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SESSION III

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Endomyocardial disease in South America—report on 23 cases in Venezuela

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Summary

Twenty-three cases of endomyocardial disease (ED)* are presented, studied in Venezuela, a tropical country in northern South America.

The diagnosis was confirmed in 18 cases by means of pathological studies, and in 5 cases by angiocardiography which showed the characteristic obliterative ventricular lesions. Eosinophilia was present in 35% of the patients. The most frequent clinical feature was heart failure associated with mitral regurgitation. Systemic embolism was the first clinical feature in 5 cases. In 2 cases, ED was associated with autoimmune haemolytic anaemia or vasculitis.

Necropsy revealed a predominance of the left-sided (9/16 cases) and biventricular (6/16 cases) types. The pathological lesions were characterised by fibrous thickening of the endocardium at the apex and the ventricular inflow tracts extending to the myocardium and involving the atrioventricular valves.

ED is frequently misdiagnosed as rheumatic valvular cardiopathy.

The two-dimensional echocardiogram is a very useful procedure for determining the spatial anatomy of ED. The echo findings were closely correlated with ventriculographic and necropsy findings. Even though ED is widely spread around the world, it is most frequently found in tropical and subtropical countries in Africa, Asia and America, such as Venezuela and Brazil. This suggests that there are aetiological factors in these latitudes, about which little is known.

*Editor's note: A synonym for endomyocardial fibrosis (EMF).

KEY WORDS: endomyocardial disease, echocardiogram, South America.

Introduction

Endomyocardial disease (ED) is geographically widespread, although it is found more frequently on the African continent (Davies, 1948, 1968; Connor *et al*, 1968; Shaper, Hutt and Coles, 1968). In America it has been reported in Argentina, Brazil, Colombia, Jamaica, Mexico, U.S.A. and Venezuela (Fig. 1) (Ruggiero *et al.*, 1969; Andrade and Guimaraes, 1964; Guimaraes *et al.* 1971, 1974; Correa *et al.*, 1963; Stuart and Hayes, 1963; Contreras *et al.*, 1971; Lepley *et al.*, 1974; Mckusick and Cochran, 1952; Suárez and Suárez, 1967, 1976; Tortoledo and Dominguez, 1969; Puigbo *et al.*, 1978; Machado *et al.*, 1979).

ED is a restrictive cardiomyopathy which frequently leads to heart failure. It is characterised by fibrosis of the ventricular endocardium with obliteration of the apex and of the inflow tract of the affected ventricle and extension of the fibrosis to the myocardium, chordae tendineae and papillary muscles and eventual mural thrombosis (Shaper *et al.*, 1968; Hutt *et al.*, 1965). The obliterative fibrotic process produces a restriction of ventricular filling, decreased ventricular distensibility and atrioventricular regurgitation. It has been argued that endomyocardial fibrosis and endocarditis parietalis fibroplastica are two aspects of one same clinical and pathological spectrum which has been given the commonly accepted name of eosinophilic endomyocardial disease (EED) (Brockington, Olsen and Goodwin, 1967; Brockington and Olsen, 1972; Roberts, Buja and

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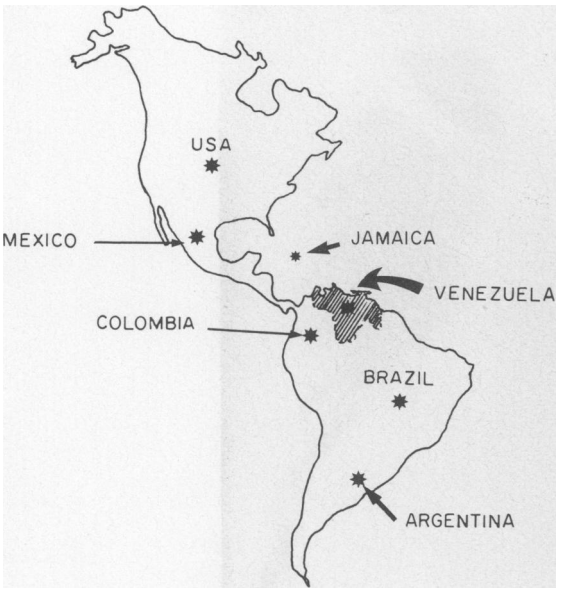

FIG. 1. Major areas of endomyocardial disease in the Americas.

Ferrans, 1970; World Health Organization Report WHO/ISFC, 1980).

The purpose of this study is to present 23 additional cases of endomyocardial disease (ED) studied in Venezuela, 18 of which have been confirmed pathologically. It considers the frequency of eosinophilia and the clinical and pathological characteristics of the process, and evaluates the role of non-invasive techniques for diagnosis of the disease.

Materials and methods

Twenty-three cases of ED studied at the University Hospital in Caracas are presented. In 18 cases, 16 by necropsy and 2 by myocardial biopsy, the pathological studies confirmed the diagnosis. In the other 5 patients, ventriculography showed the typical obliterative lesions of the apex.

Thirteen patients were female and 10 were male. The average age was 39, ranging from 13 years of age to 65. Twenty-one were racially mixed and 2 were Caucasians who had lived in rural areas in the country for more than 8 years.

The distribution of the patients by country of origin was: Venezuela—16 cases, Colombia—3 cases, and one case each from Guyana, Cuba, Spain, and Italy.

Results

Presenting clinical features

The most frequent clinical pattern was heart failure, observed in 20 cases. Heart failure was associated with a hypereosinophilic syndrome characterized by lymphadenopathy, hepatosplenomegaly, anaemia and eosinophilia in 3 cases, and with cerebral embolism in 3 cases. One patient with heart failure and a hypereosinophilic syndrome also showed signs of vasculitis.

The other 3 patients presented with peripheral embolism, cerebral embolism and ischaemic heart pain, and haemolytic anaemia with cardiac tamponade respectively. In this last case, the Coombs' test was positive and the eosinophilia preceded the cardiovascular signs by 8 years. In 8 cases (35%) there was eosinophilia of over $1{\cdot}5 \times 10^9$/litre over a period of at least 6 months. In 10 cases, the duration of the symptoms was less than 1 year, from 1 to 3 years in 3 cases, from 3 to 5 years in 5 cases and over 5 years in 5 cases.

In the 23 cases, the most frequent physical signs were: an abnormal cardiac impulse (17 cases), pansystolic mitral murmur (17 cases), loud and early third heart sound (13 cases), left parasternal systolic lift (12 cases), increased pulmonary component of second heart sound and giant 'a' wave in jugular venous pulse (7 cases). Other findings were: a fourth heart sound (5 cases), tricuspid regurgitation murmur (4 cases), pericardial rub (4 cases) and systolic 'v' wave in the jugular venous pulse (4 cases).

The predominant symptom was dyspnoea in the cases of left or biventricular form when an abnormal apical impulse, mitral systolic murmur and loud and early third sounds were commonly present. The presence of a pronounced 'a' wave in the venous pulse suggested associated restriction of the right ventricle in the biventricular form.

Radiology

Enlargement of the left ventricle (16 cases) and of the left atrium (17 cases), and pulmonary venous hypertension (14 cases) were the most frequent findings (Fig. 2). Three patients had pericardial effusions and one had endocardial calcification.

Electrocardiograph

The most frequent electrocardiographic findings were left ventricular hypertrophy (10 cases), right atrial enlargement (9 cases), left atrial enlargement (8 cases) and non-specific changes in ventricular repolarization (8 cases). A few show left or right bundle branch block and/or left anterior hemiblock.

Phonocardiography

The most frequent findings in the 8 cases studied were: reduced left ventricular ejection time (in all 8 cases), and increased pulmonary component of the

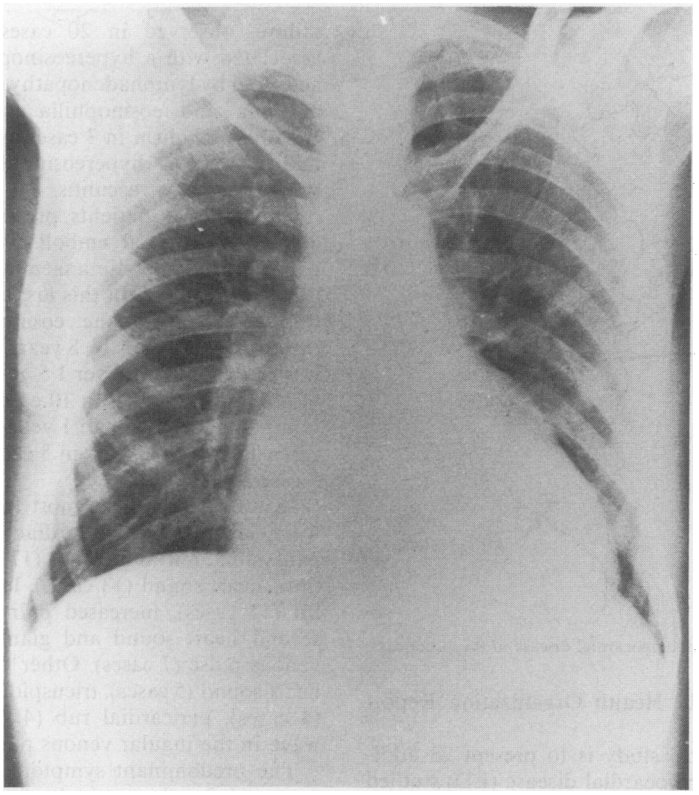

FIG. 2. X-rays: (frontal view): mitral configuration. Left atrial and auricular appendage enlargement. Pulmonary venous hypertension.

second sound, early third heart sound, mitral pansystolic murmur, prominent 'a' wave and sustained systolic phase in the right precordiogram (all in 6 cases each).

Echocardiography

M-mode. Of 7 cases studied by this technique, enlargement of the left atrium was noted in 6 cases and of the left ventricle diastolic diameter in 4 cases. In 6 cases, the ejection fraction was normal or increased and in one case it was decreased. A pattern of mitral pansystolic prolapse was found in 5 of those 7 cases, with either early outward diastolic motion of the septum (3 cases) or of the posterior wall (4 cases) (Fig. 3). Enlargement of the right ventricular chamber was found in 4 cases and a pattern of pansystolic prolapse of the tricuspid in 3.

Two-dimensional echocardiograph. Of 5 cases studied, all showed obliteration of the ventricular apex with increased reflectancy (4 cases), and enlargement of the atrium (also in all 5 cases) on both sides of the heart. Prolapse of the anterior mitral valve (3 cases), early diastolic motion of the anterior septum (2 cases), and tricuspid valve prolapse (2 cases) were also observed.

Cardiac catheter studies. These were done in 5 cases.

On ventriculography, apical obliteration of the left ventricle was found in all 5 cases, with enlargement of the left atrium and mitral regurgitation in 4 (Fig. 4a and b). One patient had apical obliteration of the right ventricle and another enlargement of the right atrium. Raised left and right ventricular end diastolic pressures were found in 4 and 5 cases respectively. The end diastolic pressure/peak systolic pressure ratio was high in the left ventricle in 2 cases and in the right ventricle in 4 cases. A 'dip and plateau' appearance was found in one case.

Pathology results

Sixteen cases were studied at autopsy. The weight of the heart in 13 cases varied from 290 to 400 g. In 3 cases the heart weighed 450, 510 and 510 g respectively. There were 9 cases of left sided disease, 6 cases of biventricular and one case of pure right sided disease.

In left sided disease, the most important lesions were endocardial fibrosis of varying thickness, generally from 2 to 5 mm, which had spread to the inflow

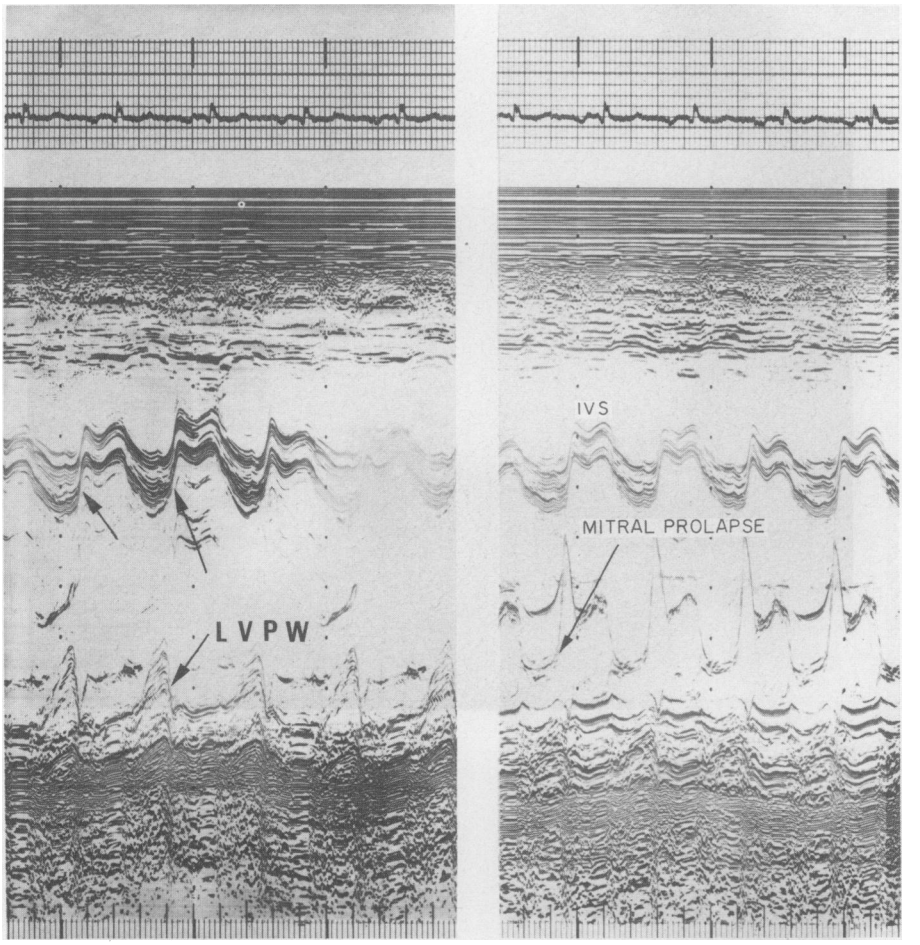

FIG. 3. Echocardiogram M-mode. Normal left ventricular diastolic and systolic diameter. Early outward diastolic motion of the septum and posterior wall. Pattern of mitral pansystolic prolapse. LVPW = left ventricular posterior wall. IVS = interventricular septum.

tract. The ventricular chamber was found to be normal, slightly restricted or enlarged.

The fibrous papillary muscles in most of the cases were in the posterior pillar, the fibrotic lesions produced a certain degree of rigidity of the mitral valves, especially the posterior leaflet. None of the cases showed spread of the fibrotic process to the mitral valves themselves. Narrow bands of connective tissue went from the fibrous plaque to the subendocardial myocardium. Mural thrombosis in different organisational stages was observed in 6 cases.

There were 6 cases with ventricular disease where the fibrous thickening of the endocardium spread to the inflow tracts of both ventricles. The fibrosis extended to the pillars and mitral chordae tendineae in all cases and to the tricuspid chordae in 3. Four cases showed mural thrombosis of the left ventricle. No thrombus was found in the right ventricle.

In the single case of right sided disease there was considerable deformity of the heart due to the gross enlargement of the right atrium, and this case showed the greatest obliteration of the right ventricle which was marked in the inflow tract. The pillars and chordae tendineae of the tricuspid valve were affected by the spread of the fibrosis. A notch on the right edge of the heart was noticed due to the obliteration of the apex of the right ventricle. The other findings in the 16 cases included slight fibrosis irregularly distributed on the pericardium, with no adhesions (in 5 cases) and pericardial effusion in 2

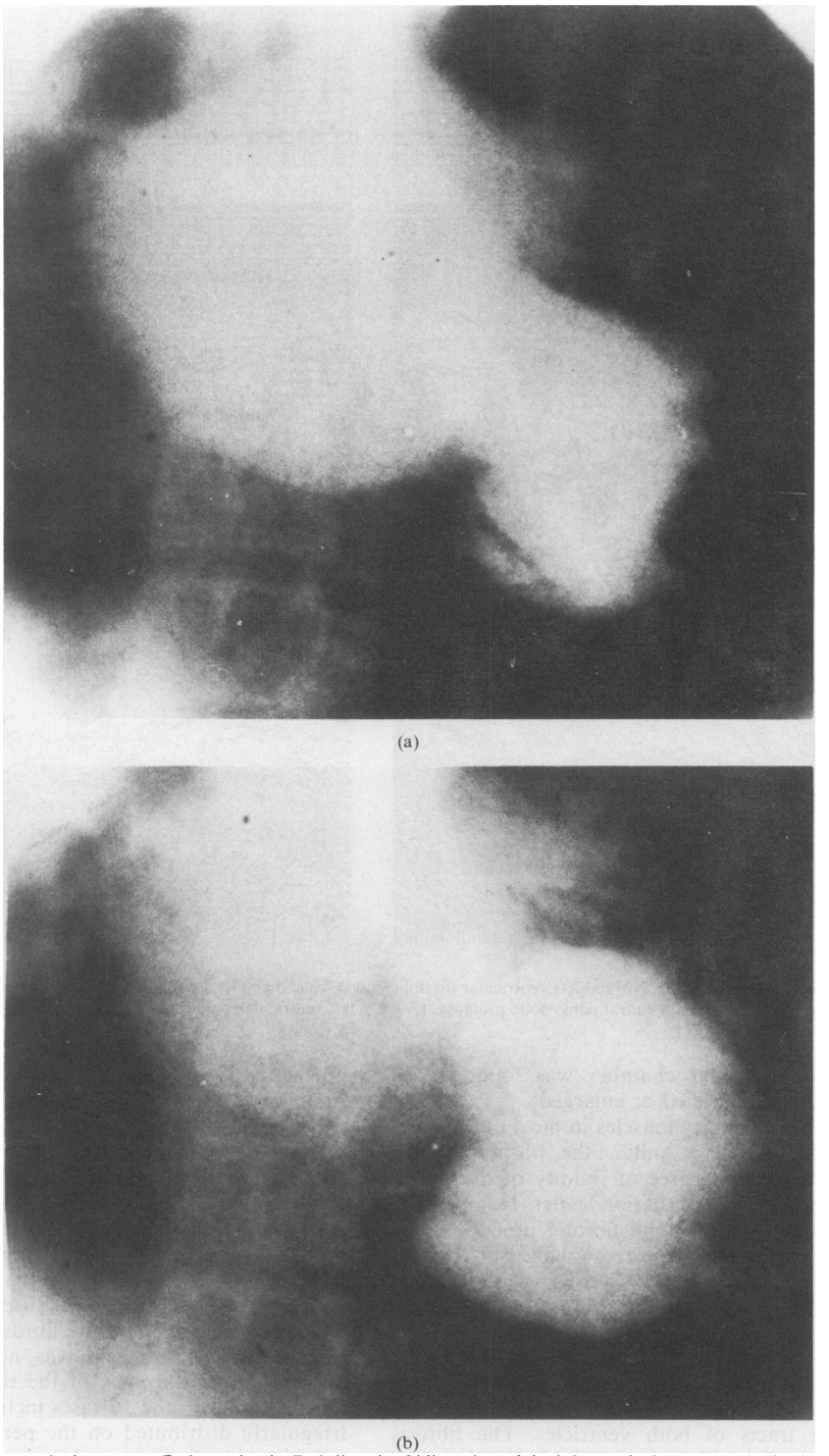

FIG. 4. Left ventriculogram (a) End-systole. (b) End-diastole. Obliteration of the left ventricular apex and mitral regurgitation.

cases. The coronary arteries were normal and no other associated pathology was found.

Microscopic. There was marked thickening of the mural endocardium of both ventricles due to connective tissue with scarce cells and abundant collagen. There was a tendency to a certain degree of stratification, with (1) a layer of mural thrombosis, (2) a band of lax connective tissue, thinner than the previous one, with blood vessels, arterioles and venulae, (3) a variably thick layer in the deeper part, parts of which were very thin and made up of laminae of elastic fibres, fragmented in some areas.

The underlying myocardium showed some bands of collagenous tissue which grew out of the endocardium and showed superficial penetration. The myocardial fibres showed minimum changes.

The 2 cases in which a myocardial biopsy was performed showed thickening of the myocardium with fibrosis spreading to the myocardium; in one case there was eosinophilic infiltration of the myocardium.

Discussion

In Venezuela, the first pathological cases of ED were described in 1967 (Suarez and Suarez, 1967). Although the disease is found in temperate climates, it is more frequent in tropical and subtropical areas, as may be seen from this relatively large series of 23 cases in one hospital in Venezuela, a country of only 16 million inhabitants. Of the total number of cases presented in our study, 21 were racially mixed and 2 were Caucasians who had spent considerable time in rural regions of country. Europeans long domiciled in the tropics have been shown to have the disease elsewhere (Brockington *et al.*, 1967).

In this material, marked eosinophilia was found in 35% of the cases, including 3 cases with a hypereosinophilic syndrome (Cushid *et al.*, 1975).

In 1973, Brockington and Olsen showed that Löffler's endomyocardial disease and endomyocardial fibrosis could not be differentiated from a pathological viewpoint which led to the premise that they were one and the same pathological process at different evolutionary stages; the term eosinophilic endomyocardial disease was proposed for both disorders (World Health Organisation, 1980). Transitory eosinophilia in the early stages has suggested the importance of the eosinophil in the pathogenetic role of endocardial lesions (Spry and Tai, 1976). The association of eosinophilia in 35% of our cases, present in one 8 years before the cardiovascular signs appeared, strengthens this hypothesis and shows an aetiopathogenic similarity with the cases described in Europe. A role for the eosinophil in the genesis of endocardial and endothelial lesions (Oakley and Olsen, 1977) and the importance of degranulation of the eosinophils (Olsen and Spry, 1979) has been proposed.

In most of the cases, the clinical presentation was heart failure, although in over a fifth, systemic embolism was an early or presenting event.

The disease was left sided in 11 cases, biventricular in 11 cases and right sided in one case. This is a frequency that differs from that found in Africa where the biventricular and right sided form predominate.

In the biventricular form, a giant 'a' wave on the jugular pulse, the pansystolic murmur of mitral regurgitation and the early and high frequency third sound were the major physical findings. The giant 'a' wave of endomyocardial disease can be an expression of the right intrachamber obliteration, secondary to the pulmonary arterial hypertension or to a combination of both factors, in the absence of tricuspid stenosis. The early and loud sound has been described as the most important physical sign. In this series it coincided with a sudden anterior protodiastolic motion of the interventricular septum in 3/6 cases, abrupt backward motion of the posterior wall of the left ventricle in 4/6 cases or with both motions in 3/8 cases. These findings reinforce the idea that the early and loud third sound is brought about by a sudden distension of the rigid ventricular chamber ('endocardial knock').

It has been considered that the systolic murmur of mitral regurgitation of the left endomyocardial disease is brought about by the spread of the scar tissue to the chordae tendineae and to the posterior mitral valve. The pattern of prolapse of the mitral valve may be interpreted as being due to the spread of the scar tissue to the posterior mitral valve, with a loss of valvular support, together with the restriction of the ventricular chamber. This pattern of prolapse has a different pathological substratum from that of the prolapse due to myxomatous degeneration of the mitral valve. The same interpretation could be true for the tricuspid valve prolapse.

From the radiological and electrocardiographic viewpoint in this series, predominant enlargement of the left sided chambers was observed. Together with the clinical findings, these suggested mitral and/or tricuspid heart disease of rheumatic origin. The pattern of pericardial effusion with normal sized cardiac chambers and a non-enlarged pericardium on pneumopericardium was seen in 2 cases. Left endocardial calcification is characteristic, but exceptional, in this series.

The findings in the two-dimensional echocardiograph of apical obliteration, reduction of the ventricular diastolic area and atrial dilatation were closely correlated with the results of the angiocardiographs

and postmortems in 5 cases. The two-dimensional echo is therefore most important for the clinical and preoperative evaluation of ED.

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