Case reports

Coronary artery disease in young patients with systemic lupus erythematosus: two case reports

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The cardiovascular system is often involved during systemic lupus erythematosus (SLE), but only few studies have documented myocardial ischemia and myocardial infarction in young patients. We observed 2 cases of coronary artery disease in young patients with SLE and different clinical presentations. In the first case, a 26-year-old woman, with SLE diagnosed at the age of 12 years, was evaluated for angina (CCS class II). Myocardial scintigraphy revealed a clear reversible thallium-201 apical perfusion defect. During the following 5 years worsening effort angina led to coronary angiography which revealed the presence of a complete obstruction of the left anterior descending coronary artery (LAD) treated with surgical myocardial revascularization (internal mammary artery implantation on the LAD). The second patient had myopericarditis and an acute myocardial infarction 1 year before coming to our observation. Coronary angiography revealed the presence of 100% obstruction of the LAD. On this basis, a diagnosis of SLE was made. Our data constitute two relevant examples of coronary artery disease with different clinical presentation in young SLE patients.

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Introduction

Myocardial ischemia and myocardial infarction have not been often documented in young patients with systemic lupus erythematosus (SLE): in the literature there is evidence of coronary artery disease in young patients with SLE[1-3].

We describe 2 cases of young patients with SLE, one female and one male, both 26 years old and presenting with severe coronary artery disease.

Description of cases

Case 1. A 26-year-old woman complained of mild effort angina during a recrudescence of SLE (CCS class II). The diagnosis of SLE was made at the age of 12 years on the basis of the revised criteria of the American Rheumatism Association[4]. The family history was negative for coronary artery disease. She did not have a history of arterial hypertension and she was initially treated with hydroxychloroquine and steroids adjusting the dosage on the basis of her clinical symptoms and laboratory results. The patient initially had renal disease with urinary protein excretion requiring high-dose steroid therapy. Subsequently, her renal function normalized. The serum levels of antiphospholipid antibodies were within the normal range. The patient had also been treated with immunosuppressant agents (e.g. cyclosporine, azathioprine). She was a smoker and had sometimes been on oral estrogens, but her lipid profile was normal.

At the time of admission, the cardiac enzymes were in the normal range. The patient was moderately hypertensive and ECG showed Q waves in leads V_3-V_4 without any ST segment or T wave abnormalities. All previous ECGs were normal. Doppler echocardiography was substantially normal. The patient underwent exercise thallium-201 (Tl-201) myocardial scintigraphy. Exercise testing was positive for angina. Scintigraphy showed a mild reversible Tl-201 apical perfusion defect, but the patient refused coronary angiography for 5 years. During this period the patient had recurrent episodes of angina pectoris. Worsening of the effort angina led to a new Tl-201 single photon emission computed tomography imaging, which showed a clear reversible apical perfusion defect

(Fig. 1); the patient accepted to undergo coronary angiography, which revealed the presence of a complete obstruction of the left anterior descending coronary artery (LAD) with the development of anastomotic net which permitted perfusion of the ischemic myocardium. There was no evidence of myocardial necrosis; contrast ventriculography showed regular chamber dimensions and normal left ventricular wall motion and Tl-201 redistribution at rest. She underwent surgical revascularization with implantation of the internal mammary artery on the LAD. During the following 3 years the patient remained asymptomatic; clinical evaluation, ECG and exercise Tl-201 myocardial scintigraphy were all normal.

Case 2. A 26-year-old male patient was evaluated for chest pain at rest. The year before the patient had a single episode of myopericarditis and 2 months after an acute antero-apical myocardial infarction. He was not a smoker, his lipid profile was normal and his family history was negative for coronary artery disease.

Coronary angiography showed complete proximal LAD occlusion. A stent coronary angioplasty was performed on the LAD with an optimal post-procedure outcome. Our clinical evaluation included an exercise Tl-201 myocardial scintigraphy without symptoms or ST-segment modifications, but with a clear anterior and apical non-reversible perfusion defect at rest and after reinjection (Fig. 2). We hypothesized that a systemic

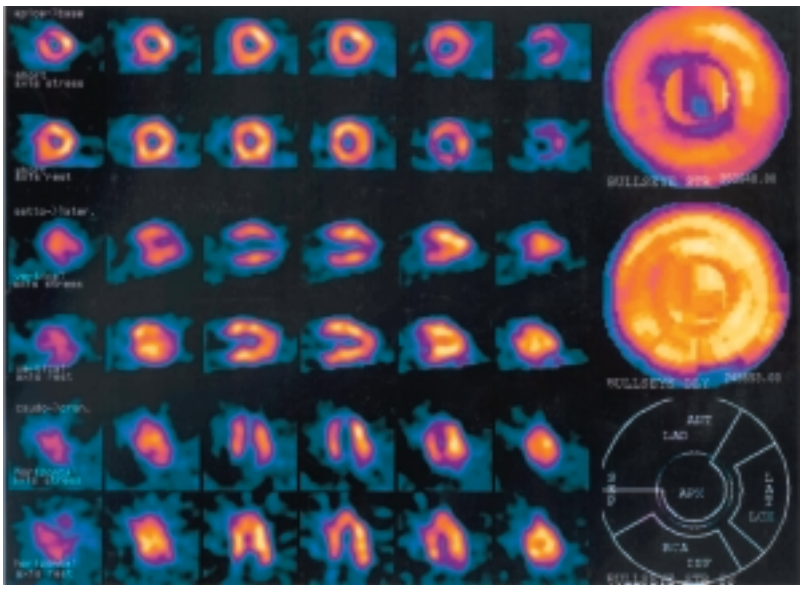

Figure 1. *Case 1: thallium-201 myocardial scintigraphy which showed a clear reversible apical perfusion defect.*

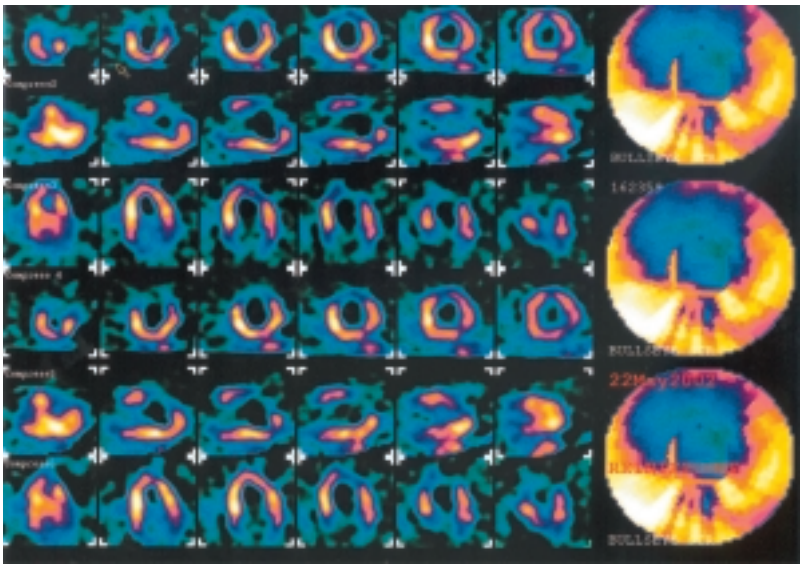

Figure 2. *Case 2: thallium-201 myocardial scintigraphy which showed a clear non-reversible anterior and apical perfusion defect.*

inflammatory disease was responsible for the coronary disease and myopericarditis. Laboratory analysis revealed high levels of inflammatory markers (fibrinogen, alpha-2 globulin, C-reactive protein, erythrocyte sedimentation rate). The antistriate muscle antibodies, anticardiolipin antibodies and anti-DNA were positive as were the antinuclear antibodies and antiextractable nuclear antigens (homogeneous pattern, 1/80 titer). Homocysteine levels were also increased. Laboratory analysis also revealed renal impairment (creatinine 1.6 mg/dl; severe proteinuria). Renal biopsy confirmed the presence of diffuse membranoproliferative glomerulonephritis; therefore a diagnosis of SLE was made[4] and the patient was placed on corticosteroids and immunosuppressive drugs (cyclophosphamide).

The patient is now asymptomatic and the inflammatory tests are negative.

Discussion

The presence of coronary artery disease in young patients with SLE has been well documented[1-3]; the frequency was not elevated but the incidence was certainly superior if compared with that of subjects of similar age[5,6]. Histopathological studies showed the presence of significant coronary damage in a higher percentage[7], without parallel clinical demonstrations of a similar frequency and importance. An important increase in mortality related to premature atherosclerosis with coronary artery disease and stroke has been reported in patients with SLE[8]. However, previous reports have shown the presence of Tl-201 perfusion defects in about 40% of patients with SLE although not correlated with clear clinical signs of myocardial ischemia[9-11]. The inflammatory angiopathy predominantly involves the small blood vessels of the kidney[12,13], as in our 2 patients, or more infrequently other structures, whereas inflammatory disease of large and intermediate-sized arterial vessels is rare. Our patients did not present with any clinical or instrumental (echo-Doppler) evidence of the involvement of large arterial vessels.

Our observations constitute examples of coronary artery disease in young patients with SLE but with different clinical pictures. In the first case the coronary disease progressed until complete occlusion of the LAD. The presence of collateral vessels and the absence of myocardial necrosis let us to believe that the coronary occlusion was progressive and consequent to a thrombotic and atherosclerotic mechanism promoted by corticosteroid therapy[14]. In the second case the patient had an acute myocardial infarction in the absence of any symptoms of systemic inflammatory disease. In view of the patient's previous myopericarditis we hypothesized a coronary occlusion consequent to a vasculitis-related thrombotic mechanism. In this case the diagnosis of SLE underlying the myocardial ischemia was made 1 year after the acute myocardial infarction without previous corticosteroid and immunosuppressive drug interactions.

The hypothesis is that immunological mechanisms eventually leading to coronary vasculitis could be activated during the phases of recrudescence of SLE. The cellular pathology of vascular disease in SLE can be classified into two broad categories: inflammatory and thrombotic[12]. The first mechanism involves inflammatory angiopathy and it is held that the pathogenetic mechanism includes immune complex deposition and complement activation in the vicinity of the blood vessel wall. This is followed by infiltration of the vessels by leukocytes which release lysosomal enzymes and oxygen radicals. Simultaneously or alternatively a Shwartzman phenomenon could occur with up-regulation of the intercellular adhesion molecule-1 and E-selectin on the endothelial cell surface and engagement of polymorphonuclear leukocytes until vascular occlusion. The second mechanism involves a thrombotic phenomenon[12] associated with the mechanism of interaction between the clotting system, antiphospholipid antibodies[15], increased platelet aggregation, vascular endothelial function and antiendothelial cell antibodies[12,16]. This may explain the predisposition to a prothrombotic state[17]. This predisposition could be enhanced by hyperhomocysteinemia, that is frequently observed in SLE[18], with an impaired nitric oxide synthesis and endothelial disorders[12].

The accelerated progression of atherosclerosis in patients with SLE does not depend only on the classic risk factors identified in epidemiological studies (advanced age, high cholesterol levels, hypertension, diabetes, obesity) but also on the processes of vasculitis and thrombotic or atherosclerotic vascular disorders which are favored by prolonged steroid therapy. This was the case in the first patient. We could define SLE as an independent risk factor in the pathogenesis of coronary artery disease[19].

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