MYOCARDIOPATHY IN CHAGAS' DISEASE

I. Comparative Study of Pathologic Findings in Chronic Human and Experimental Chagas' Myocarditis

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I. Comparative study of pathologic findings in chronic human and experimental Chagas' myocarditis

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Great emphasis has been placed in the past on the importance of scattered fibrotic plaques found in heart musculature presenting chronic inflammation due to *Schizotrypanum cruzi* (*S. cruzi*).

Dias and associates[1] have stressed the presence of thinning of several regions in the free ventricular walls, and Laranja and associates[2] have found marked thinning of the left ventricular apex in 3 necropsy cases. These changes have been attributed by other authors[3-8] to confluent fibrotic processes predominating at the apex, producing at times aneurysm-like dilatations of the affected ventricular wall.[3,5,6,8]

Moia[6] was the first to describe thinning of the free ventricular wall and the formation of aneurysms in a case of Chagas' myocarditis at a site other than that classically described. Frequent discrepancies have arisen, also, in regard to the pathogenetic mechanism responsible for the degenerative changes observed in muscular fibers and replacement of them by collagen fibers. It has been suggested that the causative factors of the histologic changes produced by *S. cruzi* are: mechanical destruction of fibers by the parasite,[9-13] toxic[3,14-16] or immunoallergic mechanisms[8,16-28] neurogenetic factors,[23-25] vascular factors,[2,5,26-29] and anoxia of the fibers due to hypertrophy of the interstitial space.[6,30-31]

In the present study, an analysis is made of the pathologic findings in dogs with chronic experimental *S. cruzi* infection. These findings are compared with those in human autopsy material from the Institute of Pathology of the Universidad Central de Venezuela. Finally, an attempt is made to study the changes produced in the ventriculogram by the areas of fibrosis in experimental Chagas' myocarditis, and in the anatomic-electrocardiographic correlations in human beings.

Material and method

Twenty-nine hearts from patients showing a chronic inflammatory process at autopsy were studied histologically. The findings obtained were correlated with corre-

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sponding electrocardiographic changes. The selection of cases was based on clinical and pathologic data. At this point, we should like to add that autopsies 1 to A.2503 were performed without following specific criteria. Although our impression is that there were some cases of chagasic myocardiopathy among them, the correct diagnosis was not confirmed except in Cases A.826, A.1217, A.1731, A.2199, and A.2503. Clinically, the cases selected for study were those which had a suggestive epidemiologic background, a positive complement fixation reaction (CFR) for *S. cruzi*, and clinical and electrocardiographic evidence compatible with that observed in chronic Chagas' myocarditis. From the pathologic point of view, the cases were selected on the basis of macroscopic flaccidity of the myocardium and dilatation of the chambers, with or without mural thrombosis. Microscopically, all these cases had a focal or diffuse inflammatory reaction in the free ventricular and atrial walls of the heart, and an absence of inflammatory reaction in other organs.

A correlation between pathologic and electrocardiographic findings was made in experimental animals. Techniques of infection in dogs, the evaluation of myocardial damage, and the tracing methods employed have been described previously.[30-31] An absence of atherosclerotic coronary lesions was stressed in all of the cases studied.

Preparation of the hearts was as follows: the organ was separated from the structures to which it was attached and was removed from the thoracic cavity. Care was taken to obtain sufficiently long pulmonary and caval veins. After initial washing, 10 per cent formalin was injected into the left and right chambers. The left chamber was injected via a pulmonary vein, with ligatures placed on the other pulmonary vein and the aorta; and the right chamber was injected via a superior vena cava, with previous ligation of the inferior vena cava and the pulmonary artery. Injection pressure was 50 ml. of water. The heart was then submerged in 10 per cent formalin for 5 days so that it would retain its natural shape and size.

Sections perpendicular to the longitudinal axis, from apex to base, were made at 5-mm. intervals. For histopathologic study, blocks were taken from the anterior, lateral, and posterior surfaces of the left ventricle, and from the anterior and posterior surfaces and edge of the right ventricle. Superior, middle, and inferior areas of these were selected for sectioning. Blocks from the middle, superior, and apical areas of the interventricular septum were also taken.

Areas of intense and generalized fibrosis and their surroundings, and areas with thinning of the ventricular wall were included in those blocks in order to analyze the affected regions plus the ones around them. Sections were stained with hematoxylin-eosin, Gomori, and Van Gieson stains.

An important reduction in thickness was taken as the criterion of thinning of the free ventricular wall, together with normal thickness in the neighboring areas. In the right ventricle, with normally thin walls, the criterion for decreased thickness was translucency of a given area.

Results

I. Gross anatomy. Hearts from patients with chronic myocardiopathy of chagasic origin present a macroscopic increase in total volume due to dilatation of the chambers. The degree of dilatation was significant and was present in all chambers in most of the cases studied; Table I shows the degree of dilatation, on a scale of I to IV, in each case. Only 3 cases (A.2769, A.3057, and A.3293) showed scant dilatation, but this was in conjunction with hearts of smaller size.

An important reduction in the thickness of the free ventricular wall was found in the majority of cases. Few hearts had walls of normal thickness, for the reason that hypertrophy of the heart was related to weight, which varied from 260 to 785 grams.

In experimental cases, chronic Chagas' infection (with a duration longer than 1 year and frequent reinfections) produces significant dilatation of all chambers, although the right ventricle is found to be affected more frequently. Fig. 8 shows the results of a 5-year infection in a dog; there is dilatation of all chambers, with a significant decrease in the thickness of the free left ventricular wall and thinning and fibrosis of the free right ventricular wall.

Table I. *Postmortem findings in 29 human cases*

Autopsy number	*Dilatation*							*Thrombosis*					
	Age (yr.)	*Sex*	*LA*	*RA*	*LV*	*RV*	*RVOT*	*RA*	*LAAp*	*RAAp*	*LV*	*RV*	*Heart weight (Gm.)*
A. 826	26	F	III	IV	IV	IV	IV			+	+	+	630
A.1217	48	M	II	III	III	IV	III				+		685
A.1731	21	M	III	IV	IV	IV	III			+	+	+	600
A.2199	50	F	II	III	III	III	III			+	+		520
A.2503	66	F		I	I	II	I				+		316
A.2721	36	F	II	II	III	II	I				+		480
A.2769	45	F			I	I							260
A.2930	15	F	I	I	III	II	III			+	+		455
A.2952	64	M	II	II	II	I	II			+			498
A.2954	44	F	I	II	II	II	III						490
A.2971	40	M	II	III	II	III	III			+	+	+	436
A.2981	40	M	III	III	IV	IV	IV			+		+	424
A.2984	66	M	II	III	III	II	III	+		+	+		464
A.3057	22	F		I		I	II						275
A.3093	68	F	II	III	II	II	II		+	+			502
A.3096	32	M	II	II	II	III	III			+	+		414
A.3116	18	F	II	III	II	III	III						400
A.3177	66	F	II	III	II	II	III					+	370
A.3183	32	F	III	III	III	III	III						665
A.3185	58	M	III	IV	IV	III	IV			+			498
A.3197	34	M		I	II	II	II			+			438
A.3199	64	F	II	III	II	III	II			+			320
A.3247	54	M	I	III	III	II	II						510
A.3250	55	F	I	II	II	II	II			+	+	+	300
A.3253	66	M	II	III	III	III	III				+	+	532
A.3286	33	M	III	IV	IV	IV	IV			+	+		785
A.3293	48	M				I	I				+		290
A.3320	55	M	II	III	II	III	III			+	+		620
A.3362	45	M	III	III	II	III	III			+			487

LA: Left atrium. *RA:* Right atrium. *LV:* Left ventricle. *RV:* Right ventricle. *RVOT:* Right ventricular outflow tract. *LAAp:* Left atrial appendage. *RAAp:* Right atrial appendage.

Table II. *Type and distribution of lesions in human cases (postmortem study)*

Single lesion: (5 cases)	3 cases with fibrosis and thinning at LV apex 1 case with fibrosis and thinning at the superior aspect of the RV posterior wall 1 case with fibrosis and thinning at the superior aspect of the posterior wall of the LV
Multiple lesions:	6 cases: LV apex—Posterior wall LV 1 case: LV apex—Lateral wall LV (high) 1 case: LV apex—Anterior and lateral walls LV 1 case: LV apex—Anterior and lateral walls LV Posterior wall RV 1 case: LV apex—Posterior wall LV—Middle intraventricular septum 1 case: LV and RV apex—Anterior wall LV 2 cases: LV and RV apex—Posterior wall LV 1 case: LV and RV apex—Lateral and posterior wall of LV 1 case: LV and RV apex—Posterior wall LV Posteroinferior intraventricular septum 1 case: RA—Posterior and anterior walls RV

Both the human and canine hearts showed significant muscular flaccidity; the organs were easily depressed under pressure and showed creases when placed over a hard surface.

Of the 29 human cases studied, 21 presented the previously described anomalies; 8 did not show thinning or extensive fibrosis in the cardiac walls. Of the 21 pathologic cases, 5 showed a single lesion (fibrosis and thinning of the right or left free ventricular wall) and 16 showed multiple lesions (fibrosis and thinning in several zones of the heart). The distribution of the anomalies is shown in Table II. The lesions found were of an irregular round shape, and they varied in size from 1 to 4 cm.

Fig. 1 (A.3185) shows the typical ventricular dilatation with thinning of the ventricular wall in the anterior and posterior regions. The lateral wall shows a semicircular fibrotic zone extending from the anterolateral surface to the posterior surface, and small foci of fibrous tissue in the subendocardium. The translucent zone at the apex of the left ventricle is due to an extensive area of fibrosis which produced a foliaceous thinning at that level.

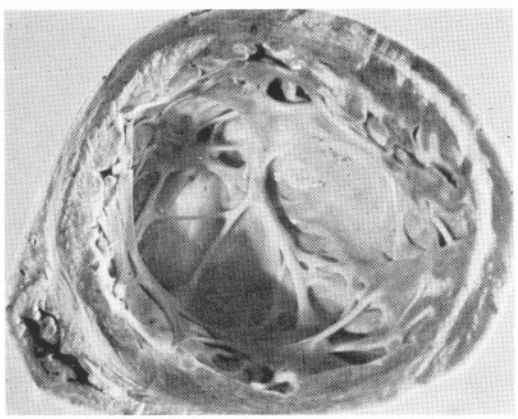

Fig. *1*. Transverse section at the level of the inferior half of a heart (A.3185) with chronic myocarditis of *S. cruzi* origin. Marked dilatation of the LV is observed, with an increase in trabeculation and significant thinning of the wall. Heart weight was 498 grams. There is an extensive and dense fibrotic plaque at the lateral aspect of the wall, and smaller fibrous plaques dispersed through the muscular tissue. The apex of the LV is translucent as a result of thinning of the foliaceous type consisting of collagenous connective tissue.

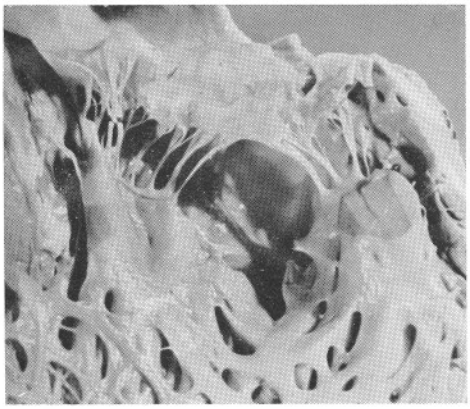

Fig. *2*. Aneurysmal dilatation, 4 by 3 cm., located at the posterosuperior zone of the LV wall, immediately below the A-V sulcus. As seen from the interior of the LV chamber, the wall is translucent at the subvalvular mitral area. Wall thickness was 1 mm. and consisted of a fibrous plaque. Heart weight was 320 grams (A.3199). Dilatation was most marked in the right chambers.

Eight of the same 29 human cases had aneurysmal formation as follows: at the level of the left ventricular apex in 6, and in the posterosuperior portion of the left ventricle in the subvalvular zone of the mitral valve in 2.

Fig. 2 (A.3199) shows an aneurysmal dilatation in the superior portion of the posterior wall of the left ventricle. When seen from the inside of the left ventricle, this area shows translucency of the wall behind and below the posterior leaflet of the mitral valve.

Fig. 3 (A.3286) is from another case with striking thinning of the left ventricular wall at two places. One site is at the apex and the other is in the posterior wall at the level of the atrioventricular sulcus, immediately behind the posterior mitral leaflet. This zone also shows aneurysmal formation, 3.5 cm. in diameter, which extends through the thinnest area. It is important to emphasize that not all the attenuated areas showed aneurysmal dilatations.

Thinning and fibrosis were equally evident in the experimental animals. Fig. 4 is from a dog (LXI, P8) with a 2½-month-old infection. Fibrotic foci (localized at the subepicardium) are observed at the apices of both the left and the right ventricles, more extensively at the inferior portion of

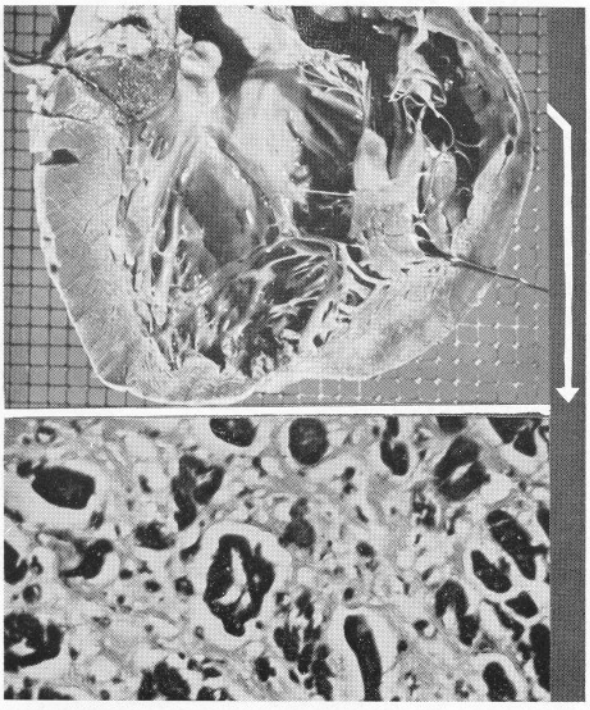

Fig. *3.* Anteroposterior section parallel to the interventricular septum (A.3286). Marked dilatation of the LV chamber and an increase in trabeculation is observed. Heart weight was 785 grams. Significant dilatation of the free ventricular wall seen at the apex and in the superior aspect of posterior wall of the LV. The latter one, localized below the A-V sulcus and behind the posterior mitral leaflet, shows a 3.5-cm. aneurysm. Histologically, this consisted of dense collagenous connective tissue with islets of muscular fibers undergoing variable degrees of degeneration (Gomori trichrome, ×320).

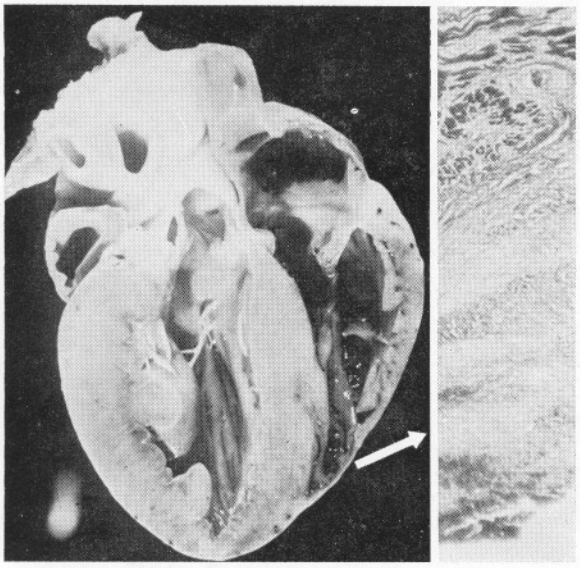

Fig. *4.* Dog heart (LXI, P8) as seen from its posterior aspect. Duration of *S. cruzi* infection, 2½ months. Marked dilatation of the RV chamber and, in lesser degree, of the RA are seen. Thinning of the wall at the inferior aspect of the anterolateral surface of the RV. Intramural thrombus adhered to the endocardium. Extensive fibrosis consisting of collagenous connective tissue and muscular islets. Fibrotic plaques became confluent near the subepicardium (Gomori trichrome, ×125).

the anterolateral surface of the right ventricle. The ventricular wall is considerably diminished at this level, having a thickness of 0.5 mm. at the most affected portion.

In both the human and animal hearts an attempt was made, by the use of serial sections, to find vascular changes, especially around the compromised tissues. Arterial or arteriolar lesions were not found in any of the cases studied. No necrotic areas were found in either the sites of wall thinning or in any other myocardial region.

II. Microscopic anatomy. Fibrotic foci were found in the markedly thin regions of the free ventricular walls. Histologically, these were composed of collagen fibers. In those cases depicted in Figs. 1 and 2 the translucent zones were 1 mm. in thickness and were composed of scar connective tissue and scanty inflammatory infiltrates. Similarly, the marked thinnings observed in the hearts of chronically infected dogs were composed predominantly of collagen fibers and some mononuclear cell infiltrates. In some dogs the Leishmanial form of the parasites were present in the myocardial fibers. The parasites were not encountered in human hearts.

Fig. 4 (LXI, P8) shows in the anterolateral surface of the right ventricle a 0.5-mm. thin area which is formed by dense collagenous connective tissue, with some islets of muscular fibers that show various degrees of degeneration and few inflammatory infiltrates.

Muscular fibers located within fibrotic tissue were more abundant in the less involved areas. These islets of muscle with variable degenerative changes are particularly evident in the subepicardium; on the

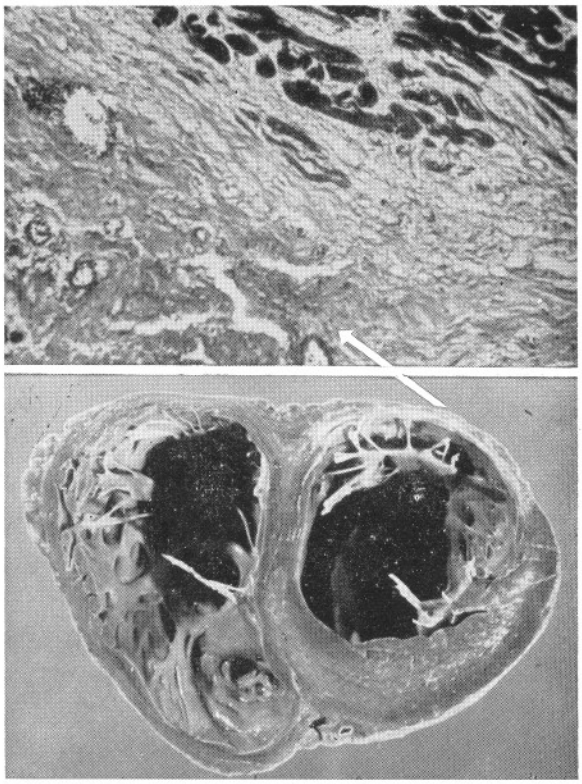

Fig. 5. Transverse section at the superior third of a human heart (A.3183). Marked dilatation of both ventricular chambers and the right ventricular outflow tract is observed. Thinning of the LV posterior wall consisting of a fibrous plaque which is most dense at the subendocardium. The plaque consists of collagenous connective tissue and muscular islets. The latter are scarce in the subendocardium but become numerous as the subepicardium is reached, where bundles are more dense and widespread (Gomori trichrome, ×250).

other hand, fibrous tissue predominates in the subendocardium. The mononuclear cell infiltrate was greater in those subepicardial areas in which muscular islets were more numerous.

Fig. 5 (A.3183) shows a heart with dilatation of both ventricular chambers. The posterior wall of the left ventricle is moderately thinner than the posterior wall of the right ventricle. It consists of a plaque of dense subendocardial fibrous tissue. Histologic study showed fibrous tissue with few inflammatory infiltrates in the subendocardium, and collagenous plaques with interposed muscular islets in the subepicardium. Variable degenerative changes were observed in the muscular fibers.

The microscopic study of the coronary system indicated an absence of atherosclerotic degenerative lesions in both the arterial and arteriolar segments. This was also true in the vessels located around the thin fibrotic areas.

III. Correlation between histologic and electrocardiographic findings. A study of the morphology of ventricular complexes of supraventricular or ectopic origin demonstrated the presence of areas of fibrosis.

Fig. 6 is from a patient (A.1731) with thronic Chagas' myocarditis. The heart weighed 600 grams and showed marked dilatation of all chambers. The thickness of both ventricular walls was markedly diminished; extensive confluent scars which formed large fibrous plaques were observed at the anterior surface of the left ventricle, from the anteroseptal region to the apex. An aneurysm, 1.5 cm. in diameter, was observed at this level. Equally large fibrous plaques were observed on the anterior surface of the right ventricle, becoming more confluent in the transtrabecular area. The electrocardiogram showed: first-degree A-V block, notched, full P wave of 0.12 sec. duration in the standard leads and diphasic, with slow negative phase, in Precordial Lead V_1, slightly acuminated in Leads II and V_F. QRS and P voltages were similar

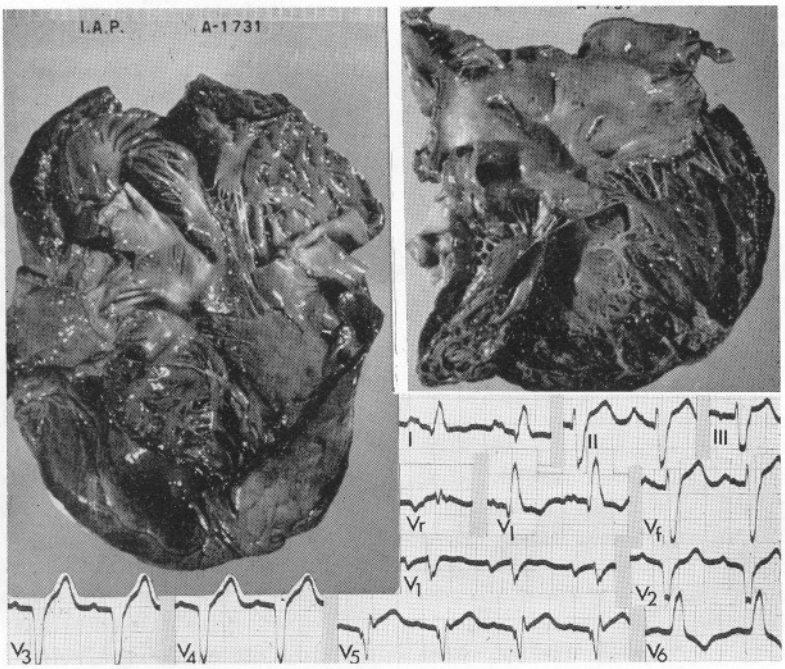

Fig. 6. Correlation between histologic and electrocardiographic findings in case A.1731. Ventriculograms show morphologies of type rS in V_1 and QS in V_2-V_5, indicating a zone of nonexcitable tissue oriented toward the anterior surface of the heart. Marked dilatation of the heart. Heart weight was 600 grams. Extensive fibrous plaques on the anterior surface of the heart (trabecular zone of RV, anteroseptal surface and apex of LV). V_5, oriented toward the apex, shows a discrete positive imbalance of the ST-T segment, indicating the presence of an aneurysm at the LV apex. The coronary system was intact.

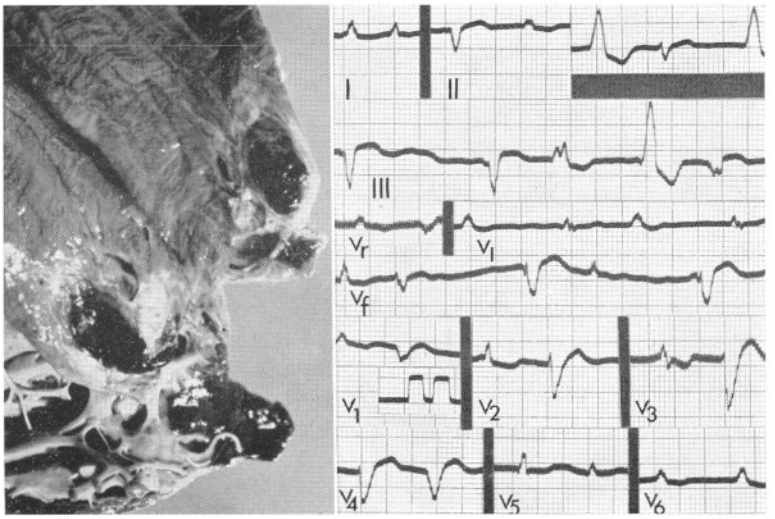

Fig. 7. Same correlation as in Fig. 6, in case A.2199. Extrasystolic ventricular complexes of QS type in V_2 and V_3, and qrS morphologies in V_F indicate the presence of a posteroinferior nonexcitable zone. Extrasystolic QS from V_1 to V_4 and the decrease in R in the extrasystolic complex in V_2-V_4 indicate an anteroseptal and LV apical nonexcitable zone. There was thinning and confluent fibrosis in these areas, with large irregular plaques in the posteroinferior and anteroseptal aspects and apex of the LV. The positivity of the ST-T in V_2, V_3, V_F, V_1-V_4 corresponds to aneurysmal formation at the apex. The coronary system was intact.

in the left ventricle. These changes correlate well with the marked dilatation observed in both atrial chambers. QS complexes observed in Leads V_2 to V_5 indicate the presence of an electrically inactive zone throughout the anterior surface of the heart. Histologic sections of the anterior surface of both ventricles demonstrated that the fibrous plaques present consisted of dense collagenous connective tissue with small muscular bundles and few inflammatory infiltrates. The wall was composed exclusively of collagenous connective tissue at the level of the trabecula and apex of the left ventricle.

The heart depicted in Fig. 7 (A.2199) showed marked dilatation and a decrease in ventricular wall thickness. The wall was 10 mm. thick in the superior portions but decreased to 2 mm. at the apex. There was a diffuse fibrosis throughout the wall, and this became interrupted at the apex and at the anteroseptal and posteroinferior surfaces of the left ventricle, forming quite extensive irregular plaques. Several aneurysms with thrombi were observed at the left ventricular apex. The electrocardiogram showed a complete arrhythmia due to atrial fibrillation and frequent multifocal ectopic beats. The extrasystolic morphology is of the QS type in Leads II and III, and of the qrS type in Lead V_F, indicating the presence of an unexcitable area at the posteroinferior surface of the heart. Extrasystoles of the QS type are observed in Precordial Leads V_1 and V_4. A significant decrease in the R voltage in the extrasystolic complex is observed from Lead V_2 to Lead V_4; these changes suggests a nonexcitable zone at the anteroseptal and apical surfaces of the left ventricle. The ventricular wall was found to be formed by dense collagenous connective tissue and a few bundles of muscle fibers forming isolated islets.

The electrocardiographic tracings in animals demonstrated a correlation with those recorded in human beings. Fig. 8 shows the heart of an animal with a chronic infection; there is a marked dilatation and decreased thickness of the free ventricular walls. Fibrous and irregularly distributed plaques are observed on the epicardial surface, and at the lateral surface of the right ventricle. The wall is formed by collagenous connective tissue and a few inflammatory infiltrates in the inferior and trabecular regions. Confluent interstitial connective tissue and intermediate muscular islets are seen in the

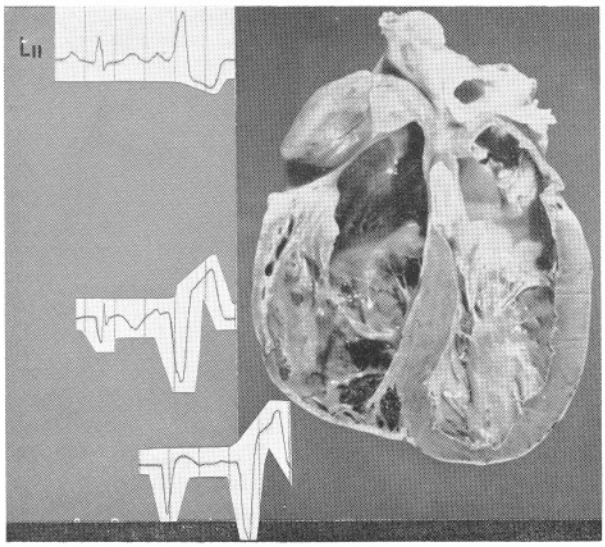

Fig. 8. A similar correlation in a dog with chronic *S. cruzi* infection of 5 years' duration. Unipolar epicardial tracings of supraventricular and ectopic ventricular origins (RV) obtained at the trabecular zone show morphologies of the QS type, indicating the presence of a nonexcitable zone in the area neighboring the one studied. Those of the lateral aspect of the RV wall show morphologies of QRs type in the supraventricular complexes, and of QS type in those of ectopic origin. The trabecular zone consisted of collagenous connective tissue. The lateral aspect showed interstitial connective tissue confluent in the subendocardium and subepicardium, forming dense areas of fibrosis. The mid-portion of the wall showed muscular islets surrounded by collagenous connective tissue. The coronary system was normal.

subendocardium and subepicardium at the middle zone. Unipolar epicardial tracings from the inferior and trabecular zones showed QS morphology in supraventricular or ectopic complexes originating in the right ventricular wall. Supraventricular complexes obtained at the middle zone of the right ventricular wall showed QS morphology. Extrasystolic complexes originating in the right ventricle were of the QS type. These findings suggest the presence of a nonexcitable zone adjacent to the origin of the leads, which coincides with the areas of fibrosis described.

Discussion

Flaccidity and dilatation are commonly seen in chronic inflammatory cardiopathies, both in those of *S. cruzi* origin[1-8,32,33] and in those of any other etiology.[20,34-36] Flaccidity was found in all of our human and experimental cases. Dilatation of the chambers was marked in 25 of the autopsy cases, moderate in 1 (A.2503), and slight in 3 (A.2769, A.3057, and A.3293). The left atrium was less affected by dilatation in those cases of slight or moderate hypertrophy, but showed a dilatation proportional to that of the other chambers when hypertrophy became marked. In 2 of the cases with slight cardiac enlargement (A.3057 and A.3293) the right chambers were affected the most. In the third case (A.2769), dilatation was evident in both ventricles. The cases with marked enlargement showed dilatation of all chambers, with no particular pattern of predominance.

Intramural thrombosis was a frequent finding, as demonstrated by Tejada and Castro[8] and Franco de Oliveira.[7] The frequency of this finding was 79.3 per cent in our study in the human cases with predominance of the right chambers (right atrial appendage–RAAp: 3.4 per cent; RA: 58.9 per cent; RV: 24.1 per cent) as compared to the left chambers (LA: 3.4 per cent; LV: 51.7 per cent). No thrombi were found in the left atrial appendage (LAAp) or in the right ventricular outflow tract (RVOT), in spite of the marked degree of dilatation evident in both the LAAp and the RVOT. Independently of other chambers, the left ventricle showed a higher frequency of thrombi than did the right ven-

tricle, as has been reported previously by Tejada and Castro.[8]

In general, hearts with more marked dilatation showed a greater frequency of thrombosis in the various chambers, although marked cardiomegalies without accompanying thrombosis were also observed (A.3116, A.3183, and A.3247). In general, slight dilatations are not accompanied by thrombosis; in our 3 cases, thrombi were not found in 2 (A.2769 and A.3057), and a left ventricular thrombosis was seen in 1 (A.3293). It was noted that the thrombosis appeared in a left, nondilated chamber.

Laranja and associates[37] found that chronically infected dogs showed, after a few months, hypertrophy of the right chambers. In our series, dilatation was found in all chambers in advanced stages of the disease; predominance of the right chamber was observed only in the early phases. Intramural thrombi were found in 11 per cent of the animals with chronic infection, as compared with a higher percentage in human beings; these thrombi were localized, 8 per cent in the right ventricle and 3 per cent in the left ventricle.

Thinning of the free ventricular walls was a frequent finding in our autopsy material. Similar findings had been reported earlier in pathologic studies of chronic Chagas' myocardiopathy.[10,14] Dias and associates[1] and Laranja and associates[2] stressed the frequency of thinning at the left ventricular apex, as produced by confluent fibrosis,[3-8] which subsequently produces aneurysmal dilatation at times.[3,5,6,8] Moia[6] reported the first case with thinning and aneurysmal formation in a different localization. Two of his 3 cases presented the classic findings, but the third one had aneurysmal formation in the anterior surface of the left ventricle, below the atrioventricular sulcus. Frequency and distribution of thinning and aneurysmal formation were analyzed from a statistical point of view by Suarez,[38] whose figures are very similar to those in the present study.

Chagas' infection causes in animals (monkeys, dogs, etc.) a degeneration of cardiac fibers and the proliferation of fibroblasts in a relatively short period of time. These changes appeared in some of our animals during the fourth week after primary infection, coincidental with an intense inflammatory infiltrate. Torres and Tavares[39] found that degeneration of cardiac fibers becomes evident 3 months after inoculation in the species *Macacus cebus*. This period can be considered to be a time of expected fluctuation in the appearance of fibrotic lesions in experimental myocardiopathy. Fibrosis appeared very early in some of our dogs, with a decrease in the thickness of the wall being evident 2½ months after the primary infection. Thinning plus extensive fibrosis were more common in the free wall of the right ventricle in experimental animals.

Microscopic study of the thin areas demonstrated that the histologic pattern is the same in human and experimental cases. When thinning is extreme (foliaceous type) and extensive, fibrous plaque is found, which consists of collagenous fibers and almost no inflammatory infiltrate. In less extensive lesions, bundles of muscular tissue are seen within the fibrous tissue; these islets show fibers undergoing variable degenerative processes, and are more numerous in the cases of less pronounced thinning. Mononuclear cell infiltrate is greater in those areas in which islets are abundant.

Laranja and associates[2] explain the decrease in the thickness of the walls as a result of extensive destruction of myocardial fibers, together with replacement by connective tissue. The destruction is the result of a diminishing supply of blood, which is, in turn, secondary to hyperplasia of the intima and thickening of the medial arteriolar layer, with a subsequent reduction in the caliber of the lumen of the vessel. Wainrach and associate[4] interpret the fibrosis as scarred infarcts which result from the inflammation of capillaries, arterioles, and perivascular tissue which produces coronary thrombosis. Coronary or necrotic lesions were not found in our study; therefore, the fibrosis cannot be ascribed to myocardial infarction.

Moia[6] did not find arterial lesions in 2 of his 3 patients, but reported moderate arteriosclerotic lesions in the larger coronary branches in the third one, a 52-year-old woman. Tejada and Castro[8] failed to find vascular changes in 8 patients with widespread fibrosis. On the basis of all these reports, it is our thought that fiber degeneration and fibrous replacement with subsequent thinning of the wall cannot be

explained by ischemia due to coronary occlusion.

Moia[6] believes that the causative factor is the myocardial inflammatory process originated by the disease per se; he suggests that the dense fibrosis of limited areas is related to regions in which inflammation and destruction of muscular elements are more intense. Pifano and associates[30] and Anselmi and associates[31] demonstrated that the close relationship between the degree of degeneration of muscular elements and the intensity of the inflammatory process in experimental myocarditis originated from alterations in the supply of oxygen caused by increases in the interstitial space due to edema and inflammatory infiltrate. In chronic Chagas' myocardiopathy it has been possible to demonstrate that rapid ventricular complexes in the electrocardiogram identify electrically nonexcitable zones which correspond to fibrous areas[40,41]; this has been confirmed in our study, in both autopsy and experimental series. Nonexcitable zones are related to a predominance of fibrous tissue in the areas to which the exploratory electrode is directed. Replacement of muscular tissue by collagen fibers caused important changes in supraventricular and ectopic ventricular ventriculograms. QR, Qr, and QS extrasystolic morphologies, indicative of nonexcitable zones, were the ones most usually observed. An analysis of the different leads permitted an appraisal of the localization and extent of the areas of fibrosis. The physiopathology of ventricular activation which originates these morphologies has been demonstrated in experimental studies[42,43]; their appearance depends on the presence of ventricular fibrosis or necrosis.

In cases of aneurysmal dilatation it was possible to observe the classic positive imbalance of the ST-T segment which is pathognomonic of these pathologic findings.[44] Even when electrocardiographic findings of ischemia are related to the presence of inflammatory infiltrates in Chagas' myocardiopathy,[31] the combined presence of nonexcitable tissue and areas of injury should suggest the presence of aneurysms in the wall.

Summary

Pathologic findings in 29 individuals with a clinical picture of chronic Chagas' myocardiopathy are analyzed. Both macroscopic and microscopic changes are studied, and are correlated with similar findings in dogs infected with strains of *Schizotrypanum cruzi*.

Flaccidity and dilatation was frequently found in both the human and experimental cases. Dilatation was more common in the right chambers of the hearts of the dogs, particularly in the right ventricle. Intramural thrombosis was frequent in human subjects (79.3 per cent), but was observed with less frequency in animals (11 per cent). Thinning of the wall and plaques of fibrosis were found, respectively, in 72.4 and 42 per cent of the cases in the human and animal groups. Parietal aneurysms localized in the areas of fibrosis and thinning were found in 27.6 per cent of the autopsy cases. Aneurysms of the wall were not found in dogs, but they were seen in the trabecular zone of the right ventricle in 7 animals. Aneurysms were of variable diameter (1 to 3 cm.) and disappeared when the animal died. Thinning of the wall by fibrous replacement of muscular tissue was found in all of the cases.

The histologic pattern of the thin areas was similar in both groups; large areas of collagenous connective tissue at the subendocardial level were found. Also, islets of muscular bundles were found at midwall and subepicardium. They were particularly abundant in the latter localization.

An electrocardiographic correlation demonstrated that epicardial unipolar leads obtained at the areas of fibrosis in dogs had the ventricular morphology of nonexcitable zones. In human beings, ventriculograms of both supraventricular and ectopic ventricular origin always indicated the presence of areas of fibrosis, the localization and extent of which could always be determined by an analysis of the different leads.

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