Acute Heart Failure Without Prior History of Myocardial Dysfunction

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Clinical Presentation

M.C.O.M., female, 62 years old, admitted in the emergency room with sudden and progressive onset of dyspnea for about an hour before admission. Refers rheumatoid arthritis and upper airways infection (UAI) for about a week. On examination, the patient was tachycardic, tachypneic, and hypotensive (96 × 60 mmHg), presenting jugular venous distention and plethora in the face, neck, and upper chest. Cardiac auscultation showed hypophonic sounds.

Diagnosis, Assessment, and Treatment

The patient was intubated in the emergency room, being placed on mechanical ventilation and initiated continuous infusion of noradrenaline (0.2 mcg/kg/min). Electrocardiogram (ECG)

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at admission showed atrial fibrillation (AF) and arterial blood gas values for PCO_2, 54 mmHg; pH, 6.58; PO_2, 52 mmHg; HCO_3, 9.9 mEq/L; and SO_2, 54%. Still had WBC, 14,350/mm^3; band cells, 4%; platelet, 130,000/mm^3; C-reactive protein (CRP), 1.07 mg/dL (Reference Value – RV, 0.5 mg/dL); troponin, 0.846 ng/ml (RV < 0.016); and CK mass, 17.9 ng/mL (RV < 3.4).

Transthoracic echocardiogram showed severe left ventricular dysfunction and mild to moderate pericardial effusion with the collapse of the right ventricle. The patient was subjected to pericardiocentesis with removal of a small amount of liquid (130 ml) and transferred to intensive care unit (ICU), where a catheter was inserted for invasive hemodynamic monitoring (Swan-Ganz) in the left subclavian vein and continuous blood pressure (BP) in MSE.

Another echocardiogram showed severe biventricular dysfunction (EF 15%) (Fig. 1, ECO transthoracic). A progressive increase of noradrenaline (01 mcg/kg/min), associated with dobutamine (08 mcg/kg/min) and vasopressin (0.04 U/min), was necessary. Held chemical cardioversion of AF with amiodarone and electrical cardioversion. Intra-aortic balloon was installed without significant improvement in hemodynamic

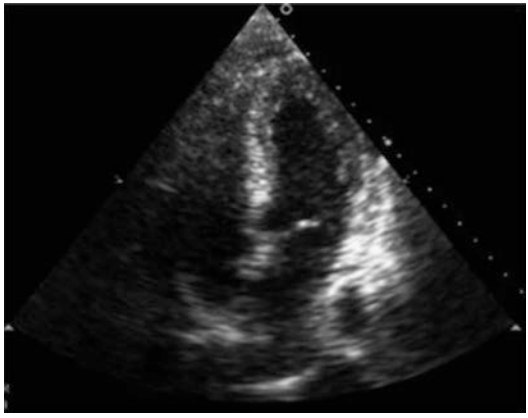

Figure 1 ECO transthoracic (EF, 15%)

condition. Arterial blood gas analysis showed severe respiratory acidosis with pH, 7.2 (RV = 7,35–7,45); blood lactate, 28 mg/dL (RV = 4,5–14,4 mg/dL); PCO_2, 58 mmHg (RV = 35–45 mmHg); PO_2, 68 mmHg (RV = 80–100 mmHg); HCO_{3-}, 29 mmHg (RV = 22–36 mmHg); SpO_2, 83% (RV = 95–100%); SVO_2, 65% (RV = 68–77%).

Considering the refractory cardiogenic shock and clinical progression with multiple organ failure, it was decided by the installation of circulatory assist device – extracorporeal membrane oxygenation (ECMO) in venoarterial mode with right femoral vein (23F Maquet cannula) and femoral artery (17F Maquet cannula) cannulation by the Seldinger technique. Patient progressed after 6 h of ECMO installation with hemodynamic improvement, being possible to reduce vasoactive amines (noradrenaline, 0.5 mcg/kg/min; dobutamine, 8 mcg/kg/min; vasopressin, 0.02 U/min) and improvement of metabolic acidosis, with blood gas pH, 7.3; PO_2, 105 mmHg; PCO_2, 45 mmHg; HCO_3, 20 mEq/L; and SpO_2, 94%. Echocardiogram after installation of ECMO showed moderate decompression of the heart chambers but maintenance of biventricular dysfunction (ejection fraction, 15%).

By completing 24 h of circulatory assistance, continuous infusion of heparin (10 U/kg/h) was started. Patient presented bleeding puncture and melena, and endoscopy showed gastric ulcer. After 48 h of circulatory assistance, she returned to present AF, despite of the continued use of amiodarone and multiple electrical cardioversion, requiring increased vasoactive amines. There was the need for blood transfusions with packed red blood cells (04 IU) and platelets (15 IU). Another echocardiography showed biventricular asystole and strain of the cardiac chambers. Exams on the second day of circulatory support showed arterial gasometry – pH, 7.38 (RV = 7,35–7,45); pCO_2, 58 mmHg (RV = 35–45 mmHg); PO_2, 71 mmHg (RV = 80–100 mmHg);HCO_3, 34 mEq/L (RV = 22–26 mEq/L); SpO_2, 94% (RV = 95–100%); SVO_2, 77% (RV = 68–77%); WBC,12,000/mm^3 (RV = 5.000–10.000/mm^3); band cells, 10% (RV = 2–6%); platelet, 74.000/mm^3 (RV = 150–400/mm^3); PCR, 144 mg/dL (RV = 0,4–0,5 mg/dL); troponin, 0.705 ng/ml (RV = < 0,030 ng/mL); CK mass, 2.10 ng/ml (RV = < 4,94 ng/mL); fibrinogen, 230

mg/dL (RV = 150–370 mg/dL); Hb, 10,6g/dL (RV = 12–16 g/dL); Ht, 32% (RV = 35 a 45%); lactate, 25 mg/dL (RV = 4,5-19,8 mg/dL); albumin, 3.5 g/dl (RV = 3,5 a 5,2 g/dL); urea, 81 mg/dL (RV = 16–40 mg/dL); creatinine, 0.98 mg/dL (RV = 0,6–1,2 mg/dL); and Na+, 150 mmol/L (RV = 135–145 mmol/L); K+, 3.5 mmol/L (RV = 3,5–5,5 mmol/L). Research for rheumatic disease and autoimmune were negative: CH50 < 60 U/CAE (RV = 60–144 U/CAE); C3, 35 mg/dL (RV = 84–193 mg/dL); C4, 9 mg/dL (RV = 16–47 mg/dL); negative anti-CCP; anti-DNA < 1.0 U/mL (RV = < 68, 6 U/mL); FAN, nonreactive (RV = nonreactive); ANCA C and P, nonreactive (RV = nonreactive); and FR, < 9.3 UI/mL (RV = < 14,0 UI/mL).

Hemodynamic instability, due to the persistence of atrial arrhythmia (atrial fibrillation), is not responsive to electrical cardioversion therapy coupled with the strain of the cardiac chambers and reduced urine output with increased slag, determining the replacement of ECMO to paracorporeal biventricular circulatory support device (CentriMag). The procedure was performed in the operating room under general anesthesia by median thoracotomy and extracorporeal circulate. Two drainage cannulas were installed, one in the right atrium and the other in the left atrium, the last positioned in the left ventricle under the guidance of transesophageal echocardiography. Two return cannulas were installed in the main pulmonary artery and the ascending aorta (Fig. 2).

Upon returning to the ICU, the patient developed hemodynamic instability in the early hours of biventricular assistance, managing to restart weaning amines 24 h after installation of the devices, and maintained only dobutamine (8 mcg/kg/min). There was improvement in urine output due to the diuretic stimulus. Patient needed another transfusion (CH, 03 IU) due to the worsening of the white blood cell count (23,200 with 19% rods), and Vancomycin was started. Sedation was suspended to assess the level of consciousness. As the service protocol, daily echocardiography was performed to evaluate ventricular function, which showed progressive improvement. Patient maintained minor bleeding through mediastinal drain and puncture sites, and anticoagulation control was done by tempo de coagulação ativado activated coagulation time

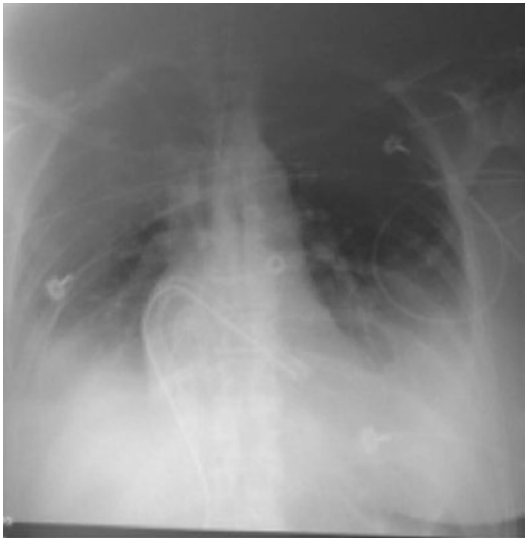

Figure 2 XR after installation of biventricular CentriMag

(ACT) every 2 h (within the range therapy). There was the need for blood transfusion. Considering the positive accumulation of fluid balance, dialysis was started from the fifth day of circulatory support with good tolerance.

By completing 9 days of circulatory assistance, there was full recovery of biventricular function (CentriMag Biventricular®), being decided by the weaning and explantation of the devices. Procedure was performed in the operating room under general anesthesia. In the ICU, tracheostomy was done to facilitate weaning, which was achieved 13 days after explantation of the devices.

She was discharged from ICU 31 days after explant of circulatory assist devices.

Questions

1. How is the cardiogenic shock diagnosis done?

According to the 2016 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure, cardiogenic

shock (CS) is characterized by marked persistent (>30 min) hypotension with signs of hypoperfusion, blood pressure (BP) <90 mmHg, decrease in cardiac index < 2.2 L/min/m^2, and elevated ventricular filling pressure (pulmonary capillary wedge pressure > 18 mmHg/central venous pressure > 20 mmHg). Other markers of metabolic and invasive hemodynamic monitoring in CS are also mentioned, such as systemic vascular resistance > 2000 dines/s/cm^3/m^2 and increased arteriovenous difference of O_2 > 5.5 ml/dl. The identification of the shock etiology is crucial in order to establish the appropriate treatment and the consequent hemodynamic stabilization and/or reversal of dysfunction.

2. What is the best treatment choice for the cardiogenic shock?

For the patient with suspected cardiogenic shock, the initial workup includes chest X-ray, electrocardiogram, and echocardiogram.

The pharmacological management is the use of inotropic and vasopressor agents. There is a constant monitoring of hemodynamic perfusion. In this case, the pulmonary artery catheterism should be considered. Dobutamine is the most constant inotropic. Norepinephrine is an important vasopressor. The use of intra-aortic balloon, although questionable, as the latest guideline of heart failure of the European Society of Cardiology (ESC 2016) and other publications, can be used, especially if there are no more effective devices. However, often the use of circulatory assist devices should be considered when there is not an adequate response [1].

3. What is myocarditis?

Myocarditis corresponds to the inflammation of the heart muscle due to exposure to external antigens such as viruses, bacteria, parasites, drugs, or internal trigger such as autoimmune activation against autoantigens. This inflammation is also associated with any form of injury to the heart, including ischemia, by mechanical trauma and genetic conditions.

The pathological diagnosis according to the Dallas criteria calls for the presence of inflammatory cells simultane-

ously with myocyte necrosis in the same microscopic preparation. However, the criteria have become very criticized for being too narrow and difficult to apply. Thus, myocarditis became an exclusion diagnosis. The own diagnostic definition has become broader, including the presence of viral genome or molecular markers of immune activation, in agreement with the advent of new techniques of molecular diagnosis.

This existing failure in accurate diagnosis or the failure to detect subclinical cases is reflected in the difficult affirmation of the true incidence of myocarditis, always depending on the inclusion and applied diagnostic criteria. In young adults who had sudden death, it was suggested a higher incidence of myocarditis up to 8.6%. This shows that myocarditis is not clinically suspected, leading to death or severe heart failure [5].

4. What is the pathophysiology of viral myocarditis?

According to the 2013 Brazilian guidelines on myocarditis and pericarditis, the pathophysiology of viral myocarditis can be divided into acute, subacute, and chronic phases.

The acute phase is characterized by the presence of viremia. The virus reaches the myocardium through hematogenous or lymphatic dissemination. There is loss of myocytes by necrosis due to direct action of the virus, cytotoxic effects of inflammatory mediators, and oxidative stress products associated with endothelial dysfunction and ischemia. The direct action occurs by the entry of the virus into the cell, through membrane receptors such as CAR (coxsackie-adenovirus receptor) and cytoplasmic and nuclear injuries. As the viral aggression progress, there is an activation of a mechanism from the immune system with important inflammatory infiltrate with natural killer cells and macrophages. The production of cytokines (interleukin 1 and 2, interferon γ and tumor necrosis factor) is part of this inflammatory response, which can damage myocytes depending on the time and exposure levels of these cells.

The subacute phase starts from the 4th day of inoculation and extends until the 14th day. The T lymphocyte infiltrate

continues in myocardial invasion, peaking 7–14 days after viral inoculation. In this phase occurs the main myocardial cell damage. There is also B lymphocytes infiltration, and the proportion increases gradually during the first to the third month. The humoral immune response has an important role in myocardial injury and dysfunction. The direct or indirect myocyte injury releases myosin into the circulation, and the presence of this protein promotes the release of antibodies against the myosin heavy chain and stimulates CD4 + T lymphocytes, which can perpetuate and amplify the lesion of cardiac cells. This amplification stimulated by CD4 T lymphocytes occurs by stimulating B lymphocytes in the production of anti-myosin antibodies and by stimulating the cytotoxic presence of CD8 T lymphocytes. Cross-reaction of antibodies between viral antigens and myocardial cells also provides damage to myocytes.

The third phase begins on the 15th day and continues until the 90th day after viral inoculation and is characterized by the intense deposition of collagen in the myocardial interstitium with myocardial fibrosis evolving to dilation, dysfunction, and heart failure.

5. What are the indications for mechanical circulatory support in cardiogenic shock?

According to the Guideline of Mechanical Circulatory Assistance from the Brazilian Society of Cardiology (2016), the following considered indications for implantation of mechanical circulatory assist devices (MCAD) in cardiogenic shock, in the context of acute insult: post-acute myocardial infarction cardiogenic shock, acute fulminant myocarditis, peripartum, exogenous intoxication, Takotsubo, postcardiotomy, cardiac allograft dysfunction, right ventricular dysfunction post-implant of left MCAD, acute heart valve disease, pulmonary embolism, and sepsis.

In the case of cardiogenic shock in acute chronic patients, the following are considered indications for implantation of mechanical circulatory assist devices (MCAD): chronic cardiomyopathy with indication for heart transplantation, eligi-

ble cardiomyopathies for long-term devices, and congenital cardiopathies.

According to the Guidelines of the European Society of Cardiology – ESC 2016 – the use of mechanical circulatory support, including heart percutaneous support equipment, extracorporeal life support (ECLS), and extracorporeal membrane oxygenation (ECMO), attends in life support of patients with left ventricular or biventricular failure, until heart and other organ functions return. The use of this equipment is restricted to a few days and weeks. The score of survival after venoarterial ECMO use can help in predicting survival in patients receiving ECMO to contain refractory cardiogenic shock.

The ECLS and ECMO can be used as a bridge to decision in patients with acute and rapid deterioration in heart failure or cardiogenic shock, serving for hemodynamic stabilization and clinical evaluation for possible heart transplant procedure or a more durable mechanical circulatory support.

Regarding the guidelines from the International Society for Heart and Lung Transplantation (2013), the extended use of mechanical circulatory assistance (MCS) in patients with acute cardiogenic shock is indicated as these evidence levels:

- Evidence level B, inotropic dependent patients, representing a high mortality group even in continuous medical treatment.
- Evidence Level C, patients with ventricular function considered unrecoverable, patients with hemodynamics and vital organ function maintenance difficulties, patients with a significant capacity for recovery quality of life and organ dysfunction, and patients with irreversible organ damage.
- Evidence level C, patients with end-stage systolic heart failure, being necessary to calculate the risk and cardiopulmonary stress test.
- Evidence level C, heart failure patients at high risk of death for a year, using prognostic models, with indication for heart transplantation or MCS, as a bridge to transplantation or destination therapy.

6. How to manage a patient in use of mechanical circulatory support?

According to the Guideline of Mechanical Circulatory Assistance from the Brazilian Society of Cardiology (2016), the following actions should be taken during mechanical circulatory support:

- Monitoring of the perfusion status through continuous cardiac monitoring, pulse oximetry, invasive measurements of blood pressure, central venous pressure, and diuresis control.
- Monitoring of renal and liver function, tissue perfusion (lactate), and venous oxygen saturation index measures should be made by laboratory tests.
- Routine inspection (every 6 h) of the whole circuit with special attention to the puncture site and membrane oxygenation, measuring the drainage pressures before and after the membrane.
- Strict gasometric control, from the patient and from the circuit (pre and post membrane).
- Blood pressure control, arrhythmias, and collateral effects by use of vasoactive drugs.
- Monitoring of coagulation tests by measuring the activated partial thromboplastin time (APTT) every 6 h or thromboelastogram daily with adjustment of the heparin infusion dose and replacement of clotting factors, primarily platelets (preventing reduction to less than 60,000/mm^3).
- Hematimetric control with maintenance of hemoglobin levels above 12 mg/dL.
- Chest X-ray and daily transthoracic echocardiography, with evaluation of the positioning of the cannulas, decompression of the heart chambers, the opening of the aortic valve, myocardial contractility, and measures of the filling pressure (PASP and PVC).

The levels of renal dysfunction are high mortality factors after mechanical circulatory support implantation, as well as hepatic dysfunction. Elevated bilirubin, INR and

transaminases, ascites presence and hepatic encephalopathy, hypoalbuminemia, Model for End-Stage Liver Disease (MELD), and Child-Pugh high scores are the main hepatic alterations related with this worse prognosis.

7. What are the criteria for weaning and explant of circulatory assistance device?

According to the Guideline of Mechanical Circulatory Assistance from the Brazilian Society of Cardiology (2016) the explant or MCAD weaning should occur under the following conditions: when in minimal assistance condition (flows from 1.5 to 1.0 L/min) check the opening of the aortic valve associated with improved left ventricular function (LVEF 40–45%), cardiac chambers decrease and maintenance of adequate hemodynamic parameters.

In cases of severe complications related to the device, such as bleeding and hemolytic, thrombotic and embolic complications, it's indicated the explant [2].

8. What are the main complications in circulatory assistance?

The main complications of circulatory assistance involve problems arising from the need for continuous anticoagulation, mainly bleeding in puncture and digestive sites, as well as pericardial effusion and infection.

Hemorrhagic complications should be promptly evaluated with the objective of reversing the effects of anticoagulants and antiplatelet agents and exploration for bleeding, if necessary.

Hemolysis is associated with negative pressure elevations in the venous line, persistent maintenance of high blood flow, or inappropriate choice of drainage and infusion cannulas.

Thrombus formation in the circuit and embolic events are mainly caused by the difficulty of modulating the necessary coagulation target.

The increase in complications after mechanical circulatory assist devices (MCAD) implant is directly related to assistance time. In this way we should take into consideration the migration to other devices or assistance mode whenever there are signal of inappropriate response to therapy.

Review About the Addressed Disease or Treatment

Heart failure (HF) represents the common pathway of most heart diseases, being a growing epidemic problem. As for definition, Ponikowski et al. [1] characterize HF as an abnormality of cardiac function or structure that progresses to failure in the delivery of commensurate levels of oxygen and are determinants for tissue metabolic needs. In addition, there are hemodynamic changes involving inadequate cardiac output responses and elevated pulmonary and systemic venous pressures. This reduction in cardiac output contributes to a state of inappropriate tissue perfusion [7].

Another necessary point is the correlation of the diagnosis of HF and the initial symptoms, such as cardiogenic shock (CS), identifying details that may conclude in the diagnostic description. The CS relates to the inability of the cardiac muscle to provide adequate output to the needs of the organism, which generates signs and symptoms of low cardiac output associated with degrees of pulmonary congestion. Persistence of the shock frame results in the onset and worsening of hypoxia, with accumulation of metabolites, acidosis, and endothelial and cellular damage. As a consequence, there are interferences on inotropism and/or cardiac chronotropism, which decreases cardiac work, contributing to the onset of arrhythmias, inflammation, and myocardial ischemia, among other complications [6].

All this dysfunction of the heart muscle may also be associated with the so-called myocarditis, which indicates the classic paradigm of cardiac injury: the pathogenesis of myocarditis followed by an inflammatory immune response of the host, such as cardiac inflammation. The consequences of this intense immune response, as in the case of viral myocarditis, may be dilated cardiomyopathy and acute heart failure with refractory cardiogenic shock.

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