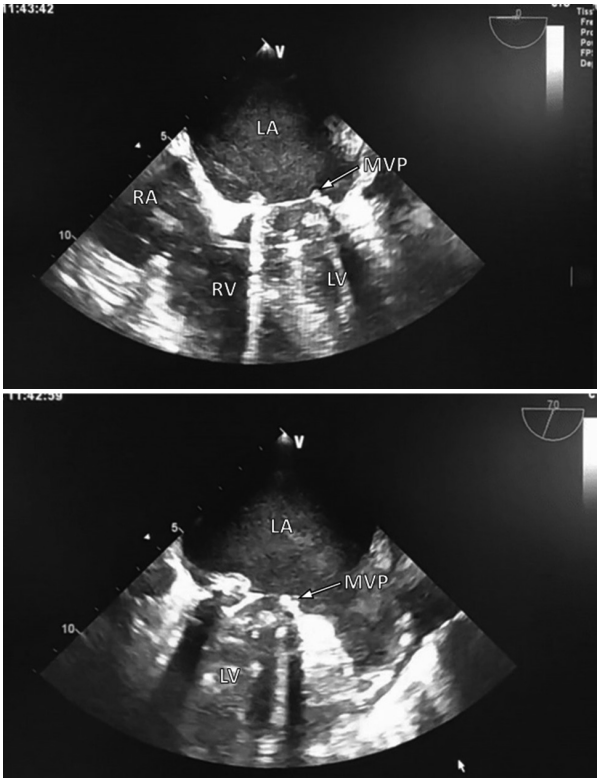

Figure 3. Transesophageal echocardiography of the prosthetic valve: thrombosis with multiple thrombi floating between the left ventricle and left atrium
Slika 3. *Transezofagealna ehokardiografija veštačke valvule: tromboza sa multiplim trombima koji flotiraju između leve komore i leve pretkomore*
Legend: LA – left atrium; LV – left ventricle; MVP – mitral valve prosthesis; RA – right atrium; RV – right ventricle
Legenda: LA – leva pretkomora; LV – leva komora; MVP – veštački mitralni zalistak; RA – desna pretkomora; RV – desna komora

surgery in general endotracheal anesthesia with extracorporeal circulation. Thrombectomy of the prosthetic valve was performed, which was sufficient for complete restoration of the mechanical valve function, as confirmed by perioperative TEE. The postoperative course was uneventful, the patient was stable and without any symptoms, so she was discharged on the 8th postoperative day in good general condition. Her VKA dosage was carefully up-titrated in order to reach and retain the target INR of 3.0. Subsequent control TTE showed normal function of the mechanical prosthesis, with normal pressure gradients across the valve.

Discussion

Prosthetic valve thrombosis is one of the most dangerous complications following surgical valve replacement and it is associated with high morbidity and mortality. Dysfunction of the prosthetic valve, with or without thrombosis, may clinically manifest as progressive dyspnea and signs of heart failure [5]. Prosthetic valve thrombosis may be detected incidentally during routine echocardiography examination. Also, in every patient with acute or subacute development of symptoms and progression of transprosthetic gradient (compared to previous echocardiography examination) there is a suspicion of a possible prosthetic valve dysfunction [6–8]. This case report presents a way to detect and solve a complex problem called mechanical valve thrombosis.

The intensity and duration of anticoagulant therapy depend on the type of prosthesis, risk of bleeding, and thromboembolic complications [9–12]. Patients with implanted mechanical valve require lifelong anticoagulant therapy with VKA [13]. Lin et al. described several predictors of mechanical valve thrombosis and they include occlusive mobile mass, increased transvalvular pressure, and INR $\leq$ 2.5 [14]. In the German Experience with Low Intensity Anticoagulation study, patients with mechanical valve at the mitral position and low INR were associated with lower survival rates compared to patients with higher INR values of 2.5 - 4.5 [15]. According to the latest recommendations, in patients with mechanical valve at mitral position, anticoagulant therapy with VKA is indicated to achieve the INR target value of 3.0 [16]. One of the possible explanations for the thrombosis of the mechanical valve in our patient may be inadequate anticoagulant therapy and subtherapeutic INR value of 2.3 on admission, which can be affected by a number of factors such as age, weight, diet and interaction with other drugs [17].

The TTE is the first line test for the diagnosis of prosthetic valve dysfunction [18]. Although this method has many advantages, such as assessment of hemodynamics and valve motility, TTE is limited in morphological characterization of the etiology of mechanical valve dysfunction. Acoustic shadowing caused by the prosthesis itself can make visualizing blood clots, pannus, and vegetation more difficult, but other factors can also affect the accuracy of this method, such as the presence of pericardial effusion, previous sternotomy, and obesity [18]. Due to the above mentioned, for better evaluation of prosthetic valve dysfunction after TTE, TEE should be performed, which has a significant role in guiding the therapeutic strategy. Furthermore, in left-sided prosthetic valve thrombosis, the presence of thrombus favors surgery because fibrinolysis carries a significant risk of embolism. The mobility of the mechanical valve can also be assessed by cinefluoroscopy, which enables the assessment of the opening angles of the prosthesis [16]. In a number of cases, multidetector computed tomography (CT) can provide an accurate assessment of prosthetic valve structure and functional status [19, 20]. According to the latest recommendations for the treatment of valvular heart diseases, every patient with suspected mechanical valve thrombosis needs an urgent evaluation by TTE, TEE and/or multidetector CT [16, 21]. Following the latest recommendations, our patient underwent TTE, TEE and cinefluoroscopy, which altogether gave insight into the correct diagnosis and enabled an adequate treatment strategy.

There are several therapeutic options for mechanical valve thrombosis, including emergency surgery, thrombolytic therapy, and anticoagulation therapy. According to the 2020 American College of Cardiology/American Heart Association recommendations [16], the decision on either emergency surgery or systemic fibrinolysis should be made by the heart team based on the individual characteristics of each patient. Emergency surgery is recommended for patients with NYHA functional class III or IV and/or large thrombus (thrombus area $\geq$ 0.8 cm^2), while NYHA classes I and II, high operative risk, low risk of bleeding, and a small thrombus favor fibrinolysis as a therapeutic option. In contrast, according to the 2021 European Society of Cardiology and the European Association for Cardio-Thoracic Surgery guidelines [21], surgery is preferred and fibrinolysis should only be used when surgery is not an option. Due to the presence of a large thrombus, acute heart failure, absence of significant comorbidities and low operative risk in our patient, emergency surgery was indicated as a therapeutic option. In their meta-analysis, Karthikeyan et al. included several studies comparing surgery and fibrinolysis as therapeutic options for mechanical valve thrombosis [22]. They concluded that emergency surgery led to complete success in 86.5% of cases and fibrinolysis in 69.7%. Significant bleeding was less common in operated patients (1.4% vs. 5%). Stroke was less common in the group of operated patients compared to patients undergoing fibrinolysis, and also repeated mechanical valve thrombosis occurred less frequently in operated patients.

Conclusion

Prosthetic valve thrombosis is a serious life-threatening condition that requires urgent management. Multimodality imaging is crucial for evaluating the artificial valve function and establishing the correct diagnosis. Coordination and cooperation of the whole heart team is necessary for optimal choice of treatment, which primarily includes either surgery or fibrinolysis.

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