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Artículo:

Fibrosis endomiocárdica (enfermedad de Davies) asociada a Lupus eritematoso sistémico

ENDOMYOCARDIAL FIBROSIS (DAVIES DISEASE) COINCIDENTAL WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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RESUMEN

FIBROSIS ENDOMIOCÁRDICA (ENFERMEDAD DE DAVIES) ASOCIADA A LUPUS ERITEMATOSO SISTÉMICO

Los autores presentan el caso de una mujer de 27 años, con signos y síntomas de insuficiencia cardiaca congestiva rebelde al tratamiento, anemia, úlceras en la mucosa gingival, fotosensibilidad y alopecia. Los datos electrocardiográficos, ecocardiográficos, angiográficos y hemodinámicos orientaron el diagnóstico de cardiomiopatía restrictiva, insuficiencia mitral secundaria a prolapso mitral y dilatación biauricular. El examen histológico de la biopsia endomiocárdica, tomada durante el cateterismo cardiaco, mostró signos de fibrosis endomiocárdica y el examen inmunológico resultó compatible con lupus eritematoso sistémico. Hasta donde sabemos, éste es el primer caso de fibrosis endomiocárdica (enfermedad de Davies) asociado con lupus eritematoso sistémico publicado en la literatura médica. Permanece incierta la etiología de la fibrosis endomiocárdica y su asociación con lupus eritematoso sistémico sugiere el probable origen autoinmune de este padecimiento.

SUMMARY

This is the case of a 27 years-old woman with signs and symptoms of severe untreatable congestive heart failure anemia, gingival mucosa ulcers, photosensitivity and alopecia. The electrocardiographic, echocardiographic, angiographic and hemodynamic data oriented the diagnosis of restrictive cardiomyopathy, mitral insufficiency secondary to mitral prolapse and bi-atrial dilation. The histologic study of the endomyocardial biopsy, performed during catheterization, showed signs of endomyocardial fibrosis, and immunological analysis was compatible with systemic lupus erythematosus. As far as we know, this is the first case of endomyocardial fibrosis (Davies disease) associated with systemic lupus erythematosus published in the medical literature. The etiology of Davies disease remains unrevealed and its association with systemic lupus erythematosus suggest a probable autoimmune origin.

RESUME

FIBROSE ENDOMYOCARDIQUE (MALADIE DE DAVIES) ASSOCIÉE AVEC LUPUS ERYTHÉMATEUX DISSÉMINÉ

Les autheurs présentent le cas clinique d´une femme âgée de 27 ans, avec des signes et symptômes d'insuffisance cardiaque rebelle au traitement, des ulcères dans la muqueuse gingivale, photosensibilité et alopécie. Les données cliniques, électrocardiographiques, échocardiographiques, angiographiques et hémodynamiques ont orienté le diagnostic vers la cardiomyopathie réstrictive, l´insuffisance mitrale secondaire au prolapsus mitral avec dilatation biauriculaire. L´examen hystologique de la biopsie endomyocardique, obtenue au cours du cathétérisme cardiaque, montra des signes de fibrose endomyocardique et l'examen immunologique était suggestif de la présence de lupus erythémateux disséminé. D´après nous, on présente ici le prémier cas de fibrose endomyocardique (maladie de Davies), associée à lupus erythemateux disséminé, publié dans la littérature médicale. L´etiologie de la fibrose endomyorardique n'est pas définie et son association avec le lupus erythemateux disséminé suggère l´origine autoimmune de cette maladie.

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Palabras clave: Cardiomiopatía restrictiva. Fibrosis endomiocárdica. Enfermedad de Davies. Lupus eritematoso sistémico.
Key words: Restrictive cardiomyopathy. Endomyocardial fibrosis. Davies disease. Systemic lupus erytematosus.

INTRODUCTION

The endomyocardial fibrosis (EF) has been related to the patients habitat, low socioeconomic status, malnutrition, diet rich in bananas, presence of carcinoid heart disease, virosis, bacterial (streptococcal) infections, parasitosis (filariasis),[1-9] immunological response to malaria[10] and collagenosis.[11] The purpose of this article is to present the case of a patient with clinical, echocardiographic, hemodynamic and histopathological signs of EF, with clinical manifestations and laboratory data compatible with sistemic lupus erythematosus (SLE).

CASE REPORT

This is the case of a 27 years-old woman belonging to a low socioeconomic class, with history of cardiac failure, an indefinable heart murmur and mucocutaneous alterations (oral ulcers, photosensitivity and alopecia). She was admitted with symptoms of heart failure unresponsive to pharmacological treatment, pale, emaciated, with a body temperature of 36.7°C, hypotensive (90/60 mm Hg), tachycardic (110 min^{-1}), tachypneic (20 min^{-1}), with important neck vein distention, hepatomegaly, ascites and peripheral edema. A mitral and tricuspid systolic murmur was heard in the *mesocardium*. The chest roentgenogram of the patient showed signs of cardiomegaly (cardiopulmonary index 0.58) and right pleural effusion *(Figure 1)*. The electrocardiogram at rest showed an atrial flutter (231 min^{-1}) with 2:1 A-V block, RBBB of intermediate degree and dilation of both *atria* and of the right ventricle *(Figure 2)*. The echocardiogram (not illustrated) showed signs of mitral prolapse, paradoxical septal motion, left ventricular hypokinesia (ejection fraction 0.52), right and left atrial enlargement, and mitral and tricuspid regurgitation. The Doppler echocardiography showed signs of restrictive flow pattern. The abdominal echogram (not illustrated) showed signs of hepatomegaly, ascites, right pleural effusion, and bilateral infiltrate in the renal cortex. The intravascular catheterization revealed hypertension of the pulmonary artery (67/38-47 mm Hg), right ventricle (62/22 mm Hg) and right *atrium* (18 mm Hg) with a domi-

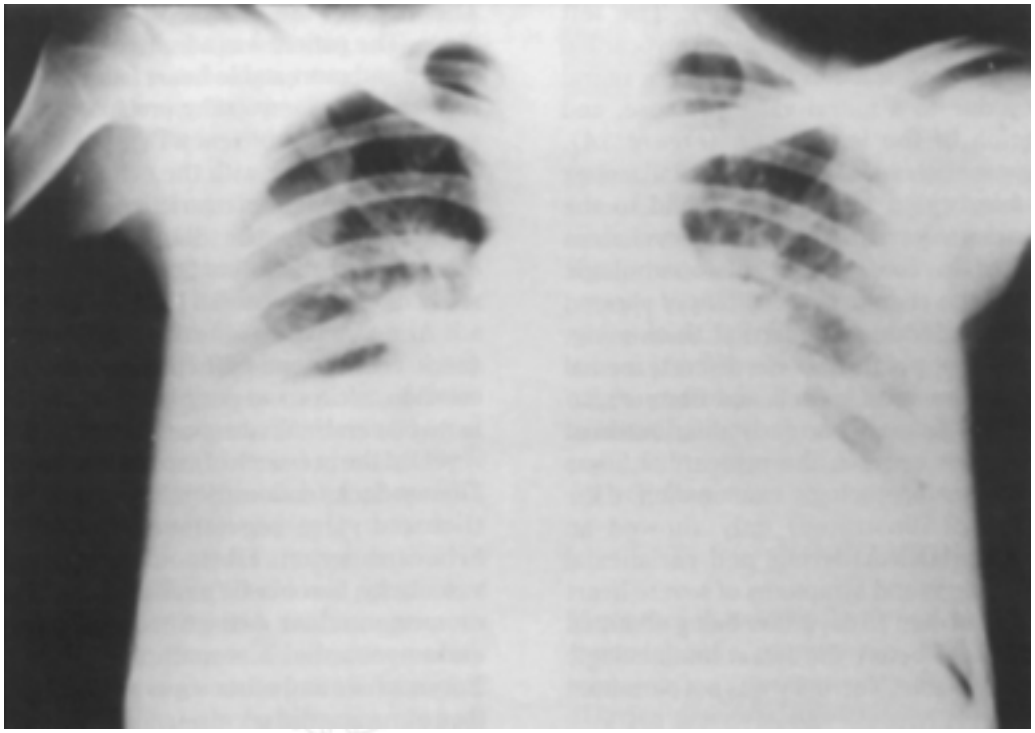

FIG. 1: Chest roentgenography showing signs of cardiomegaly and right pleural effusion.

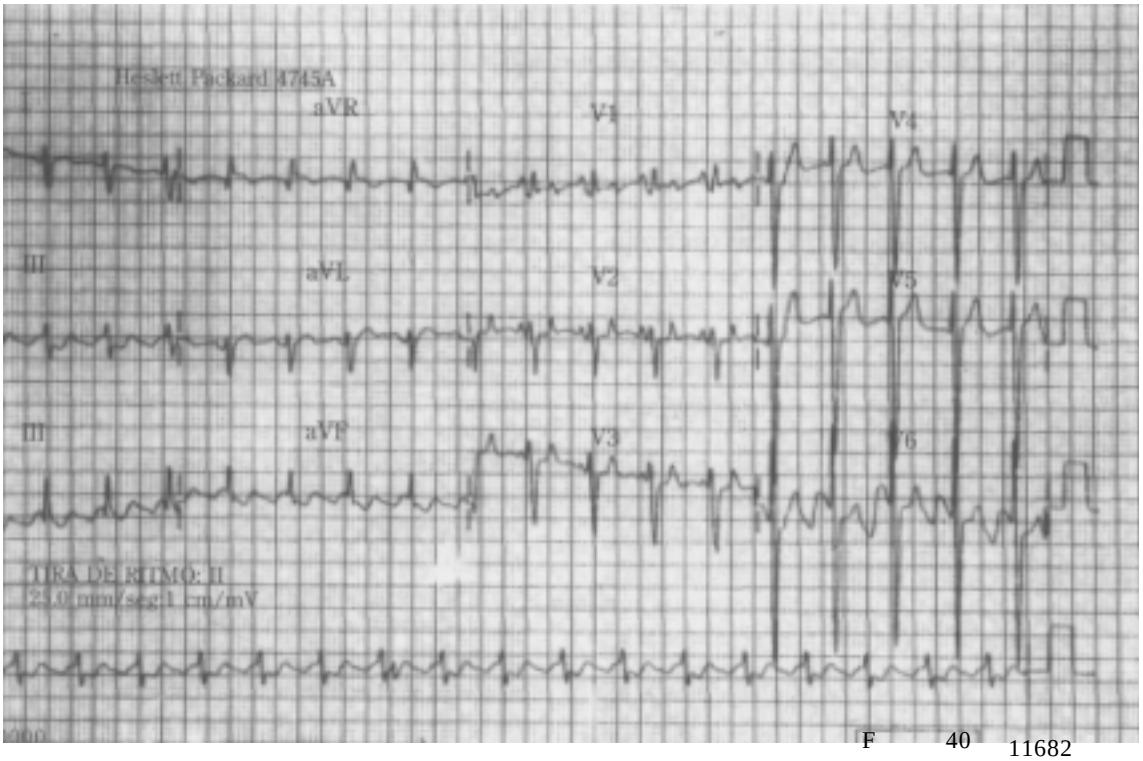

FIG. 2: Electrocardiogram at rest showing signs of atrial flutter 231/min with 2:1 AV block RBBB of intermediate degree, dilation of both atria and of the right ventricle.

nant "v" wave; hypotension of the left ventricle (75/20 mm Hg) and aorta (80/58-66 mm Hg) and low cardiac index (1.6 L min^{-1} M^{-2}). The left ventriculogram showed signs of reduced myocardial contractility (ejection fraction 0.50), severe mitral insufficiency due to a mitral valve prolapse, and severe dilation of the left *atrium (Figure 3A)*. Radiopacity was observed at the left ventricular apex during systole, which might correspond to the papillary muscles *(Figure 3B)*. The laboratory analysis data are listed in *Table I*. The histopathologic examination of the endomyocardial biopsy showed signs of EF: moderate endocardial thickening, discrete hypertrophy of the muscle, discrete medial hypertrophy of the small vessels and fibrous *septi* with granulation tissue irregularly distributed at different distances between the myocardial fibers *(Figure 4)*. The histopathologic examination of the skin biopsy (not illustrated) only showed an inespecific mononuclear dermal and perianexial infiltrate. With signs and symptoms of severe heart failure, the patient died 15 days after being admitted to the hospital, and before the *serum* immunologic analysis were available. Necropsy was not permitted by the patient relatives.

DISCUSSION

The onset of the disease in our patient was insidious. The patient was admitted to the hospital with severe and untreatable heart failure, resulting from restrictive cardiomyopathy, prolapsed mitral valve and severe mitral insufficiency. Bi-atrial dilation *(Figures 2 and 3)*, together with the echocardiographic and angiographic signs of restrictive cardiomiopathy *(Figure 3)* lead to the diagnosis of EF (Davies disease)[1,12] that was confirmed by the microscopic study of endomyocardial tissue *(Figure 4)*.

Aside from the signs of congestive heart failure (neck vein distention, hepatomegaly, right pleural effusion, ascites and peripheral edema), the patient had a bilateral infiltrate of renal cortex. Blood analysis revealed the presence of autoantibodies. Contrary to Libman-Sacks endocarditis, in our patient mitral and tricuspid valve vegetations were absent at the echocardiogram. Fibrinoid necrosis, increased vascularity, fibroblastic proliferation and neutrophils or mononuclear cells were also absent at the endomyocardial histopathologic examination.[13] Eosynophilia and other signs of Löeffler endocarditis, e.g., myocardial necrosis and eosynophilic infiltrate, were absent too.[14] On the

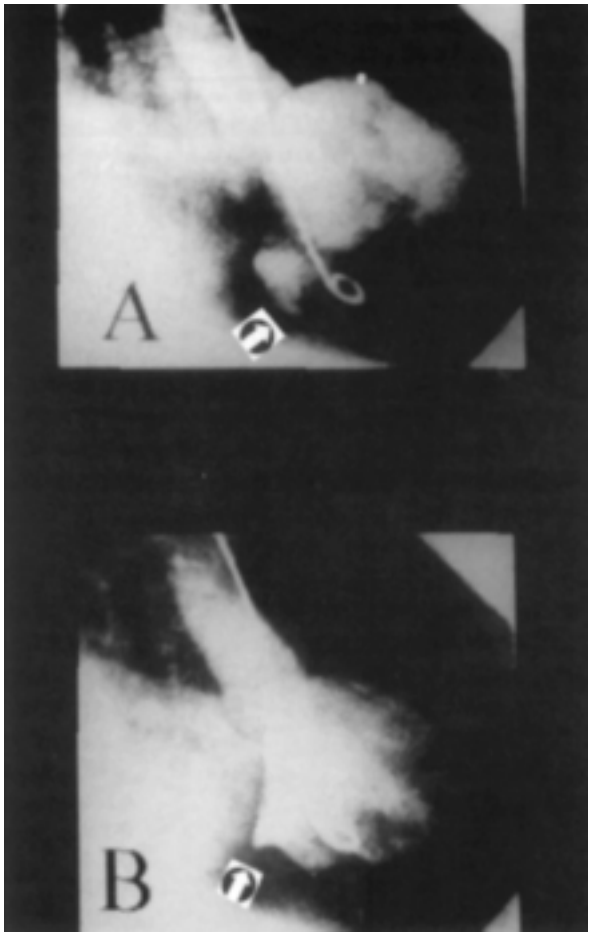

FIG. 3: The left ventriculogram (A, systole and B, diastole) showing signs of reduced myocardial contractility, severe mitral insufficiency resulted from prolapsed mitral valve (arrow), and severe dilation of the left *atrium*. Radiopacity was observed at the left ventricular apex during systole.

other hand, histologic examination of the endomyocardial biopsy of our patient was characteristic for endomyocardial fibrosis: endocardial thickening, collagenous *septi* and granulation tissue, which differentiates from other entities, like endocardial fibroelastosis.[15] In the absence of eosinophilia, Löeffler endocarditis was an uncertain diagnosis. The patient met classification criteria for SLE: mucocutaneous disorders (alopecia, photosensitivity and oral ulcers), hematologic disorders (anemia, leukopenia and lymphopenia), immunological disorders (increase in Ig particularly IgG, decrease in C3, presence of anti-DNA autoantibodies and positive VDRL) and presence of antinuclear autoantibodies with an homogeneous pattern in the indirect immunofluorescence assay. Althoug heart failure is a common cause of pleural effusion we cannot exclude the participation of a possible inflammatory pleural process

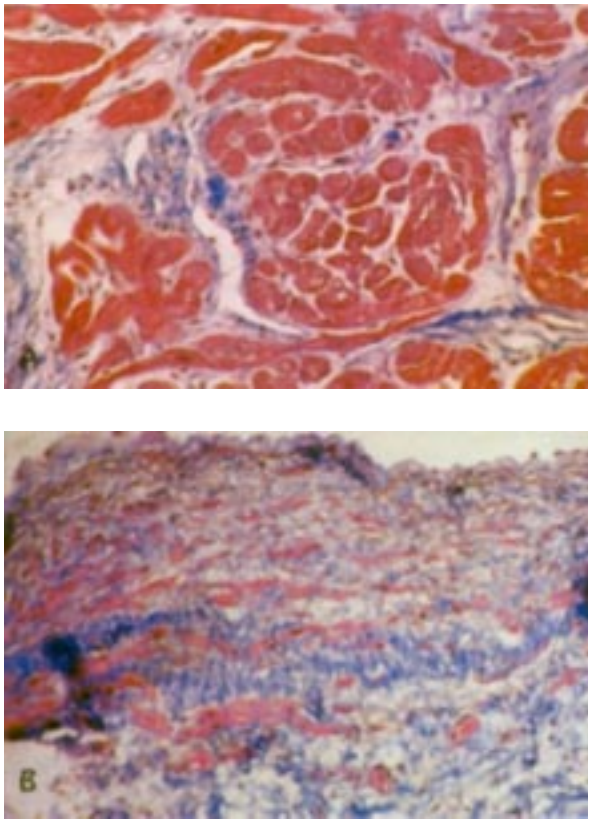

FIG. 4: The histopathologic examination (Masson stain) of the endomyocardial biopsy showing (A) signs of granulation tissue and fibrosis with *septi* formation penetrating at variable distances into myocardium and discrete medial hypertrophy of small vessels (X 16) (B) moderate endocardial thickness resulted from collagenous deposits and discrete hypertrophy of the muscle fibers (X 6.3).

(serositis) in our patient. It is well known this kind of serosal affection in some SLE patients. On the other hand, we did not investigate the presence of treponema in this patient, but the antinuclear autoantibodies often produce false-positive VDRL by crossreaction even in the absence of anticardiolipin antibodies. SLE is a multiorganic disease causing mucocutaneous, articular, neurological, hematological, renal, immunological, vascular, cardiac, pulmonary and glandular lesions.[16] In our patient, the signs of Davies disease coincided with SLE.

CONCLUSION

In conclusion, based in the clinical, echocardiographic, hemodynamic, immunologic and histopathologic examination, our patient was affected with EF (Davies disease), associated with SLE. This last diagnosis confirmed by immunological analysis. As

Table 1
Laboratory analysis

Variables	units	Observed	Normal
Hemoglobin	g dl^{-1}	10.5	12-16
Hematocrit	%	33	45-50
Leukocytes	μl^{-1}	3900	5000-10000
Eosinophils	μl^{-1}	117	50-400
Basophils	μl^{-1}	39	0-100
monocytes	μl^{-1}	156	200-900
limphocytes	$\mu 1^{-1}$	1170	1200-3800
Glucose	mg dl^{-1}	126	90-120
Creatinine	mg dl^{-1}	1.3	0.9-1.2
Urea	mg dl^{-1}	45	16-35
Uric acid	mg dl^{-1}	10	1.5-5
Albumin	g dl^{-1}	2.2	3.0-4.1
Cholesterol	mg dl^{-1}	126	170-200
Tryglicerides	mg dl^{-1}	107	< 160
IgG	mg dl^{-1}	3056	800-1900
IgA	mg dl^{-1}	570	74-436
Igm	mg dl^{-1}	409	81-200
C3	mg dl^{-1}	60	74-172
C4	mg dl^{-1}	9	14-51
Erythrocyte sedimentation rate	mm h^{-1}	33	< 20
Antinuclear antibodies*	$dilution^{-1}$	640	< 40
Anti-dsDNA antibodies**	UI ml^{-1}	135	< 135
Anticardiolipin IgG***	AU¶	0	0-1.9
Anticardiolipin IgM***	AU¶	0	0-2.4
Anticytoplasmic antibodies†	$dilution^{-1}$	10	negative
VDRL‡		positive	negative
AFB§ in pleural effusion fluid		negative	negative

* Homogeneous pattern by indirect immunofluorescence technique.
** Anti-double strand DNA antibodies by ELISA technique.
*** ELISA technique.
¶ Arbitrary Units.
† Indirect immunofluorescence in polimorfonuclear cells technique.
‡ Dilution not reported.
§ Acid-fast bacilli

far as we know, this is the first case reported with EF and SLE association. At least, two reports in the medical literature suggest the immunological origin of Davies disease.[10,11] The coincidence of both entities in our patient may give support to the idea that autoimmune dysfunction is related to the origin of Davies disease.

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