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EVOLUTION AND MANAGEMENT OF A SECOND EPISODE OF PROSTHETIC MITRAL HEART VALVE THROMBOSIS: CASE REPORT

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Palabras clave: Prótesis Valvulares Cardíacas; Insuficiencia de la Válvula Mitral; Trombosis; Terapia Trombolítica.

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ABSTRACT

Introduction: Prosthetic valve thrombosis (PVT) is a potentially fatal complication of prosthetic heart valve replacement. Treatment selection remains controversial due to the multiple pharmacological and surgical options available and the lack of prospective data and randomized clinical trials.
Case presentation: A 28-year-old woman with a history of systemic lupus erythematosus and mitral and tricuspid valve disease secondary to rheumatic fever required mechanical mitral valve replacement. In 2020, the patient visited the emergency department of a tertiary care center in Bogotá, Colombia, due to dyspnea and chest pain. A transthoracic echocardiogram was performed, revealing mechanical mitral valve prolapse, which was managed with ultra-slow thrombolysis with alteplase, although surgical intervention was not required. In 2023, the patient was readmitted to the emergency department of the same institution with oppressive chest pain, progressive dyspnea, and headache. On this occasion, a focused cardiac point-of-care ultrasound (FoCUS) was performed, showing a prosthetic valve dysfunction that indicated a new episode of PVT, which was initially treated with ultra-slow thrombolysis and alteplase. However, given the deterioration in her clinical condition, it was decided to perform surgery to clean the mechanical mitral prosthetic valve. During this procedure, the patient experienced complications and required massive transfusion and extracorporeal membrane oxygenation support. The patient's postoperative course was satisfactory, and she was discharged 26 days after admission.
Conclusion: PVT management remains controversial given the lack of prospective and randomized clinical studies on the subject and due to the high risk involved regardless of the approach taken (fibrinolysis or surgery). Therefore, it is necessary to establish treatment based on each patient's clinical condition.

RESUMEN

Introducción. La trombosis de la válvula protésica (TVP) es una complicación potencialmente mortal del reemplazo valvular cardíaco protésico, en la cual la elección del tratamiento continúa siendo controversial debido a las múltiples opciones terapéuticas farmacológicas y quirúrgicas, y a la falta de datos prospectivos y de estudios clínicos aleatorizados.
Presentación del caso. Mujer de 28 años con antecedente de lupus eritematoso sistémico y valvulopatías mitral y tricuspídea secundarias a fiebre reumática, quién requirió reemplazo valvular mitral mecánico. En 2020, la paciente asistió al servicio de urgencias de una institución de salud de cuarto nivel de atención de Bogotá (Colombia) por disnea y dolor torácico. Se realizó un ecocardiograma transtorácico en el que se observó TVP mecánica mitral, la cual fue manejada con trombólisis en esquema ultra lento con alteplasa, sin requerimiento de manejo quirúrgico.

En 2023, la joven ingresó nuevamente al servicio de urgencias de la misma institución con dolor torácico opresivo, disnea progresiva y cefalea. En esta ocasión se realizó una ecografía cardiaca focalizada a pie de cama en la que se observó disfunción de la válvula protésica, por lo que se estableció que presentaba un nuevo episodio de TVP que se trató inicialmente con trombólisis en esquema ultralento con alteplasa; sin embargo, ante el deterioro clínico se decidió realizar cirugía para limpiar la válvula protésica mecánica mitral. En este procedimiento la paciente presentó complicaciones y requirió transfusión masiva y apoyo con oxigenación por membrana extracorpórea; no obstante, en el posoperatorio evolucionó satisfactoriamente y fue dada de alta a los 26 días de su ingreso.
Conclusión. El manejo de la TVP continúa siendo controversial dada la ausencia de estudios prospectivos y clínicos aleatorizados sobre el tema, y debido a que es de alto riesgo independientemente de la opción de abordaje que se siga (fibrinólisis o cirugía), es importante establecer el tratamiento teniendo en cuenta las condiciones clínicas de cada paciente.

INTRODUCTION

Valvular heart disease can lead to serious complications such as cardiogenic shock (CS), a state of low cardiac output associated with inadequate end-organ perfusion or tissue hypoperfusion secondary to cardiac dysfunction (1). CS is an area of interest for researchers because, despite advances in mechanical circulatory support treatments, related morbidity and mortality rates remain high (2,3).

Acute coronary syndrome is the main underlying condition in CS (2). However, any cause of ventricular dysfunction or reduced cardiac output or cardiac index should be considered as a possible etiology, including heart failure, myocarditis, hypertrophic cardiomyopathy, or valvular heart disease (1,3).

The incidence of CS due to valvular heart disease is increasing (4), and valvular emergencies, such as valvular thrombosis, are currently a major cause of this complication. Nevertheless, their clinical presentation and initial diagnostic tests are often nonspecific, resulting in delayed diagnosis. Therefore, identifying these complications requires high clinical suspicion, a thorough physical examination, and early and comprehensive use of imaging studies such as transthoracic echocardiography and point-of-care ultrasound (5).

Regardless of the option chosen, the management of mechanical prosthetic valve thrombosis (PVT) carries a high risk. For example, patients with fibrinolysis may experience bleeding, systemic embolism, and recurrent thrombosis (6). As a result, treatment is complex and depends on many factors (e.g., valve position, severity of the complication, and adherence to anticoagulant therapy) and remains controversial given the lack of prospective data and randomized clinical trials on its benefits (7).

The following is the case of a female patient with mitral and tricuspid valve disease who was a recipient of a mechanical mitral prosthetic heart valve and had a history of cardiac PVT managed with fibrinolysis. She required surgery to treat a second episode of PVT.

CASE PRESENTATION

A 28-year-old female patient with systemic lupus erythematosus and mitral and tricuspid valve disease secondary to rheumatic fever that occurred at the age of 5 years required mitral valve replacement with a mechanical prosthetic heart valve and anticoagulation therapy with warfarin.

Importantly, in 2020, the patient visited the emergency department of a tertiary care center in Bogotá, Colombia, due to dyspnea and chest pain caused by valvular thrombosis, possibly related to poor adherence to anticoagulation treatment with warfarin. On that occasion, a transthoracic echocardiogram was performed upon admission, revealing mechanical mitral valve thrombosis (thrombus measuring 2x2.40 cm in diameter) and high transvalvular pressure gradients, suggesting acute prosthesis dysfunction.

Given the findings, 11 hours after admission, controlled thrombolysis was initiated by slow infusion of alteplase (25mg administered intravenously over 25 hours, without bolus), followed by treatment with unfractionated heparin (70IU/kg bolus, followed by 16units/kg/hour continuous infusion). The patient was treated with noninvasive mechanical ventilation and vasopressor support, with subsequent resolution of mechanical valve dysfunction without the need for surgical intervention. Anticoagulation therapy with warfarin (20mg) was restarted at full dose for one week, and home hospitalization was recommended to begin cardiac rehabilitation and monitor the international normalized ratio (INR). During follow-up, it was determined that it was not possible to achieve the results expected for the INR due to interaction with other medications prescribed at that time to control a psychiatric illness that had been diagnosed. Upon discharge from hospital, it was decided to continue anticoagulant treatment with enoxaparin 1mg/kg every 12 hours only, a regimen that the patient maintained until the second PVT event occurred.

In 2023, the patient returned to the emergency department of the same institution due to oppressive chest pain, progressive dyspnea, and headache occurring over the previous 12 days. On admission, it was found that the patient had tachycardia (120bpm), mild hypoxemia (92% with FiO_2 at 28%), and normal blood pressure. No abnormal findings were observed during cardiopulmonary auscultation. The emergency department requested an electrocardiogram, which showed an S1Q3T3 pattern (McGinn-White sign), as well as laboratory tests that showed a subtherapeutic INR (value of 1.0), leading to the suspicion of pulmonary

embolism. Based on the findings, a CT angiography of the chest was performed on the same day of admission, ruling out the diagnosis of pulmonary embolism and incidentally identifying pulmonary edema.

Seven hours after admission, the patient's condition progressively deteriorated, with increased respiratory distress, hypotension (blood pressure of 79/57 mmHg), cool peripheries, and prolonged capillary refill. Since all this suggested CS associated with pulmonary edema, she was transferred to the resuscitation room where she underwent invasive mechanical ventilation and was given vasopressin (3IU/h intravenously) and norepinephrine (0.5mcg/kg/min intravenously).

Given her clinical deterioration, two hours after admission to the intensive care unit, a point-of-care focused cardiac ultrasound was performed, showing a mechanical mitral valve prosthesis with limited leaflet opening (Figure 1) and color Doppler evaluation indicating prosthetic valve dysfunction (Figure 2). This, combined with hemodynamic findings suggesting significant prosthesis stenosis (mean gradient: 19 mmHg, maximum velocity [Vmax]: 2.7 m/s, MV VTI to LVOT VTI ratio: 5.9) (Figure 3), allowed us to establish that the patient was experiencing a new PVT episode.

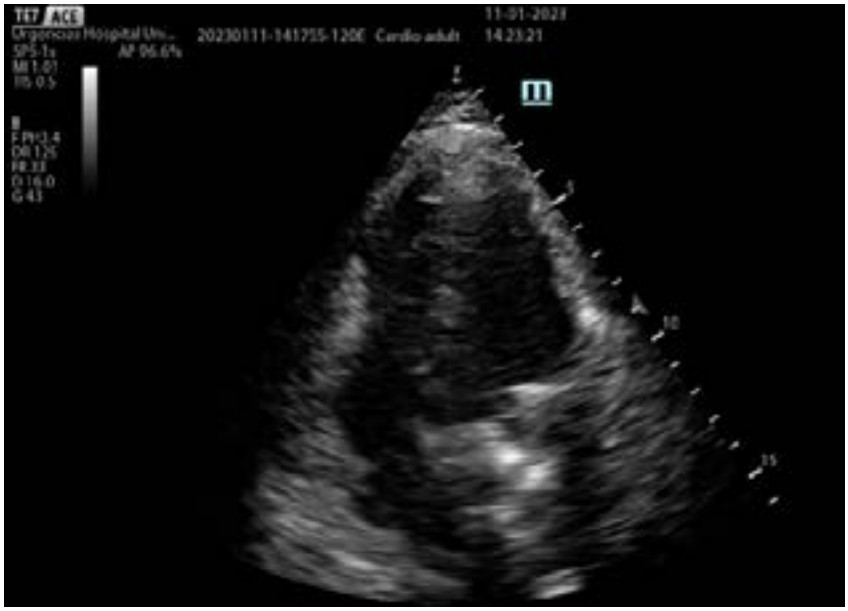

Figure 1. Point-of-care focused cardiac ultrasound showing limited opening of the mechanical mitral valve prosthesis leaflets.

Source: Image obtained while conducting the study.

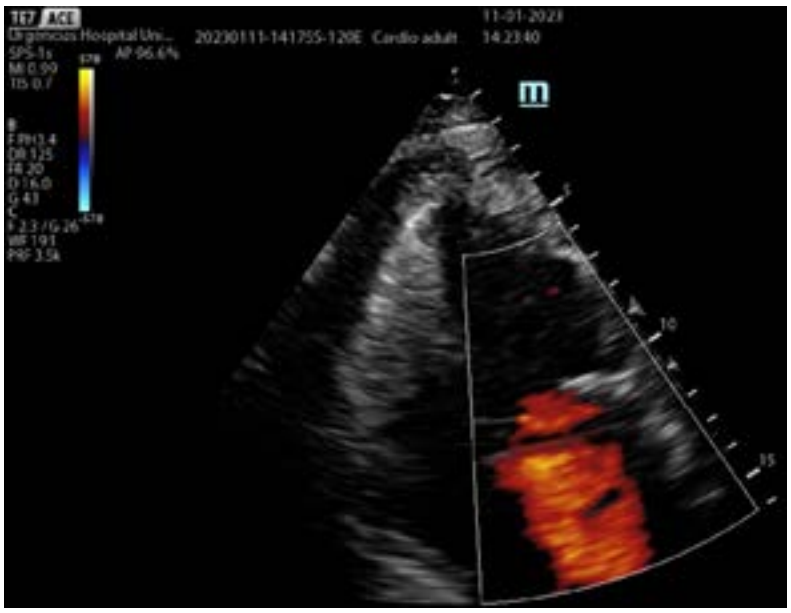

Figure 2. Point-of-care focused cardiac ultrasound in color Doppler mode showing periprosthetic regurgitation.

Source: Image obtained while conducting the study.

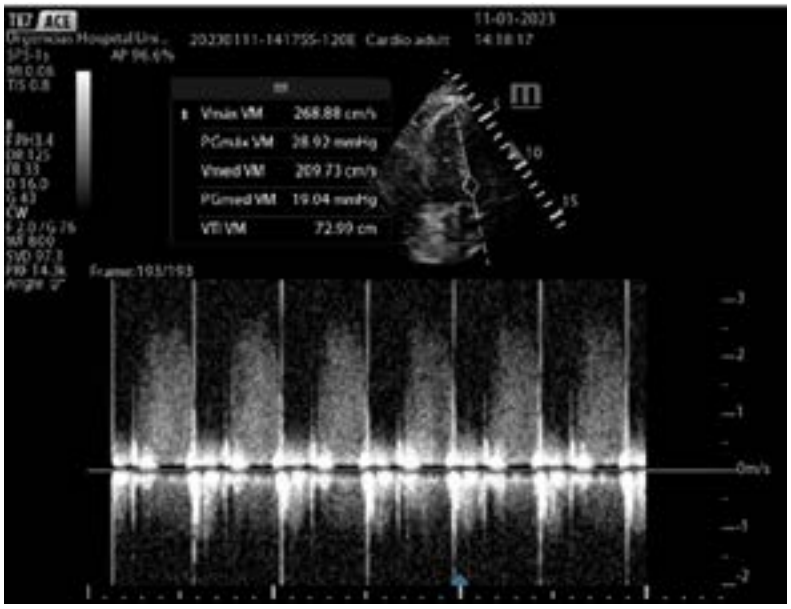

Figure 3. Point-of-care focused cardiac ultrasound showing prosthetic valve stenosis due to altered mean gradient.

Source: Image obtained while conducting the study.

Given the context of CS of valvular etiology (classified as stage D according to the Society for Cardiovascular Angiography and Interventions classification) (8) and in view of the high surgical risk, it was decided to implement once again a controlled thrombolysis protocol involving a slow infusion of 25mg of alteplase intravenously over 25 hours. The patient was transferred to the intensive care unit (ICU) 11 hours after admission, where she continued thrombolysis treatment with alteplase and received invasive mechanical ventilation and dual vasopressor support.

However, her condition did not improve and hemodynamic instability persisted, so after spending 8 hours in the ICU, it was decided to perform surgery to clean the prosthetic mitral heart valve, achieving adequate movement of the leaflets. During the procedure, the patient developed coagulopathy, ventricular dysfunction, pulmonary dysfunction, and pump failure, requiring massive transfusion and extracorporeal membrane oxygenation (ECMO) support upon her return to the ICU.

The patient progressed satisfactorily and tolerated the removal of the mediastinal packing and ECMO system. She was transferred from the ICU to a general ward after 10 days and was discharged 26 days after admission with resolution of the CS.

DISCUSSION

CS is a hemodynamically complex syndrome characterized by low cardiac output that often culminates in multiple organ failure and death, with a short-term mortality rate >40%. The main causes of CS include valvular dysfunction, myocardial dysfunction, and arrhythmia (9).

Given the diversity of manifestations, overlap with other shock states, poorly understood pathophysiology, complex and multifactorial causes, and varied hemodynamic parameters, CS can be difficult to identify in the emergency department (1). However, diagnosis can be supported by physical examination, electrocardiogram, laboratory tests, and, when available, point-of-care ultrasound (9), as in the present case.

PVT is more common in mechanical valves than in biological valves, with an annual rate for the former ranging from 0.1% to 5.7% (10). This condition should be suspected in patients with recent dyspnea, chest pain, or embolic events, as well as in patients with CS and acute pulmonary edema (6,10), as in the present case. The most important risk factor for PVT is inadequate anticoagulation or discontinuation of anticoagulation with vitamin K antagonists such as warfarin (10).

Although physical examination may alert physicians to the presence of PVT, diagnostic methods are often required to assess prosthesis function. One of these methods is echocardiogram, in which a high gradient is evidence of limited valve movement (stuck valves), while the presence of thrombi is often associated with valve obstruction, regurgitation, or embolism (11).

The treatment of mechanical PVT involves a high risk. Firstly, fibrinolysis can lead to hemorrhage, systemic embolism, and recurrent thrombosis (6), and, secondly, surgical management can cause, besides embolism or bleeding, non-embolic and non-hemorrhagic complications such as postoperative infection, acute kidney disease, tamponade, prolonged endotracheal intubation, tracheal stenosis, multiple organ failure, and arrhythmias, which can compromise surgical success and increase mortality (7).

In this regard and given the lack of prospective data and randomized clinical trials, PVT treatment remains controversial to date (7). The guidelines for the diagnosis and treatment of valvular heart disease published in 2021 by the European Society of Cardiology (6) recommend considering surgery for the treatment of mechanical PVT when there are large non-obstructive thrombi (>10mm) complicated by embolism or persisting despite optimal anticoagulant therapy, as well as fibrinolytic management in cases in which surgery is not available or involves a high risk, or to treat right-sided prosthetic valve thrombosis. These recommendations are based on an individualized assessment of the risks and benefits for each patient.

Similarly, other studies and guidelines recommend treating left mechanical PVT with slow-infusion low-dose thrombolysis (25mg of alteplase over 6 hours) or emergency surgery (7,10,12). For example, in 2013, Özkan *et al.*, (12) in a prospective study (TROIA trial), compared different thrombolytic therapy regimens (rapid infusion of streptokinase; slow infusion of streptokinase; high-dose infusion of alteplase [100mg]; slow infusion [6 hours] of medium-dose alteplase [50mg]; and slow infusion [6 hours] of low-dose [25 mg] alteplase), finding that slow infusion of low-dose alteplase, without bolus and repeated as needed, had the lowest combined rates of mortality and major non-fatal complications, being the safest and most effective option in patients with PVT (12).

That same year, Karthikeyan *et al.* (13) published a systematic review and meta-analysis of observational studies comparing the efficacy and safety of urgent surgery and fibrinolytic therapy for the treatment of left-sided PVT. They reported that, although urgent surgery was not superior to fibrinolytic therapy in terms of complete restoration of valve function, it substantially reduced the incidence of thromboembolism (1.6% vs. 16%), major bleeding (1.4% vs. 5%), and recurrent PVT (7.1% vs. 25.4%).

In 2015, Özkan *et al.* (14), in a study evaluating the efficacy and safety of ultra-slow infusion of low-dose alteplase (25mg over 25 hours) for the management of PVT (PROMETEE trial), reported a success rate for this regimen of 90% and a complication rate of 6.7%, of which 3.3% were major non-fatal complications, 2.5% were minor, and 0.8% were fatal.

More recently, in 2022, Özkan *et al.* (7) conducted a prospective study comparing thrombolysis with low-dose alteplase (25 mg) administered by slow infusion (6 hours) or ultra-slow infusion (25 hours) with surgical management in

patients with mechanical PVT and reported that the success rate in the thrombolysis group was 90.4% with a mean dose of alteplase of 59mg (IQR: 37.5-100mg). The rates of minor complications, major complications, and mortality were significantly higher in the surgery group: 38.7% vs. 8.4%, 41.3% vs. 6.0%, and 18.7% vs. 2.4%, respectively. These findings suggest that thrombolysis with low-dose alteplase, administered by slow or ultra-slow infusion, may be an effective and safe therapeutic strategy in patients with mechanical PVT.

Even though, as noted in the preceding paragraphs, the evidence suggests good clinical outcomes with the use of slow or ultra-slow alteplase infusion protocols in PVT settings, the patient in this report experienced different outcomes during both episodes, requiring surgical support in the latter. Therefore, deciding which treatment to choose for PVT (medication versus surgery) should be based on each patient's clinical situation and its progression.

CONCLUSION

CS as a complication of PVT is a major cause of morbidity and mortality, so timely and specific etiological diagnosis of this condition is of great importance. Point-of-care focused cardiac ultrasound is an extremely useful tool in the emergency department because, together with high clinical suspicion and a thorough physical examination, it facilitates its identification. Concerning treatment, thrombolysis has been reported to have better outcomes in terms of safety and efficacy than surgery. However, thrombolytic treatment of choice, optimal dose, and standard infusion time still need to be established, as well as the time to consider initial surgical management to reduce morbidity and mortality.

Therefore, PVT constitutes a challenge for the treating medical team due to the lack of standardization in its management, so individualization for each case remains essential to determine the most appropriate treatment.

ETHICAL CONSIDERATIONS

This case report was prepared upon authorization from the patient, who signed the informed consent form at the Hospital Universitario San Ignacio, and with the approval of the clinical ethics committee of the same institution.

CONFLICTS OF INTEREST

None stated by the authors.

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