Sudden death in infective endocarditis

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ABSTRACT

The case fatality rate of infective endocarditis (IE) is high and is associated with varying causes. Among them, acute myocardial infarction due to an embolism in a coronary artery is rare; the incidence of this complication in the setting of IE is reported to be up to 1.5%. We report a case of sudden death in a 22-year-old woman diagnosed with systemic lupus erythematosus who was referred to the Cardiology Center for the treatment of mitral valve incompetence due to IE. She was hemodynamically stable with antibiotic therapy and vasoactive drugs, despite severe mitral valve regurgitation. Unexpectedly, she presented cardiac arrest and died. The autopsy showed total occlusion of the left main coronary artery by septic embolus, which originated from the mitral vegetation, as the cause of death. Thus, although a rare complication, it should always be kept in mind that a coronary embolism can be a lethal complication of IE, and the possibility of surgical treatment combined with the underlying antibiotic therapy should be raised.

Keywords
Lupus Erythematosus, Systemic; Endocarditis; Heart Arrest; Embolism; Coronary Vessels

CASE REPORT

A 22-year-old female patient was recently diagnosed with systemic lupus erythematosus (SLE). The symptoms were fatigue, malaise, low-grade fever, muscle pain, and arthritis. The laboratorial work-up revealed normocytic anemia, leukopenia with lymphopenia, cylindruria, proteinuria at the nephrotic range, and hematuria; an elevated erythrocyte sedimentation rate; high titers of antinuclear antibody anti-double stranded DNA, and a positive Immunoglobulin G response to anticardiolipin. Soon after the diagnosis, the creatinine determinations rose substantially and rapidly, requiring hospitalization. With the hypothesis of progressive glomerulonephritis, the patient was prescribed a 3-day pulse therapy of methylprednisolone with further creatinine normalization. A renal biopsy was not performed. Over the following weeks she became febrile, and blood cultures disclosed oxacillin sensitive \textit{Staphylococcus aureus} on two separate occasions. A new systolic murmur in the mitral area was heard, and petechiae appeared on the conjunctiva. A transthoracic echocardiogram detected vegetation on the posterior mitral leaflet. The patient's fever subsided, and her general status improved after oxacillin administration. However, 2 weeks later, she...
developed acute pulmonary edema, along with the intensification of the regurgitant murmur in the mitral area. Rupture of the chordae tendineae was suspected, and she was transferred to the cardiology center for surgical evaluation.

On admission, she reported intense fatigue. She was afebrile, with a blood pressure of 100/60 mmHg and a pulse rate of 96 beats per minute. Oximetry was normal at the expense of oxygen supplementation. Neither jugular distention nor peripheral edema was present. The heart auscultation disclosed a loud holosystolic murmur in the mitral area, with axillary irradiation. The pulmonary auscultation demonstrated sparse rales on the pulmonary bases, and peripheral perfusion was slightly diminished. Abdominal examination revealed a slight hepatomegaly but the spleen was not enlarged.

A laboratory work-up disclosed hemoglobin of 8.0 g/dL (reference value [RV]: 12-14 g/dL), leukocytes of 6,900/ mm$^3$ (RV: 4.4-11.3 × 10$^3$/mm$^3$) without a shift to the left, and platelets of 194,000/mm$^3$ (RV: 150-400 × 10$^3$/mm$^3$), creatinine of 1.3 mg/dL (RV: 0.4-1.3 mg/dL), and normal electrolytes. Bedside transthoracic echocardiogram showed normal left ventricular size and function. The mitral valve showed a marked regurgitation and a large vegetation attached to its posterior leaflet. Intravenous dobutamine was initiated, with overall improvement. Suddenly, the patient presented cardiac arrest and died. This occurred 47 days after the diagnosis of SLE and monitoring at the rheumatology unit, and fever with the diagnosis of endocarditis, during the last 10 days of life.

**AUTOPSY FINDINGS**

A huge vegetation (20 × 15 × 4 mm), tissue corrosion on the posterior leaflet, anterior commissure of the mitral valve, and rupture of some chordae tendineae at that point was evident (Figure 1).

At histology, the vegetation was composed of fibrin and neutrophils with numerous Gram-positive cocci and granulation tissue at the base (Figure 2).

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**Figure 1.** Gross examination of the formalin-fixed heart showing the mitral valve with large vegetation (arrow) at the posterior leaflet, near to the posterior commissure, with the rupture of some chordae tendineae (arrowhead). LA = left atrium; MV = mitral valve.
The examination of the coronary arteries displayed complete occlusion of the left main artery by an embolus with the same histological composition of the vegetation (Figure 3). There were no histological signals of myocardium infarction due to the short time that had elapsed since the patient’s death. In addition, there was also embolization to the skin, kidneys, spleen, and central nervous system, which formed small abscesses in organization. There were no signs of active SLE at the other organs.

DISCUSSION

This case illustrates a fatal outcome of infective endocarditis (IE) in a young patient diagnosed with SLE who was recently submitted to corticoid pulse therapy.

The prevalence of cardiac involvement in patients with SLE varies from 30-50% to 52-80%.¹

All the cardiac layers may be involved in SLE. The coronary arteries might be affected by vasculitis, thrombi, and atherosclerosis. The most common

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Figure 2. Photomicrography of the vegetation showing clumps of Gram-positive cocci (Staphylococcus aureus): A - Low magnification of the vegetation showing the base of granulation tissue and the top composed of fibrin with polymorphonuclear leukocytes interspersed with bacteria clumps (arrows) (H&E, 25×); B, C - Detail of the top and the region near the base of the vegetation. The arrows points to some clumps of bacteria and the asterisk is at the granulation tissue area at the base, which is consistent with the time history of the endocarditis (H&E, 200× and 400×, respectively); D - The Brown-Hopps stain shows the coccus-shaped bacteria colonies (arrow) with a change in the dye affinity (red), with very few of them purple (Gram-positive) due to the antimicrobial treatment (Brown-Hopps, 1000×).
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There have been signs of inflammation in 75% of the cases at autopsy, either active or quiescent. Pericarditis is clinically evident in 20-30% of the patients along the course of their disease. Cardiac tamponade is rare, with an incidence ranging from 1.23% to 2.5% in two large retrospective series. Clinical manifestations of myocarditis are also rare; however, the signs of inflammation have been seen in 40-80% at autopsy. Libman and Sacks described a particular type of nonbacterial endocarditis, which constitutes one of the most common cardiac manifestations of SLE. These vegetations are sterile, small, flat, granular or verrucous and occasionally sessile. They firmly adhere to the endocardium and may cover a large area of the valve surface, with extension to the atrial and ventricular endocardium, chordae tendineae, and valve pockets. The mitral valve is the most commonly affected, and usually at the ventricular surface. The antiphospholipid syndrome accompanies SLE in 50-70% of cases, which increases the risk of coronary thrombosis, intramural thrombi, and valvar dysfunction.

Although the Libman-Sacks endocarditis should always be remembered, in patients with SLE, there was no doubt that our case was infective in nature. This patient had two major criteria (typical microorganism isolated on two settings of blood cultures, and vegetation on the echocardiogram) and one minor criterion (fever) for the definite clinical diagnosis of IE according to Duke’s modified criteria.

The overall mortality for IE remains high, ranging between 20% and 25%. Fabri et al. studied 629 patients with IE and found the occurrence of 21.1% for embolic events, 47.4% for central nervous system involvement, 42.9% peripheral organs involvement, 9.7% for both central nervous system and peripheral organs involvement, and 1.5% for coronary arteries. Systemic embolization complicates IE in 22-50% of cases. Up to 65% of the embolic phenomena involve the central nervous system, leading to ischemic strokes, cerebral abscesses, and mycotic aneurysms, which occasionally rupture. These are accompanied by mortality rates of around 80%.

The risk of embolization increases with (i) involvement of the mitral valve; (ii) vegetation size of more than 10 mm; (iii) the growth of vegetation size despite adequate therapy; and (iv) endocarditis caused by fungus or staphilococci. Embolization to coronary arteries represents another site with prognostic impact. Septic coronary embolism is an infrequent but dramatic complication of IE. The embolization to the coronaries as a cause of acute myocardial infarction is considered rare; the incidence of this event, which is secondary to IE, is hard to estimate. The literature includes case
reports and case series describing mostly autopsy findings, after Virchow’s original report in 1856 of coronary emboli secondary to IE due to puerperal sepsis.\textsuperscript{14-17} Wenger et al.\textsuperscript{18} described 15 cases of embolization to the coronaries as the immediate cause of death, in which 8 cases had cardiac vegetation as the embolic source. The same authors, in a retrospective analysis of the literature, found 74 case reports of coronary embolization, and IE was the cause of the embolization in 47 cases (63%). Two-thirds of these cases had a fatal outcome. In more than half of these cases, the left main coronary artery and/or the descending anterior artery were involved, possibly due to the greater caliber and higher flow to this segment and the more favorable anatomy when compared to the right coronary artery. An embolectomy by a large lumen aspiration device could be a preferential therapeutic option.\textsuperscript{19,20}

CONCLUSION

IE still has a high mortality rate. An embolism to major vascular beds carries ominous prognostic implications. An embolism to the coronaries is often overlooked as a cause of acute myocardial infarction and may determine a fatal outcome, as was presented here. The postmortem examination was essential to clarify the cause of death in this young patient.

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