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CHRONIC CHAGAS HEART DISEASE AND OTHER CARDIOMYOPATHIES IN VENEZUELA

by

J.J. PUIGBO, J.A. SUAREZ, I. BOCCALANDRO, J.R. NAVA-RHODE & J.A. VALERO

Department of Clinical Cardiology, University of Caracas, Venezuela.

INTRODUCTION.

Human infection by *Schizotrypanum cruzi* can produce a variety of heart diseases and it can determine the appearance of immunological changes which are expressed by serological reactions highly specific for the diagnosis. The serological investigation has become a very useful instrument in the epidemiological study of Chagas' disease (Maekelt, 1960). It has been estimated that in vast areas of the American continent there is a high prevalence of human infection by Schizotrypanum cruzi (see Bibliography: Report on Research in Chagas' disease, 1965 and WHO, 1960). In our midst, it is essential to establish a distinction between chronic Chagas' cardiomyopathy and other myocardial diseases of known or unknown etiology.

In order to gain a better knowledge of chronic Chagas' heart disease, information has been gathered from three sources: a clinical and epidemiological study of a rural endemic community, analyses of pathological material and a clinical study of selected cases.

EPIDEMIOLOGICAL STUDY.

The epidemiological study carried out in a Venezuelan rural population (Belén) includes to date:

A. An initial cross-sectional study (1961), 1,210 subjects.

B. A four-year follow-up study (1961-1965), 812 subjects.

Hitherto, the general conclusions of the epidemiological study (Puigbó *et al.*, in press; Puigbó *et al.*, to be published) have been the following (Table I):

TABLE I

EPIDEMIOLOGICAL STUDY (BELEN, VENEZUELA

	CROSS-SECTIONAL SURVEY (PREVALENCE)	FOLLOW-UP SURVEY INCIDENCE IN 4 YEARS
	RATES FOR 100 INHABITANTS	
CHAGAS INFECTION	47.3	16.3
ALL FORMS OF CARDIOPATHIES	17.3	2.2
CHRONIC CARDIOMYOPATHY	16.0	2.2
CHRONIC CHAGAS' CARDIOMYOPATHY	13.2	1.9
CHRONIC CHAGAS' CARDIOMYOPATHY (UNDER 50 YEARS OF AGE)	8.7	1.7

1) High prevalence of Chagas' human infection tending to increase with age.

2) High prevalence of chronic Chagas' cardiomyopathy and low prevalence of other etiological forms of heart disease.

3) The pathological findings confirmed the clinical diagnosis of chronic cardiomyopathy with characteristic features of Chagasic etiology.

4) High incidence of human infection during the four-year follow-up study, proved by serological change. However, during this period of time, the group that suffered this change did not develop heart disease.

5) High incidence of chronic cardiomyopathy with marked tendency to predominate in the seropositive (Chagasic) group.

6) Cardiac failure and sudden death were the main causes of mortality (68.7 %) in the population under control. The fatality rate among patients under 50 years of age with chronic seropositive heart disease was high (7.4 %).

7) Evolutive electrocardiographic patterns were found.

CLINICAL EVOLUTION OF CHRONIC CHAGAS HEART DISEASE.

Based on the information gathered from the epidemiological and clinical study it has been possible to establish tentatively, different evolutive stages of chronic Chagas' heart disease.

The general approach for the diagnosis should be based upon: history of exposure to Chagas' infection, positive complement fixation test specific for Chagas' disease and the exclusion of ischemic, hypertensive, valvular, congenital, pulmonary and obstructive cardiomyopathy.

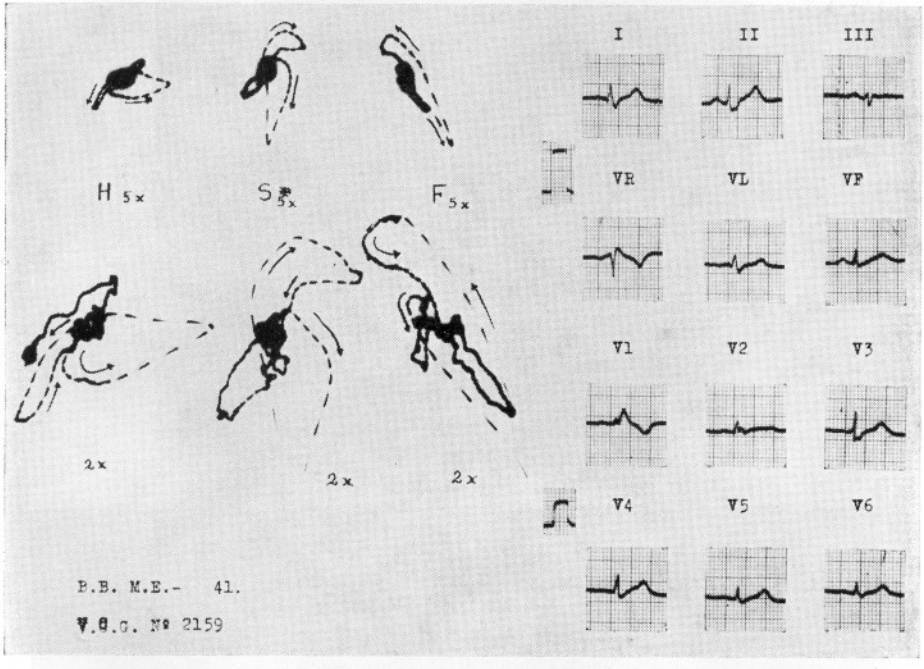


FIG. 1. — E.C.G. : Right bundle branch block. V.C.G. : Right bundle branch block. Absence of important displacement of QRS loop.

Initial stage (Figs. 1, 2)

From a clinical point of view, the patient might be asymptomatic or he might manifest symptoms, generally related to rhythm disturbances, expressed by palpitations, faintness and syncopal attack. There is neither enlargement of the heart nor cardiac insufficiency. The electrocardiogram can show: a) Different evolutive stages of right bundle branch block. Absence of ÂQRSF deviation or slight ÂQRSF deviation

towards the left (up to —30°). b) A primary, persistent, marked and extensive ventricular repolarization disturbance. c) Multifocal ventricular extrasystoles or, d) A combination of these three different abnormalities. In the vectocardiogram no marked displacement of the QRS loop is observed. The X-rays shows an absence of cardiomegaly and, frequently, a localized diminution of the cardiac pulsation.

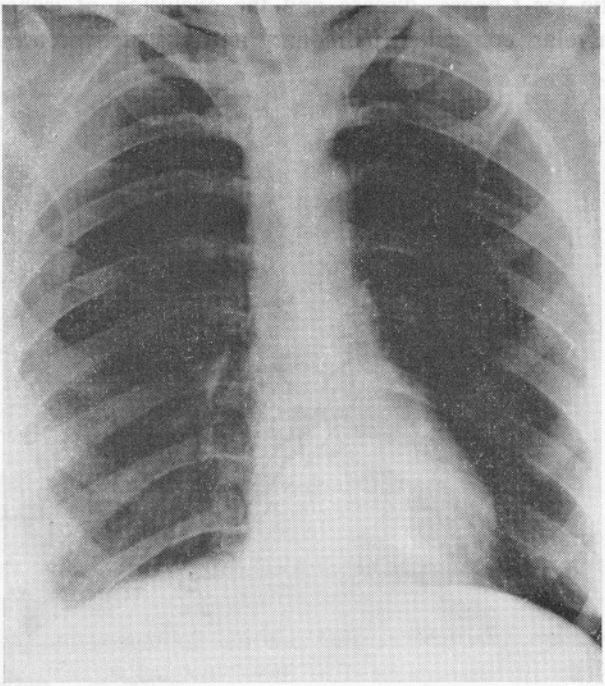


FIG. 2. — Absence of cardiomegaly.

Intermediate stage (Figs. 3, 4)

At this stage, the clinical manifestations either persist or increase. There is slight to moderate cardiomegaly related to the enlargement of

FIG. 3. — E.C.G. : ÂQRSF-50°. Right bundle branch block. Ventricular repolarization disturbance. Possible enlargement of the left ventricle and electrically inactive zone at the anterolateral wall and the apex. V.C.G. : QRS loop deformity due to an inactive zone at the anterolateral wall and the apex. Septal vector was present. rsr' morphology of the E.C.G. in V1 and V2 is related to the displacement of the QRS loop toward the right, due to the presence of the inactive zone. Upper increase of vector 2 in sagittal and frontal planes. Ventricular repolarization disturbance.

FIG. 4. — a. Moderate cardiomegaly. — b. Diminution of the cardiac pulsations of the left ventricle.

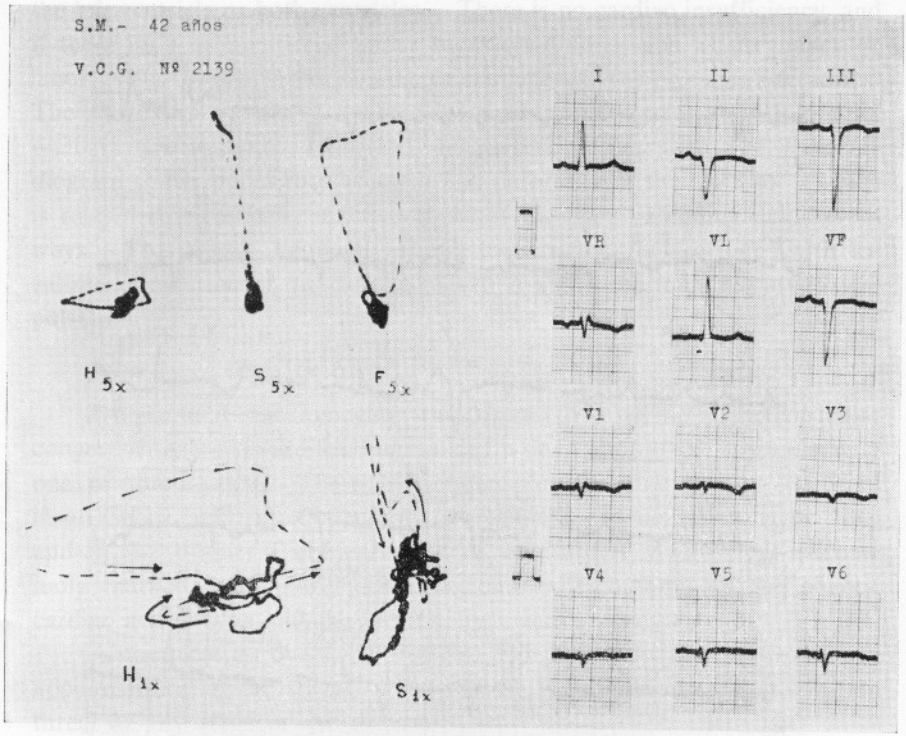
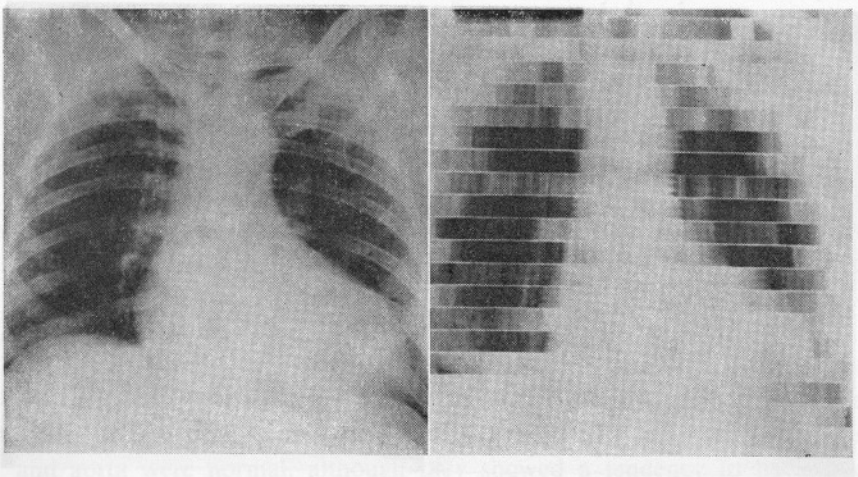

S.M.- 42 años
V.C.G. Nº 2139
I
II
III
VR
VL
VF
V1
V2
V3
V4
V5
V6
H 5x
S 5x
F 5x
H 1x
S 1x

FIG. 3.



a b

FIG. 4.

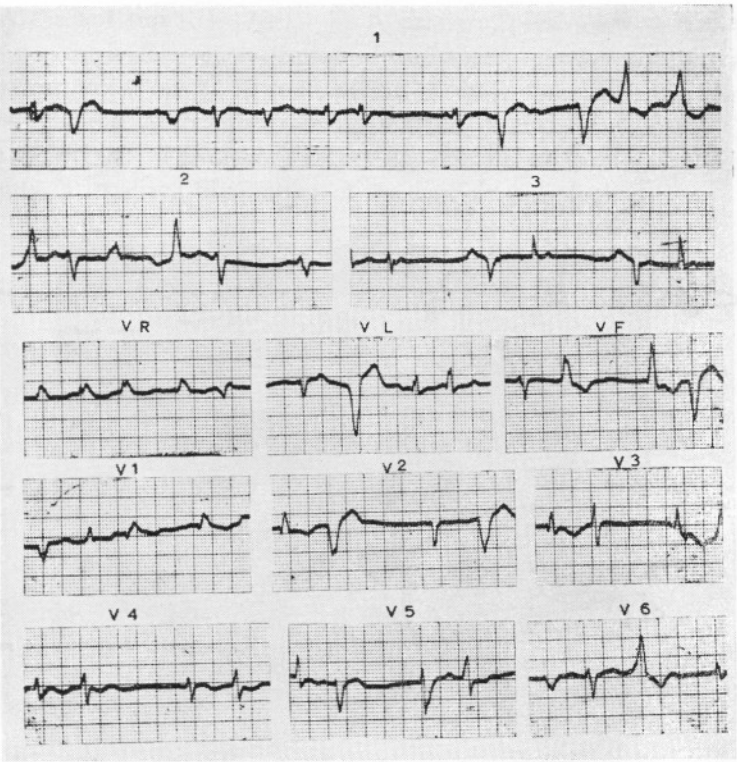
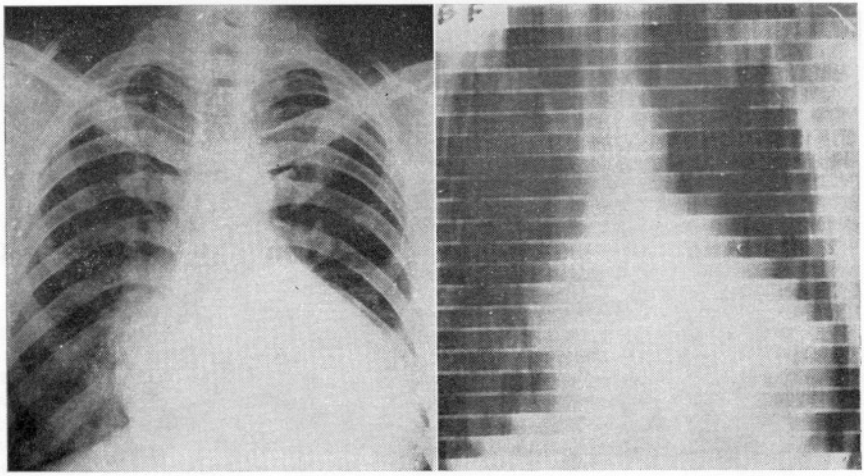


FIG 5. — E.C.G. : Complex arrhythmia of the chaotic cardiac action type.



a b

FIG. 6. — a. Extreme cardiomegaly. — b. Diminution of the cardiac pulsations

the left ventricle or both ventricles. There is no cardiac insufficiency, and if there is, it is manifested under stress conditions such as pregnancy or labor. The electrocardiogram displays increase of the previous alterations. The ÂQRSF is markedly deviated towards the left and upwards (> than —30°). Occasionally, electrically inactive zones appear. The vectocardiogram shows upper displacement and deformity of the QRS loop which is related to electrically inactive zones at the apex extending in different ways. The X-rays frequently shows biventricular enlargement with localized diminution of the cardiac pulsation and, occasionally, paradoxical pulsation.

Final stage (Figs. 5, 6)

Exaggerated cardiomegaly (moderate to extreme). Biventricular congestive heart failure leading to death in a period of approximately one to three years. There is frequent functional mitral or tricuspid insufficiency and thromboembolic phenomena, particularly in the lung and in the brain. Electrical signs of myocardial involvement become more marked, particularly different complex arrhythmia of the chaotic cardiac action type and the electrically inactive zones extend.

A complete atrioventricular block with Stokes-Adams syndrome can appear in any of the stages of the disease. Sudden death is a constant threat at any stage of the disease.

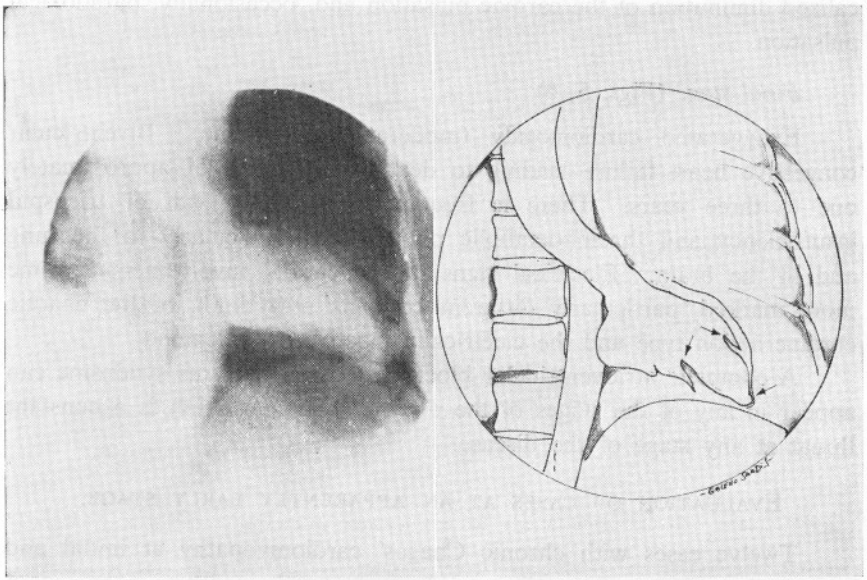
EVALUATION OF CASES AT AN APPARENTLY EARLY STAGE.

Twelve cases with chronic Chagas' cardiomyopathy at initial and intermediate stages of the disease were selected in order to carry out a thorough cardiovascular study, including cineangiocardiography (Puigbó *et al.*, to be published). The electrocardiographic data were extremely useful for the evaluation and localization of the myocardial damage. Complete right bundle branch block associated with an upper displacement and deformity of the QRS loop (related to an electrically inactive zone extending in different ways) was correlated with a higher degree of apical lesion, from a cineangiocardiographic viewpoint, than an isolated right bundle branch block. The kymograms registered localized diminution of the cardiac pulsation in 10 cases.

The hemodynamic data regarding flow, gas analyses, response of arterial pressure to Valsalva's maneuver and on effort, were normal. The values for pressure in the right cavities, pulmonary artery, left cavities and aorta were normal, although they showed a tendency to be at the upper normal limits.

Cineangiocardiographic features of the apical lesion

The cineangiocardiographic study was very useful in establishing and evaluating the myocardial involvement. A slight general dilatation of the ventricular cavity associated with a morphological (apical deformity and mural thinning) and dynamic alteration (emptying and defective contraction of the apex) showed a higher degree of myocardial involvement (Figure 7).



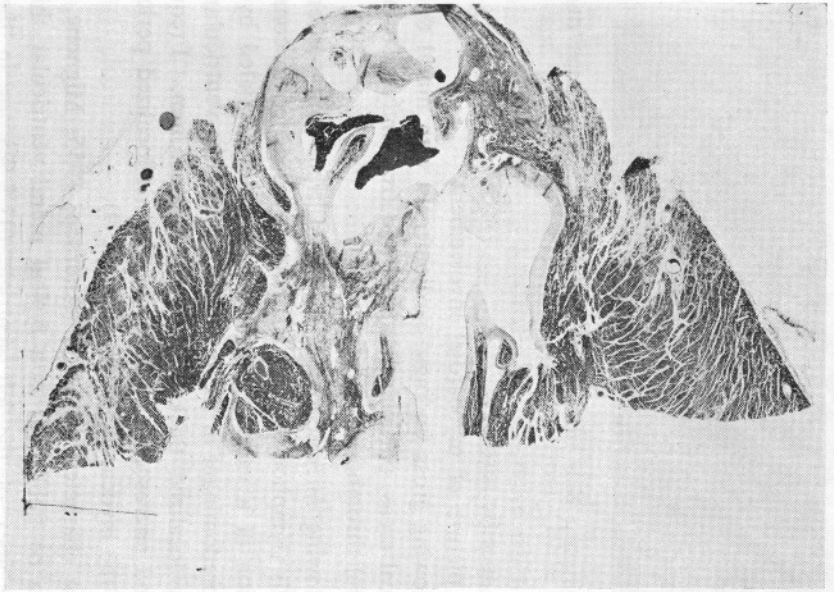
a b

FIG. 7. — Enlargement of the left ventricular cavity. Large deformity of the apical zone. Two fillings defects are present : one at the free border and one at the diaphragmatic border of the left ventricle.

These modifications are probably related to myocardial and endocardial fibrosis of the ventricular apex which becomes a rigid structure with decreased or paradoxical pulsations. The filling defects might be related to folds that occur at the upper level of the apical lesion.

PATHOLOGICAL STUDY OF CHRONIC CARDIOMYOPATHIES IN VENEZUELA.

210 cases of chronic cardiomyopathies have been studied from a pathological point of view, in order to establish and evaluate the patho-



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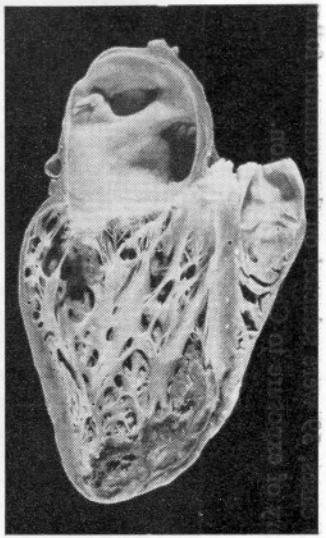

b

FIG. 8. — a. Combined mural thinning at the apex and at the base of the posterior wall of the left ventricle. — Apical mural thrombosis. — b. Frontal section of the apical zone. — Apical thinning of the left ventricle.

logical criteria for chronic Chagas' cardiomyopathy and to classify the material studied (Suarez *et al.*, to be published).

Of these 210 cases, 39 were selected on the common following basis:

a) Past history of exposure to Chagas' infection.

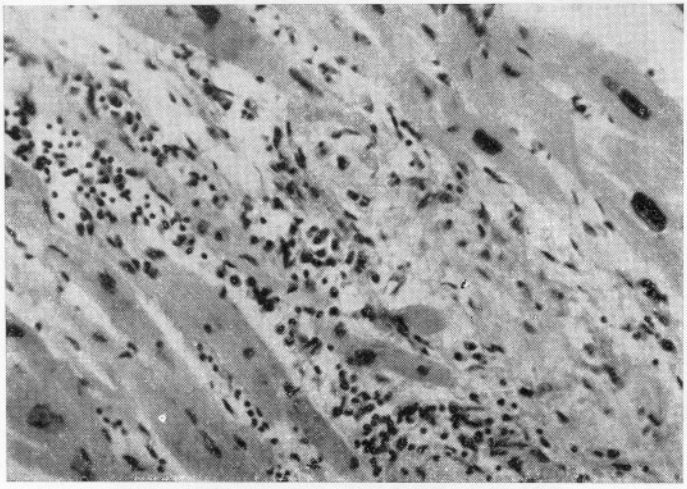

FIG. 9. — Mononuclear cells infiltration associated with myocardial fibrosis.

b) Positive specific serology.

c) Clinical picture of myocardial involvement.

d) The following gross findings: cardiomegaly with mural thinnings localized in typical areas, particularly apical and frequently associated to fibrosis and mural thrombosis.

e) The following microscopic findings: infiltrate with predominant mononuclear cells (lymphocytes and histiocytes) associated to connective tissue proliferation of a varying degree, which is evidentiated by myocardial fibrosis predominant in the inner portions of the ventricular myocardium and by localized thickening of the myocardium. Frequently, there is gross and microscopic evidence of chronic localized pericarditis and of lesion of the myocardial fibers (Figs. 8, 9).

Grossly, the characteristic lesion (Andrade, 1955; Mignone, 1958; Suarez *et al.*, to be published) is a typical mural ventricular thinning, localized at the apex of the left ventricle (91.5 %), or in the right (14.4 %). Other frequent localizations were: posterior wall (21.2 %), lateral wall (11.9 %) and anterior wall (5.9 %) of the left ventricle.

There were isolated forms (64.5 %) or combined (35.5 %). The more frequent combination was the apical thinning and the one at the base of the posterior wall of the left ventricle.

Pathological classification of the material studied.

210 cases of chronic cardiomyopathies out of 3,800 necropsies: 5.5. %

Group I. 160 (76 %) showed pathological grounds for Chagasic etiology. No megaorganisms were found.

Group II. In 22 cases (10 %), the pathological diagnosis of inflammatory cardiomyopathy was related to other entities.

Group III. 28 cases (13 %) had cardiomyopathy with no evidence of inflammatory infiltration.

Post-mortem coronary angiography (10 cases).

Did not show either obstructive vascular lesions in the main, medium sized and small arteries, or abnormal avascular areas.

Study of the intracardiac autonomous nervous system (28 cases).

Slight inflammatory lesions were observed in the ganglia (ganglionitis and periganglionitis) of the right atrium (10 %), and of the left atrium (8 %). Their number did not decrease when compared to the control group. Neuritis and perineuritis were occasional findings.

SUMMARY

This report presents our experience of cardiomyopathies in general and of chronic Chagas' heart disease in particular. It includes results obtained in 1) a follow-up study in a rural population, 2) a clinical study of hospital cases with cardiomyopathies and 3) a pathological study of cardiomyopathies of diverse origin.

1. The epidemiological study was carried out in a rural population (Belén, Venezuela) and included 1,210 persons out of a total of 1,656 inhabitants over five years of age. This study demonstrated a high prevalence of Chagas' infection (47.3 %) and of chronic Chagas' heart disease associated with Chagas' infection (84.8 %). It allowed clinical, electrocardiographic and radiological analysis. This report presents the findings of a four-year follow-up study which established the incidence of infection and that of Chagas' heart disease. The report

includes the clinical, electrocardiographic and radiological analyses of cases with heart disease in the initial survey as well as those presenting with heart disease during the observation period. Evolving electrocardiographic patterns have been found including serial electrocardiographic variations ranging from normal to definite abnormality.

2. The report includes results of a clinical study carried out in a group of hospital cases featuring different forms of cardiomyopathy and presents the findings obtained by angiocardiography and/or cineangiocardiography.

3. The report analyzes the results of the pathological study carried out in some 200 cardiomyopathy cases of diverse origin from a total of 3,800 autopsies performed at the University Hospital of Caracas (1956-1965).

Finally, the report presents the classification of the different varieties found. The great majority (approximately 80 %) displayed characteristics usually observed in chronic Chagas' heart disease. Post-mortem radiography of the coronary arteries was carried out and the intracardiac autonomic nervous system was studied in a group of hearts affected with Chagas' heart disease.

RESUME

Ce rapport présente notre expérience dans le domaine des cardiomyopathies en général et dans celui des cardiopathies chroniques de Chagas en particulier. Il comprend les résultats obtenus au cours de 1) une étude en follow-up dans une population de campagne, 2) une étude clinique des cas hospitalisés avec cardiomyopathies et 3) une étude de anatomo-pathologique des cardiomyopathies de diverses origines.

1. L'étude épidémiologique a été réalisée dans une population de campagne (Belén, Venezuela), chez 1.210 personnes sur un total de 1.656 habitants âgés de plus de 5 ans. Cette étude a démontré une prédominance importante de la maladie de Chagas (47,3 %) et des cardiopathies chroniques de Chagas associées avec l'infection par T. Cruzi (84,8 %). Elle a permis de réaliser une analyse clinique, électrocardiographique et radiologique. Ce rapport présente des observations réalisées au cours d'un follow-up de 4 ans qui a établi la fréquence de l'infection et la fréquence des cardiopathies de Chagas. Le rapport renferme les analyses cliniques, électrocardiographiques et radiologiques se rapportant aussi bien aux cas qui présentaient d'emblée une cardiopathie qu'à ceux chez lesquels l'affection cardiaque est apparue au cours de la pério-

de d'observation. Des aspects électrocardiographiques évolutifs ont été observés, y compris des altérations électrocardiographiques sériées allant d'un aspect normal à une anomalie tout à fait nette.

2. Le rapport renferme les résultats d'une étude clinique réalisée dans un groupe de patients hospitalisés et présentant les diverses formes de cardiomyopathie; les observations obtenues à l'aide de l'angiocardiographie et/ou la cinéangiocardiographie sont décrites.

3. Le rapport analyse les résultats de l'étude anatomo-pathologique réalisée dans quelque 200 cas de cardiomyopathies d'origines diverses, à partir d'un matériel autopsique total de 3.800 cas de l'Hôpital Universitaire de Caracas (1956 à 1965).

Enfin, le rapport présente la classification des diverses variétés observées. La grande majorité (approximativement 80 %) présente des caractéristiques habituellement observées dans les cardiopathies chroniques de Chagas. La radiographie post-mortem des artères coronaires a été réalisée, et le système nerveux autonome intracardiaque a été étudié dans un groupe de cœurs atteints de cardiopathie de Chagas.

RESUMEN

Este informe peresenta nuestra experiencia en al ámbito de las cardiomiopatías en general y en el de las cardiopatías crónicas de Chagas en particular, comprendiendo los resultados obtenidos en el transcurso 1) de un estudio en follow-up entre una población campesina; 2) un estudio clínico de casos hospitalizados con cardiomiopatías y, 3) un estudio anátomopatológico de las cardiomiopatías de diversos orígenes.

1) El estudio epidemiológico se ha llevado a cabo en una población campesina (Belén, Venezuela), entre 1.210 personas sobre un total de 1.656 habitantes en edad superior a los 5 años. Este estudio ha puesto de manifiesto un predominio importante de la enfermedad de Chagas (47'3 %) y de las cardiopatís crónicas de Chagas asociadas a la enfermedad de Chagas (84'8 %), habiendo permitido llevar a cabo un análisis clínico, electrocardiográfico y radiológico. Este informe brinda observaciones realizadas en el transcurso de un follow-up de 4 años que ha establecido la frecuencia de la infección y la frecuencia de las cardiopatías de Chagas. El informe abarca los análisis clínicos, electrocardiográficos y radiológicos relativos, tanto a los casos que presentaban de golpe una cardiopatía como a aquéllos en los que la afección cardiaca apareció en el transcurso del periodo de observación. Se han observado aspectos electrocardiográficos evolutivos, comprendidas alteraciones

electrocardiográficas seriadas que van de un aspecto normal a una anomalía completamente pura.

2) El informe contiene los resultados de un estudio clínico realizado en un grupo de pacientes hospitalizados y que presentaban las diversas formas de cardiomiopatía, describiéndose en el mismo las diversas formas de angiocardiografía y/o la cineangiocardiografía.

3) El informe analiza los resultados del estudio anátomopatológico llevado a cabo en unos 200 casos de cardiopatías de orígenes diversos, a partir de un material autópsico total de 3.800 casos, del Hospital Universitario de Caracas (1956 a 1965).

Presenta por último, el informe, la clasificación de las diversas variedades observadas. La gran mayoría (un 80 % aproximadamente) presenta características habitualmente observadas en las cardiopatías crónicas de Chagas. La radiografía post-mortem de las arterias coronarias ha sido realizada, habiendo sido estudiado el sistema autónomo intracardiaco en un grupo de corazones atacados de cardiopatía de Chagas.

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