Case Report

Treatment of Thrombosis of a Mechanical Aortic Valve with Fibrinolysis

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We describe the case of a 57-year-old man with a mechanical aortic valve who had discontinued oral anticoagulants for a long period and presented with symptoms of severe congestive heart failure, including pulmonary oedema and hypotension. Clinical and echocardiographic examination revealed a large thrombus obstructing the prosthetic valve. Since his critical clinical condition was not improved by heparin treatment we decided to administer intravenous fibrinolysis with 100 mg rtPA. Fibrinolytic treatment was entirely successful, with complete thrombus dissolution and restoration of clinical status. Thrombosis of mechanical prosthetic valves is a particularly serious complication with a high mortality rate. Early diagnosis and treatment are of paramount importance for these patients. Although surgical intervention is the suggested treatment in many series, fibrinolytic therapy offers a good alternative with a high success rate, especially in the critically ill patient where surgery carries a high risk of mortality.

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Thrombosis of prosthetic heart valves is a very serious and fortunately rare complication, which may present a clinical picture of either peripheral emboli or heart failure. Because of the high percentage of life-threatening complications, prompt diagnosis and treatment are of paramount importance. Although surgery has long been considered the treatment of choice in such cases it is not without risk. Fibrinolytic treatment appears to be an alternative therapy with a satisfactory success rate and a relatively low incidence of complications, especially in patients who are in a critical condition and for whom surgery is associated with high mortality.

Here we present a case of obstructive thrombosis of a mechanical aortic valve which was treated successfully by the administration of rtPA.

Case description

A man aged 57 years, who had undergone aortic valve replacement with a St. Jude mechanical valve in 2000 because of stenosis, was admitted to our department with acute pulmonary oedema. For four months the patient had reported fatigue, with dyspnoea initially on intense effort and subsequently on minimal exertion. The symptoms had worsened during the last few days, leading to dyspnoea at rest with features of orthopnoea, coughing with foamy expectoration, weakness and cold sweating (NYHA functional class III-IV). The patient had stopped taking anticoagulant medication of his own volition about a year before.

On clinical examination the patient was afebrile, with tachypnoea (30 breaths/ minute), tachycardia (135 beats/min), blood pressure 95/70 mm Hg, and rales up to the middle of both lung fields. Cardiac auscultation revealed a reduced second sound with no aortic closing click, while there was an audible 3-4/6 systolic ejection murmur at the auscultation focus of the aorta with extension towards the apex and the cervical vessels.

The ECG showed sinus tachycardia, left anterior hemiblock with signs of left

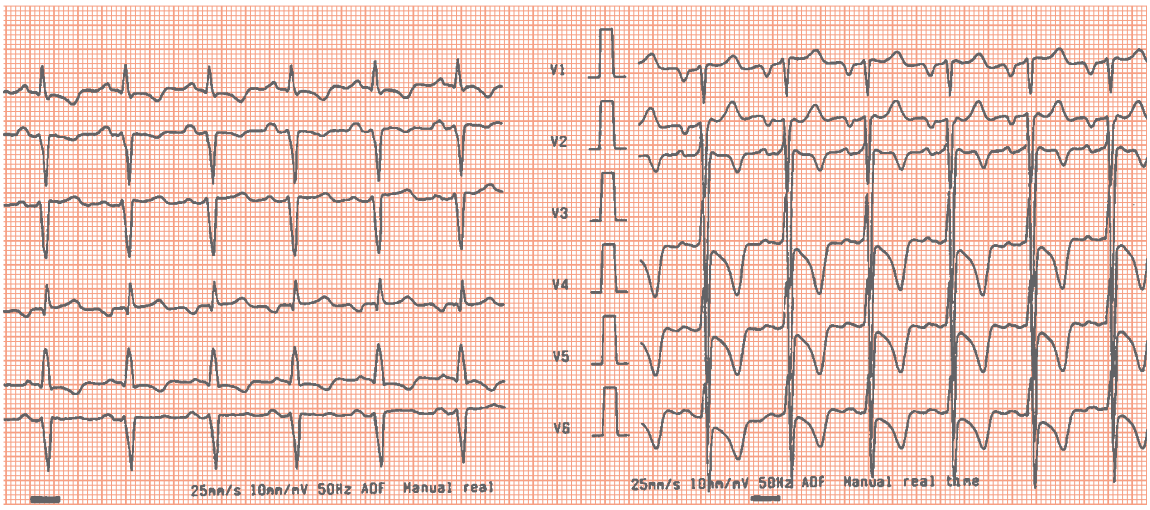

Figure 1. Patient's 12-lead ECG on admission to the department. Limb leads are on the left and precordial leads on the right. There are signs of left ventricular hypertrophy with S V_3 + R aVL >28 mV and a deep negative T in leads I, aVL, V_4-V_6.

ventricular hypertrophy (positive Cornell[1] criteria S V_3 + R aVL >28 mV) and a deep negative T wave in leads I, aVL, V_4-V_6 (Figure 1).

The chest X-ray showed a slightly elevated cardiac index, with pulmonary hilar dilation, reversal of pulmonary perfusion and fluid in the mid-lobe. Blood and biochemical tests on admission showed elevation of haematocrit and haemoglobin (Ht: 49.4%, Hb: 16.4 g/dl), white blood cells and neutrophils (WBC: 12160 with 70.8% neutrophils), as well as an increase in cardiac troponin-I, indicative of myocardial necrosis, which reached a peak value of 5.35 ng/ml, elevated CK-MB (6.8 ng/ml), transaminases (SGOT 55 IU/L, SGPT 86 IU/L) and LDH (293 IU/L), with normal values of total CK, electrolytes and renal function. The coagulation test gave an INR of 1.04.

The subsequent transthoracic and transoesophageal echocardiographic examination showed concentric left ventricular hypertrophy with slightly reduced systolic performance. There was a two-leaflet prosthetic aortic valve with stable adhesion to the annulus but with thrombus on one disk, rendering it immobile, and extrusions of thrombotic material towards the other disk (Figure 2A, B). From the Doppler study and colour mapping the peak recorded flow velocity through the valve was 5.2 m/s, corresponding to a peak pressure

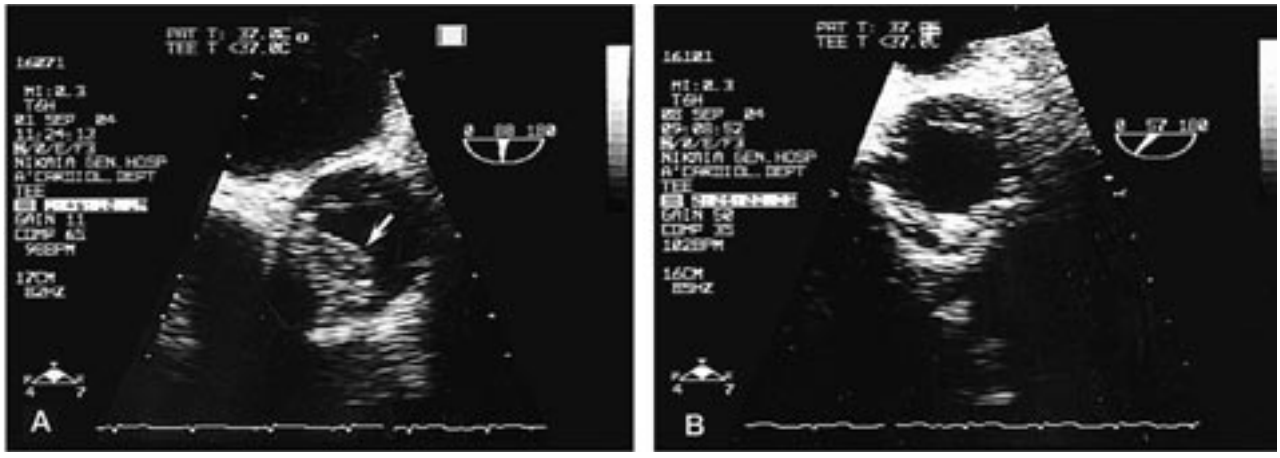

Figure 2. Transoesophageal echocardiogram showing the prosthetic valve before (A) and after (B) fibrinolytic therapy. The arrow in A indicates a large thrombus on the mechanical valve, which disappeared after the administration of 100 mg rtPA.

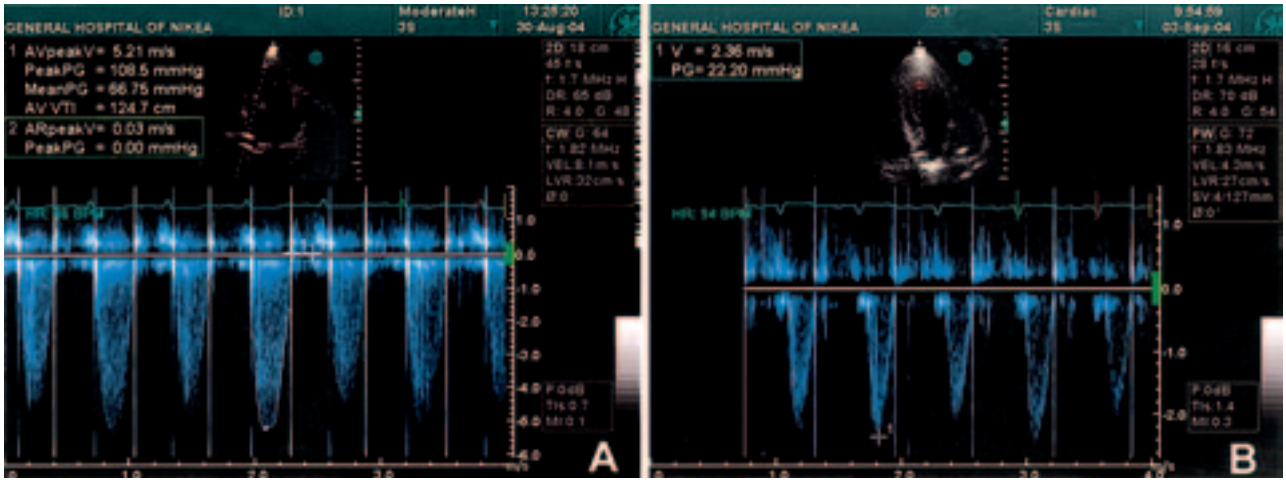

Figure 3. Pulsed Doppler flow velocity through the prosthetic aortic valve before (A) and after (B) fibrinolytic therapy. The peak flow velocity before was 5.2 m/s, corresponding to a peak pressure gradient of 108.5 mmHg and a mean pressure gradient of 67 mmHg. These values dropped dramatically after fibrinolysis (peak flow velocity 2.3 m/s, peak pressure gradient 22 mm Hg).

gradient of 108 mmHg and a mean pressure gradient of 67 mmHg (Figure 3A). A small degree of valvular insufficiency was also recorded. These findings confirmed the diagnosis of partial obstruction of a prosthetic aortic valve by thrombotic material, resulting in severe restriction of its opening.

The patient was initially placed under intravenous diuretic treatment with fractionated heparin and ramipril, but there was no notable improvement in his symptoms or clinical condition. Since his clinical picture remained marginal 24 hours after diagnosis (NYHA class IV, with low blood pressure 90-95 mmHg), it was decided to administer fibrinolytic medication. The patient was given 100 mg rtPA, with a 10 mg bolus and a 90 mg drip over 90 minutes, while the intravenous heparin was continued, aiming at an increase in APTT level to 1.5-2 times the control value, as well as acetylsalicylic acid in a daily dose of 100 mg. From the second day following thrombolysis the patient showed an improvement in his dyspnoea, with disappearance of the lung rales and the tachycardia, as well as a steady increase in blood pressure. There were also clear changes on heart sound auscultation, with a progressive increase in the volume of the aortic closing click. A later echocardiographic examination showed a reduction in peak velocity and pressure gradient across the aortic valve, with normal levels for the valve type, while the transoesophageal study showed a complete absence of thrombotic material (Figures 2B, 3B). The ECG picture also improved, with a reduction in the tachycardia, the height of the R waves and the depth of the negative T in the precordial leads, while myocardial enzymes showed a downward trend.

A few days later the patient underwent coronary angiography to rule out coronary artery disease. During a similar examination four years earlier, prior to the aortic valve replacement surgery, his coronary vessels had been free of significant obstructive lesions. The new findings were similar.

The patient continued under anticoagulant treatment with coumarin in combination with intravenous heparin, until satisfactory INR values were achieved (target INR 3.0). He was discharged on the seventh day of hospitalisation, free of symptoms, under treatment with coumarin anticoagulants and aspirin. On re-examination three months later he remained free of symptoms (NYHA functional class I), with normal haemodynamic behaviour of the aortic valve on echocardiographic examination and satisfactory results from the anticoagulant medication.

Discussion

Thrombosis of a mechanical prosthetic valve is an extremely serious complication, often being associated with emboli and with severe clinical and haemodynamic deterioration. Apart from emboli, the clinical picture can also include, as in the case described here, heart failure symptomatology with dyspnoea, pulmonary oedema and often hypotension, and it is much more severe in massive thrombosis. The valve obstruction is due to thrombus formation, or pannus, or a combina-

tion of the two. The usual cause is inadequate anticoagulation therapy, while the thrombus affects the mitral more often than the aortic valve, and older, caged ball valve types more than newer tilting disk or two-leaflet valves. The diagnosis is easily confirmed by transthoracic and transoesophageal echocardiography. Under medication with coumarin anticoagulants the incidence of prosthetic valve thrombosis has been reported to be 0.2 per 100 patient-years.[2] In patients who are not taking anticoagulants, such as the case reported here, the rate is at least four times greater and ranges from 0.9 to 3 per 100 patient-years, while it appears to be no lower in those who are taking antiplatelet drugs.[2] The guidelines of the American Heart Association and the American College of Cardiology, published in 1998,[3] make reference to the treatment of prosthetic valve thrombosis and recommend immediate surgery in patients with a large thrombus and valve obstruction, as well as in those who show the dyspnoea symptomatology of NYHA functional classes III and IV. For patients with a "small thrombus" and those who are in NYHA functional classes I and II, or who show left ventricular dysfunction, treatment with intravenous heparin is recommended, and only when the response is unsatisfactory should they be considered for possible thrombolytic or surgical therapy. In those guidelines the administration of thrombolysis to patients with severe heart failure and large thrombus, such as the case described here, is not recommended, because from an analysis of older series[4,5] the unsatisfactory outcomes reached 16-18% and the mortality 6%. More specifically, those series reported the following complication rates: thromboembolic episodes 12%, stroke 3-10%, major haemorrhagic events 5%, minor haemorrhagic events 14%, and repeat thrombosis 11%. For these reasons the 1998 guidelines recommend thrombolytic therapy as a final resort, only in patients with high surgical risk or contraindications for surgery. It is recommended that fibrinolytic therapy be given for 24-72 hours, mainly with streptokinase and urokinase.[3]

However, and in spite of the guidelines, fibrinolytic therapy has been used extensively and has been discussed as an alternative to surgery in selected patients with prosthetic valve thrombosis.[4-7]

In one centre, a very interesting recent study[8] administered fibrinolytic medication to 127 patients with prosthetic valve thrombosis, with very encouraging results. Indeed, the editorial comment accompanying the report posed the question whether the guidelines should be revised in the future to include fibrinolysis.[9] Specifically, in the series reported by Roudaut et al[8] the fibrinolytic treatment was completely successful in 70.9%, partially successful in 17.3%, with failure of treatment in 11.8% of patients. The administration of streptokinase and rtPA was superior to the use of urokinase and the fibrinolytic drugs were mainly administered with a short duration protocol of one hour and a dosage similar to that used for acute myocardial infarction (2,000,000 IU for streptokinase, 100 mg for rtPA), with concomitant administration of intravenous heparin. Fibrinolytic treatment was not given to patients with thrombus in the right atrium because of the increased risk of embolic episodes, while supplementary doses of fibrinolytic medication were given in a third of the cases in order to achieve complete dissolution of the thrombus.[8] In this series embolic episodes occurred in 15% of cases and haemorrhage in 5%: however, embolism led to stroke in only 7% of the total cases and the majority of these were not fatal. The overall mortality in Roudaut's series was 12%, so if we consider that the mortality for emergency surgical replacement of a thrombotic prosthetic valve has reached 8-20% in many series,[4,10] and exceeds 35% in patients who are in a "critical condition" requiring surgery, fibrinolytic therapy seems very promising.

Given that our patient belonged to a high-risk group for surgery, because of the symptomatology of class IV heart failure, and since the transoesophageal echo examination showed thrombus on the valve and no thrombus in the left atrium, we took the decision to apply fibrinolysis directly and administered rtPA with the very good results described above.

The presence of pannus, when it can be differentially diagnosed echocardiographically, probably renders thrombolysis ineffective. It is worth noting that the differential diagnosis of thrombus versus pannus on the basis of echocardiographic and clinical criteria is quite difficult, since the morphological features often overlap.[11] The most powerful factor for differential diagnosis on the transoesophageal echogram is the high acoustic density of the pannus imaging compared to thrombus, while as far as clinical features are concerned patients with thrombus often have inadequate anticoagulant medication and a shorter duration of symptoms that oblige them to seek medical aid.[11]

We believe it is worth providing a brief presentation of the instructions proposed by Alpert[9] with respect to thrombosis of mechanical valves, which were published in the guise of "Guidelines" even though the author himself stressed that they represented his personal views, based on his own experience, and were prompted by the publication of the study by Roudaut et al.[8]

1. All patients with suspected thrombus of a mechanical valve should undergo a transthoracic and, if necessary, a transoesophageal echo examination (level of evidence I).

2. Patients with thrombus of a mechanical valve in the right heart should be given intravenous rtPA (100 mg total, 10 mg bolus and 90 mg drip over 90 min) or streptokinase (500,000 IU over 20 min, followed by 1.5 million IU drip over 10 hours) (level of evidence IIa).

3. Patients in a severe and critical clinical condition (pulmonary oedema, hypotension, NYHA class III/IV) should receive immediate thrombolytic medication, as described above, if the presence of thrombus is confirmed echocardiographically (level of evidence IIa).

a. Supplementary doses of fibrinolysis may be given in the case of incomplete dissolution of the thrombus, as determined by repeated echocardiographic examinations (level of evidence IIa).

b. Intravenous standard heparin may be administered concomitantly with thrombolysis in order to achieve an APPT level 1.5-2.0 times the control time (level of evidence IIb).

c. Surgical evaluation of the patient should be carried out immediately. If repeated doses of thrombolytic medication are unsuccessful, surgical treatment is recommended (level of evidence IIa).

4. Patients with thrombosis of a mechanical valve who are clinically stable, i.e. in NYHA functional classes I and II, may be treated either with fibrinolytic/ anticoagulant medication, or with surgical valve replacement, depending on the preferences of the patient and physician (level of evidence IIa).

In the case we describe, a coronary angiographic examination was deemed necessary at a later stage in order to determine the coronary artery anatomy, in view of the elevation in myocardial enzymes, indicative of necrosis, and the ischaemic ECG changes. The absence of significant angiographic atherosclerotic disease suggested the likelihood of coronary artery embolism by a section of the thrombus on the prosthetic valve, manifested as myocardial necrosis with or without symptoms of angina. Similar cases have been reported in the literature.[12-14]

Despite the fact that the prosthetic valve thrombosis in our patient was not the result of inadequate anticoagulant medication, but rather its complete cessation, we would like to note the 1998 guideline of the American Heart Association and American College of Cardiology,[3] who recommended for mechanical valves in the aortic site that the INR should be maintained in the range 2.0-3.0 for a two-leaflet mechanical prosthesis or a Medtronic Hall valve, and 2.5-3.5 for a Starr-Edwards valve (cage type). The addition of aspirin, 80-100 mg daily, is recommended in patients with a mechanical aortic valve who are at high risk of thromboemboli, such as those with atrial fibrillation, previous embolism, hypercoagulant conditions, coronary artery disease and probable poor left ventricular function. A more recent meta-analysis[15] concerning the ideal INR target in patients with mechanical valves suggests that all patients, regardless of the site of the prosthesis (aortic or mitral valve), will benefit from therapy aimed at maintaining an INR >3.0. Even though this meta-analysis came in for some criticism,[16-18] we consider that an INR target of 3.0 simplifies the anticoagulant treatment without detracting from safety, and it was the one chosen in the case described here. The addition of aspirin, though not essential given that the thrombosis occurred in the absence of anticoagulants, was judged advisable for the best patient compliance.

In conclusion, the case presented here provides a re-examination of the invaluable contribution of thrombolytic therapy in prosthetic valve thrombosis, which in many cases should probably be the treatment of first choice.

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