A 51-year old female patient presented with precordial pain and dyspnea at moderate exertion, being diagnosed with severe aortic stenosis, with indication for surgical treatment.

The patient had arterial hypertension, mixed dyslipidemia, was a smoker and had systemic lupus erythematous, which initiated at the age of 16, as well as nephritis. She reported anemia and seizures, which were attributed to lupus. In the past months, she had presented with pleuritic precordial pain, which became worse in the decubitus position and improved at the sitting position, which was attributed to pericarditis.

The physical examination (25/10/2011) revealed the patient had good general status, was hydrated, eupneic, with 60 bpm heart rate, and 110 x 70 mmHg blood pressure. Pulmonary auscultation was normal, and cardiac auscultation revealed rhythmic sounds, hypophonesis of the aortic component of the second sound and systolic murmur ++++/6+. The abdominal examination was normal, with no edema, and wrists were symmetric.

ECG (31/10/2011) revealed sinus rhythm, 48 bpm heart rate, 200 ms PR interval, 113 ms QRS duration, 464 ms QT, disorder in the intraventricular conduction of the stimulus, and rate, 200 ms PR interval, 113 ms QRS duration, 464 ms QT, changes in ventricular repolarization (Figure 1).

Laboratory examinations (24/10/2011) revealed; hemoglobin, 7 g/dL; hematocrit level, 21%; MCV, 95 fL; leukocytes, 6,940/mm³; urea, 62 mg/dL; creatinine, 1.21 mg/dL (glomerular filtration, 50 mL/min/1.73 m²); AST, 36 UI/L; ALT, 42 UI/L; calcium, 4.3 mEq/L; magnesium, 2.30 mEq/L; total protein, 7.4 g/dL; lactate dehydrogenase, 447 U/L; sodium, 138 mEq/L; and triglycerides, 378 mg/dL.

The symptoms of delirium and pulmonary congestion. Antibiotic therapy was initiated with tazobactam and, two days later, vancomycin was added.

Decreasing doses of vasoactive drugs were necessary to control hypotension, and examinations on the third post-operative day (26/11/2011) showed hemoglobin levels at 7.2 g/dL; hematocrit, 23%; leukocytes, 13,900/mm³, with 92% of neutrophils, 122,000/mm³ of platelets, urea of 71 mg/dL, creatinine of 1.4 mg/dL, sodium of 143 mEq/L, and potassium of 3 mEq/L.

The patient was delusional and with pulmonary congestion. Antibiotic therapy was initiated with tazobactam and piperacillin, and, two days later, vancomycin was added. The symptoms of delirium and pulmonary congestion improved, and she was discharged from cardiac recovery on the seventh post-operative day.

Hemocultures and urocultures were negative (29/11/2011). ECG (30/11/2011) revealed sinus rhythm and inactive septal area (Figure 2).

A new laboratory evaluation (5/12/2011) revealed hemoglobin levels at 8.8 g/dL; hematocrits, 28%; leukocytes, 9,240/mm³; platelets, 34,800/mm³; urea, 50 mg/dL; creatinine, 2.92 mg/dL; sodium, 139 mEq/L; potassium, 3.6 mEq/L; PCR, 97 mg/L.
A new echocardiogram (5/12/2011) revealed aorta of 37 mm, left atrium of 41 mm, right ventricle of 25 mm, septum of 13 mm, left atrium of 41 mm, left ventricle of 53/41, ejection fraction of 35%. There was severe hypertrophy in the left ventricle, apical akinesis of the other walls and atypical movements of the interventricular septum. The prosthesis was normofunctional, with maximal gradient of 19 mmHg and mean gradient of 12 mmHg, and the relationship of velocities of exit path LV/aortic prosthesis was of 0.43.

Uroculture (7/12/2012) was negative.

Laboratory examinations (9/12/2011) revealed: hemoglobin levels at 7.8 g/dL; hematocrit, 25%; MCV, 100 fL; leukocytes, 9,040/mm³ (bands, 1%; segmented, 76%; lymphocytes, 21%; and monocytes, 2%); platelets, 330,000/mm³; urea, 60 mg/dL; creatinine, 2.48 mg/dL (FG = 22 mL/min/1.73 m²); sodium, 138 mEq/L; potassium, 3.8 mEq/L; PCR, 91.5 mg/L; PT (INR), 1.0; and TTPA rel, 1.11.

The patient was discharged with a prescription for hydralazine, carvedilol, furosemide, prednisone, chloroquine, atorvastatin, ferrous sulfate, folic acid, ASA.

The physical examination at hospital discharge showed serous secretion in the scar from the saphenous vein stripping in the left lower limb.
The patient was readmitted on 20/1/2012 (about one month after hospital discharge) due to an infection in the surgery wound from the saphenous vein stripping. Hemocultures were positive for multi sensitive Enterococcus sp, and the patient received intravenous ampicillin for 14 days.

The transesophageal echocardiogram (24/1/2012) revealed aorta of 35 mm, left atrium of 41 mm, right ventricle of 28 mm, septum of 13 mm, posterior wall of 12 mm, left ventricle of 53 mm, and ejection fraction of 35%. The left ventricle was hypertrophic, and presented apical akinesis and diffuse hypokinesis; the aortic prosthes was normofunctional, with no changes, with maximal gradient of 22 mmHg and mean gradient of 12 mmHg. The other valves were normal.

Thoracic tomography (20/1/2012) did not show signs of mediastinitis, osteomyelitis or pneumonia.

The left lower extremity Doppler was negative for deep vein thrombosis (27/1/2012).

The patient was discharged from the hospital on 3/2/2012, and the lower limb infection was considered as healed, and the wound would be healed by second intention. The prescribed medications were: 100 mg ASA, 50 mg carvedilol, 100 mg losartan, 25 mg spironolactone, 20 mg atorvastatin, 20 mg omeprazole, 20 mg prednisone, 400 mg hydroxychloroquine, 5 mg folic acid, 120 mg ferrous sulfate per day.

In a doctor’s appointment (28/3/2012), the patient complained of asthenia, and prednisone increased to 60 mg; the administration of ivermectin was added.

Thoracic radiography (in March, 2012) – Figures 3 and 4 – revealed cardiomegaly ++/4+ and free lungs.

The left lower extremity Doppler was negative for deep vein thrombosis (17/4/2012).

Three months later, she came to the emergency room of the hospital in shock, with 40 bpm heart rate and inaudible pressure, so the use of vasoactive amines and orotracheal intubation were necessary for respiratory support.

Laboratory examinations (on May, 8) revealed: erythrocytes, 1,900,000/mm³; blood cell count, 5.8 g/dL; hematocrit, 19%; reticulocyte, 12.1%; MCV, 100 fl.; leukocytes, 12,500/mm³ (bands, 15%; segmented, 79%; lymphocytes, 5%; monocytes, 1%); sodium, 139 mEq/L; potassium, 4.5 mEq/L; calcium, 4 mEq/L; ionized calcium, 1.16; magnesium, 1.8 mEq/L; arterial lactate, 14 mg/dL; PT (INR) 1; TTPA (rel) 0.76; ALT, 57 U/L; AST, 26 U/L; gamma-GT, 153 U/L; lactate dehydrogenase, 560 U/L; total bilirubin, 0.35 mg/dL; right bilirubin, 0.10 mg/dL; urine l, normal. Arterial gasometry showed: pH, 7.46; CO₂, 32 mmHg; O₂, 104 mmHg; O₂ saturation, 97.5%; bicarbonate, 22.2 mEq/L; and base excess (-) 1.1 mEq/L.

Echocardiogram (8/5/2012) showed aorta of 37 mm, left atrium of 43 mm, septum of 13 mm, posterior wall of 11 mm, left ventricle of 51/39 mm, ejection fraction of 50%, and moderate hypertrophy of the left ventricle and apical akinesis. The aortic graft presented thickened leaflets, minimum central regurgitation, and maximal transvalvular gradient was 58 mm Hg, mean gradient was 39 mm Hg; the other valves were normal.

Some hours later, the patient presented cardiac arrest caused by ventricular fibrillation. After recovery, there were three more cardiac arrests with pulseless electrical activity, which were reversed. Afterwards, there was a new cardiac arrest with irreversible pulseless electrical activity, and the patient passed away (8/5/2012).

Clinical aspects

The clinical case reports a 51-year old patient with systemic lupus erythematosus, arterial hypertension and mixed dyslipidemia, who went to the emergency room with fever and in shock.

The systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease, which is characterized by the immune complex deposition in the involved organs, including the heart. Its clinical picture is determined by periods of exacerbations and remission, with variable clinical course and prognosis.

Even though kidneys are classically the organs that are mostly affected by SLE, the heart and the heart/lung circulation can also be significantly affected. This disease can have an impact on the heart by means of several manifestations, which include arrhythmia and conduction disorders, pericardopathies, myocardopathies and coronariopathy.

These manifestations can be simultaneous and should be rapidly recognized in order to establish the proper immunosuppression combined with specific cardiology therapy. The clinical recognition of cardiovascular aggression can be difficult due to the common existence of multiple clinical problems in patients with lupus, such as infections and renal insufficiency.

The pathogenesis of the heart disease in systemic lupus erythematosus is not clear yet. The model that is traditionally considered for the pathogenesis of lupus carditis is very similar to that of other sites affected by lupus, so it is believed that the immune complex deposition and the activation of the complement would lead to acute, chronic or recurring inflammation in the vascular endothelium, pericardium, myocardium, endocardium, conduction system and valve leaflets, which can be supported by the common finding of immune complexes, complement and antinuclear antibodies in the affected tissues.

Pericarditis is the most common cardiac manifestation, which is clinically present in up to 25% of the patients. Series of autopsies and imaging methods demonstrated the pericardial involvement in more than 60% of the patients. It can occur as an initial manifestation of SLE, or at any point of the course of the disease, as was the case of the mentioned patient, or it can be a complication from chronic kidney disease.
Figure 3 – Chest x-ray (postero-anterior view)- Metallic sutures in the sternum, normal lungs and enlarged heart image.

Figure 4 – Chest x-ray (lateral view)- Metallic sutures in the sternum, prosthetic valvar ring.
Clinical picture is usually typical, and it can be manifested by fever, tachycardia, substernal pain (which is aggravated by the act of breathing, coughing or bending over), and by the presence of pericardial friction at auscultation; the electrocardiographic evaluation, with peaked T waves and increasing ST segment, usually does not differ from other causes of pericarditis.

Despite the young age presented by most patients with lupus, atherosclerosis remains as the most common cause of ischemic heart disease. In these patients, it is possible to observe the occurrence of accelerated atherosclerosis associated with the presence of its habitual risk factors, which makes this disease an independent risk factor for the cardiovascular disease, as well as rheumatoid arthritis.

It presents coronariopathy prevalence of up to 10%, and eight times more chances in relation to the general population. Some studies suggest that the acute myocardial infarction can be the cause of death in up to 25% of the cases, especially among patients who have had the disease for longer. The risk of this complication can be 52 times higher in relation to the population that is free of disease, when the time of disease evolution is longer than five years.

In the reported case, the patient presented not only SLE, but also other risk factors that contributed with the development of coronary artery disease: systemic arterial hypertension, smoking and mixed dyslipidemia.

Additional causes of acute coronary syndromes in the SLE include thrombosis – usually correlated to the presence of antiphospholipid antibodies –, embolism resulting from nonbacterial vegetative endocarditis (Liebman-Sacks), and coronary arteritis.

The myocardial dysfunction of SLE is usually multifactorial, and it can result from immunological lesion, ischemia, valve disease or coexisting problems, such as systemic arterial hypertension. The clinically evident acute myocarditis is not common, and it can present itself by the presence of thoracic pain and tachycardia, being disproportional to the presence of fever. Clinical signs and symptoms of cardiac insufficiency are uncommon, being present in only 5-10% of the patients.

Arrhythmia and conduction disorders can occur in the course of the disease, usually concomitantly to other cardiac manifestations, such as pericarditis, myocarditis and coronary ischemia.

Sinus tachycardia is the most common manifestation, being present in approximately 50% of the cases. In this case, the patient presented with sinus bradycardia, with prolonged QT interval of 464 ms. The expected corrected QT interval for that patient would be of less than 415 ms. According to Okin et al., the presence of this finding can be a predictive of morbidity and mortality.

Valve involvement is common, being demonstrated in transesophageal studies in more than 50% of the patients with LSE. Valve thickening is the most common echographic finding, followed by vegetation and valve insufficiency. Even though the severity of valve compromise is usually mild and asymptomatic, in this clinical case we observed severe valvular stenosis.

The patient was submitted to myocardial revascularization and valve replacement, in November, 2011, and on the third post-operative day, she presented with a suggestive picture of decompensated heart failure with clinical signs of low cardiac output associated with pulmonary congestion. Clinical measures were taken to compensate the picture, including the use of antibiotics, with clinical progress.

The main differential diagnoses for the clinical picture of the patient were infectious process, myocardial ischemia and lupus myocarditis.

The hypothesis of infection should be considered because the patient was in the post-operative period and had SLE, cardiopathy and nephropathy, and such conditions made her more prone to infections. The absence of fever and negative cultures made this diagnosis less likely.

Another diagnostic hypothesis to be considered in this context is coronary ischemia, since the patient had already had a previous coronary disease. Besides, the electrocardiogram and the echocardiogram presented new segmental changes, septal inactive area, and septal akinesis, respectively. In this case, thromboembolic ischemic events and/or coronary arteritis cannot be ruled out.

It is usually difficult to tell coronary arteritis from accelerated atherosclerosis. In cinecoronariography, arteritis is suggested when we find coronary aneurysms, focal lesions or ones that develop rapidly, which could have been the case of the patient assessed in this clinical case.

Based on the presented case, the factor that apparently triggered the clinical picture of the patient was lupus myocarditis, since the patient presented with new ventricular systolic dysfunction. The improved ventricular function shown in the echocardiogram conducted in May, 2012, seemed to corroborate this diagnosis, after the immunosuppressive therapy began, in the appointment of March, 2012.

The diagnosis of lupus myocarditis is usually difficult, since it normally progresses to mild and little symptomatic myocardial dysfunction, and mainly due to the concomitance of other factors that are potentially responsible for myocardial damage, such as ischemia, anemia, and secondary water retention to renal disease or to the use of corticosteroids.

On 8/5/2012, the patient was in shock and presented with bradycardia. Clinical measures to compensate the clinical picture were initiated, including the use of vasoactive amines and respiratory support. However, the patient had clinical worsening and cardiorespiratory arrest on this same day.

The main differential diagnoses for the final clinical picture were cardiogenic shock, hypovolemic shock and septic shock, to be discussed afterwards.

The hypothesis of cardiogenic shock caused by myocardial ischemia should be considered. This diagnosis is less likely because, in the echocardiogram conducted in May, 2012, no segmental changes were observed. In fact, it was possible to observe improvements in ventricular function, in relation to the echocardiogram performed in January, 2012. This improved cardiac performance can be attributed to the optimized treatment of lupus cardiomyopathy.
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The transesophageal echocardiogram also detected moderate aortic stenosis. Some level of valve dysfunction could also be present in the immediate post-operative period, as a result of the sub-stenosing graft implanted in a patient with a small caliber aorta, which, in this patient, was masked by the moderate ventricular dysfunction that occurred in the post-operative period. Another factor that could justify aortic stenosis would be a thrombotic process, especially if the patient had antiphospholipid antibodies and not under full anticoagulation. Another hypothesis is the one of hypovolemic shock due to hemorrhage. Even though the patient did not present exteriorization of bleeding, we observed important decrease in hemoglobin levels (from 7.8 to 5.8). The high levels of reticulocytes associated with low levels of bilirubin makes the peripheral destruction of erythrocytes less likely as a causative factor for this anemia.

For the presented case, the factor that apparently was the main trigger of the final clinical picture of this patient was infectious, which is corroborated by the increasing count of young neutrophils and by the reported fever, which was mentioned in the beginning of the clinical case. Among all possible focuses for this septic scenario, we cannot rule out the hypothesis of acute infective endocarditis. Infective endocarditis is the infectious process of the cardiac endothelium, which can affect any cardiac structure: septal defects, tendinous cords, mural endocardium and intracavitary and arteriovenous shunts. However, these are the most commonly involved cardiac valves, especially the mitral (40%) and the aortic valve (34%)\textsuperscript{11}.

Currently, for the diagnosis, modified Duke criteria are used, which are based on clinical, laboratory and echocardiographic findings\textsuperscript{11}. The transesophageal echocardiogram became the method of choice to visualize vegetation, especially at the presence of degenerated and calcified valves or mechanical prosthesis. Therefore, in the patient of this clinical case, the absence of vegetation at the transthoracic echocardiogram does not rule out that diagnosis.

In spite of the advancements in clinical diagnosis, of the advent of new antibiotics and the improvement of surgical techniques, bacterial endocarditis still presents high morbimortality, and its prognosis depends on the etiological agent and on cardiac status before the infectious picture\textsuperscript{12} (Dr. Wilma Noia Ribeiro, Dr. Alice Tatsuko Yamada).

**Diagnostic hypotheses**

Syndromic diagnosis: congestive heart failure; etiology: lupus cardiomyopathy; final event: septic shock (Dr. Wilma Noia Ribeiro, Dr. Alice Tatsuko Yamada).

**Necropsy**

The patient had two diseases: atherosclerosis and lupus erythematosus.

Atherosclerosis was mild in the aorta, moderate in the branches of the left coronary, and reaching 70% levels of obstruction in the right coronary artery, therefore being submitted to revascularization with saphenous vein interposition graft. At necropsy, the graft was obstructed in the ostium and fibroed, which means the premature closure after surgery. In spite of that, there was no significant myocardial ischemia injury, only areas of non-abundant myocardial sclerosis, compatible with what usually occurs at the presence of myocardial hypertrophy due to ay cause.

The lupus diagnosis is based on clinical and laboratory data. Under the morphological focus, several aspects can be attributed to the disease, and there is nothing characteristic enough to allow the diagnosis. Therefore, the surgically replaced valve had non-specific chronic valvulitis (Figure 5), which could also have had another cause, such as rheumatic disease, for example.

Necropsy showed the existence of bacterial endocarditis, caused by Gram-positive cocci that affected the aortic valve prosthesis and the ring around it ( Figures 6 and 7), as well as abundant abdominal bleeding, which was the final responsible for the death of the patient.

In other organs, the most relevant finding was segmental and focal glomerulopathy (Dr. Paulo Sampaio Gutierrez).

Main disease: bacterial endocarditis in biological aortic valve prosthesis. Baseline disease: systemic lupus erythematosus with aortic valvulopathy and arterial hypertension. Secondary disease: coronary atherosclerosis. Causa mortis: abdominal hemorrhage (Dr. Paulo Sampaio Gutierrez).

**Comment**

The cause of hemorrhage was not determined: nothing was found in the arterial territory that is normally examined during necropsies; possibly, there could be a downstream lesion, in the circulatory tree. By considering the existence of endocarditis, the main possibility is the occurrence of secondary arteritis (mycotic aneurysm). Another possibility is that the vascular lesion could be iatrogenic, since a catheter passed through that region, but at hospital admission the patient presented aggravation of previous anemia and certain level of abdominal distension.

Segmental and focal glomerulopathy are usually a result of immune complex deposition; in this case, it can be a consequence both of lupus and endocarditis.

Even with necropsy, it was not clear why the patient presented worsened cardiac function after surgery.
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**Figure 5** – Histological cut of native aortic valve removed in surgery. It is possible to observe non-specific chronic valvulitis with calcification points. Hematoxylin and eosin staining method; 5x objective lens.

**Figure 6** – Left ventricular outflow tract and aortic root with aortic valve prosthesis of biological material partially detached. It is possible to observe the presence of inflammatory tissue, both in the prosthesis (blue arrow) and in the ring around it (red arrow). It is also possible to see the occlusion in the ostium of the right aortocoronary saphenous graft (white arrow).
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