MYOCARDIUM OF THE LEFT VENTRICULAR APEX OF CHAGASIC HEARTS: MORPHOLOGIC AND MORPHOMETRIC ASPECTS

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ABSTRACT : We studied the behavior of the apex myocardium in 10 control hearts and 10 hearts with aneurysm of the apex by using morphometry. Besides the alterations in regards to the cardiomyocytes, we studied the fibrous connective tissue and vascular alterations. The results were submitted to statistical analysis by the qui-square test and confronted with the pertinent literature. Significant decrease of cardiomyocytes and capillaries was verified as well as accentuated increase in the amount of fibrous tissue. In addition, the remaining cardiomyocytes have suffered considerable hypertrophy.
KEY WORDS: cardiac ventricle; heart; lesion; Myocardium; trypanosome South American.

MIOCÁRDIO DO ÁPICE DO VENTRÍCULO ESQUERDO DO CORAÇÕES CHAGÁSSICOS: ASPECTOS MORFOLÓGICOS E MORFOMÉTRICOS

CORDEIRO, C.; PRATES, J.C.; SIMÕES, M.J. Miocárdio do ápice do ventrículo esquerdo de corações chagásicos: Aspectos morfológicos e morfométricos. *Arq. Ciênc. Saúde Unipar*, 6(2): p. 133-140, 2002.

RESUMO: Utilizando a morfometria, o autor estudou o comportamento do miocárdio apical em 10 corações controle e 10 com aneurisma de ponta. Além das alterações em relação aos cardiomiócitos, estudou o tecido conjuntivo fibroso e alterações vasculares. Os resultados foram submetidos a tratamentos estatísticos da análise do Qui-quadrado confrontados com a literatura pertinente. Foi constatada diminuição significativa de cardiomiócitos e capilares, assim como acentuado aumento na quatidade de tecido fibroso. Além disso, os cardiomiócitos remanescentes sofrem considerável hipertrofia.
PALAVRAS-CHAVE: coração; lesão; miocárdio; tripanossomose sul-americana; ventrículo Cardíaco.

Introduction

The muscular structure of the heart is constituted of fibers with longitudinal and transverse striations. The complex of fibers that forms the atria is entirely separate from that constituting the ventricles, thus the only communication way between both is the conducting system of stimuli.

For TANDLER (1929) and BENNINGHOFF (1948) the system of ventricular fibers presents more complex disposition than the atria where it one can identify a superficial, a medium and another deep layer. The fibers which origin at the tendon of the infundibulum are directed to the apex of the heart. When passing by the diaphragmatic surface, they cross the anterior atrioventricular groove, form the whirl around the apex of the heart and back toward the ventricular cavity to form the papillary muscles of the left ventricle. A number of fibers arising from the right atrioventricular ring and after crossing the diaphragmatic surface of the right ventricle, wind around the apex and return to end in the posterior papillary muscle of the left ventricle. Fibers which origin at the left atrioventricular ring cross in opposite directions to end in the papillary muscles of the right ventricle. Fibers that form the deep part of the medium layer join with fibers of the deep layer to constitute the papillary muscles at one side and to insert in the papillary muscles at the another side. All the muscular layers do not occupy the same plan in all its course, but that one which is the most superficial on the right side ends as the deepest one on the left side, and vice-versa.

It seems us that such complex disposition is so maintained to guarantee a synchronized function between ventricles and valvular system of the heart, because some bundles belong to the both ventricles and others are confined the just one. In any way, all the muscular bundles possess predominantly helical disposition and close to the apex return forming the vortex of the heart.

It is possible that the vortex becomes by constituting in a vulnerable point of the heart, predisposing it to attacks of illnesses as Chagas' disease.

The most conspicuous anatomopathological feature of the chagasic cardiopathy is the so-called aneurysm of the apex, atrophic lesion of the vortex, lesion of the apex, etc. Its specificity is so much that it is considered, for many authors, "the registered mark of the chagasic cardiopathy", since it was not still described in any other heart disease.

According to ALMEIDA (1976), the vortex lesion is found more frequently on the left side, consisting of thinning of the ventricular wall, removal of the muscular bundles and dilation circumscribed to the area of the apex. This is a lesion that appears in 53.2% of the carriers of chagasic heart insufficiency, thus it is considered pathognomonic of the chagasic cardiopathy.

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On the pathogeny of the vortex lesion, the divergent opinions lay around four hypotheses: hypoxia; disorder of the conducting system; inflammation and mechanical factor. The consulted literature reports the following citations.

Literature

The "aneurysm of the apex" was observed for the first time, as it seems, by CHAGAS (1916), when describing a localized thinning of the right ventricle "comparable to the thickness of a paper leaf". Just much later new registers of this lesion were made, when MONTES-PEREJA *et al* (1938) gave a pathogenetic interpretation to the own denomination of the lesion: "infarto de lá punta ". Years later, BERRUTTI (1947) described a "fibrous nodule of the apex of the left ventricle", which, as everything indicating, it was a vortex lesion with organized thrombosis.

ROMAÑA & COSSIO (1944) had observed a round saliency of 0.5 cm in diameter at the apex of the left ventricle, which was characterized as a "dilation of the ventricular wall" by court. The wall of this saliency measured 1mm in thickness and its cavity was filled by a thrombus adhered to the wall. By microscopic exam, it was revealed a pronounced diffuse cellular infiltration and condensed in focuses for the cases in which the process had recent and evolutionary character. In addition, the predominant cells were lymphocytes and histiocytes, and it could also be found neutrophils and eosinophils as well as very pronounced myofibrillar degenerative processes. In the old cases, they verified a numeric reduction of muscular fibers that underwent hypertrophy and degenerative processes similar to those found in the previous type, substitution of the contractile tissue for abundant fibrous and connective proliferation. These were, therefore, the first authors to characterize the lesion for thinning and dilation of the apex area, denominating her then of ventricular aneurysm.

LARANJA *et al* (1951) have described the microscopic aspects of the lesion, with emphasis in vascular lesions besides intense fibrosis and moderate inflammatory infiltration with almost complete destruction of the apex musculature. They still admitted that such vascular lesions, which had reduced the irrigation of the apex myocardium, were largely responsible for the destruction of the myocardium. Therefore, they introduced an ischemic theory to explain the appearance of the "fibrosis of the left ventricle apex".

CARVALHAL *et al* (1954) stated that in 86% of chagasic subjects submitted to necropsy, there was "apex necrotic lesion" with parietal thrombosis and that the electrocardiographic study of some patients had shown important alterations for the clinical diagnosis of the lesion.

MOIA *et al* (1955), although admitting that small vessels could present lesions both in hearts with and without apex thinning, they have affirmed that the main factor accountable for the appearance of the lesion could not be another but the own myocarditis determined by Chagas' disease. This latter would have in the fibrosis one of its fundamental components, in all the heart. They have still affirmed that the lesion could hardly occur in another generalized myocardites, because none of them reaches evolution so prolonged as the one that has been characterized in the majority of the cases of chagasic myocarditis.

Further, LARANJA *et al* (1956) when examining 21 chronic chagasic hearts, they have described that in 33.3% there was circumscribed thinning of the apex portion of the left ventricle, denominating it "pseudo-aneurysm of the apex". They admitted that the ischemic factor, important in the pathogenesis of the lesion, it would be consequence not only of vascular lesions but also that in the hearts of increased volume, a "dynamic factor" could also lead to the coronarian insufficiency.

In ANDRADE's studies (1956), 61.7% of the cases presented the apex lesion. Microscopically, besides the presence of thrombosis in organization, ANDRADE has verified fibrous thickness of the endocardium, while the underlying heart fibers were shown atrophic, sometimes necrosed in relatively extensive areas, or exhibiting another regressive alterations, such as mummification, vacuolar degeneration and turbid swelling. These degenerated fibers lie on the stroma of a fibrous interstitial tissue rich in collagen bundles, swelling, where clear fibroblastic proliferation was processed and a moderate and diffuse linforeticular infiltrate with focal areas of thickening was formed.

In spite of worrying with the general anatomical aspects of the chagasic heart, MIGNONE (1958) gave emphasis to the study of the left ventricular apex by describing the "atrophic lesion of the vortex" in 45% of the cases. As MOIA *et al.* (1955), he also admitted that such lesion corresponds to characteristic findings of the chronic chagasic cardiopathy. Microscopically, MIGNONE has described a deep disarrange of the architecture of the vortex myocardium, with diffuse sclerosis of variable intensity and cellular infiltration with occasional parenchymal focuses. The muscular fibers contained in the fibrous connective tissue were reduced in number, however they had conserved fascicular disposition. In the most advanced lesions, the muscular fibers were reduced to sparse grouping in the intimacy of the fibrous membrane. There was disappearance of the normal conformation of the myocardium of the internal layer, as well as of carneous trabecules in the apex portion. The endocardium showed discreet fibrous thickness sometimes accentuated. In the earliest phases, in which the muscular tissue was more abundant, the fibrousing-infiltrating manifestations of the inflammatory process were larger.

KÖBERLE (1958) observed that more of the half of the chagasic hearts analyzed by him presented thinning and protrusion of the apex, mainly in the left ventricle. Such lesions were considered pathognomonic of Chagas' disease for not being found in any other cardiopathy.

CAPRILES *et al* (1962) when studying the thromboembolic complications of the chagasic cardiopathy, they reported that in 37 chronic chagasic subjects, 20 (54%) presented thinning of the apex of the left ventricle, whose thickness varied from 1 to 3mm.

After dissecting the ventricular superficial muscular bundles of 40 chronic chagasic hearts, RASO (1964) identified 65% with vortex lesion predominantly on the left side. Of the left vortex lesions, 20 (83.3%) presented clear abnormal behavior of the musculature, at the point in that the muscular bundles inflect to constitute the vortex. Microscopically, RASO described the histological aspects of the "left vortex lesion" in the following way: "in the thinner portion of the wall, the primordial lesion is represented by intense numeric

reduction of heart fibrous-cells, reaching in certain cases until the complete disappearance where the entire area is constituted of fibrous connective tissue. The staining for elastic tissue did not demonstrate neo-formation of this element in the vortex area. In the cases of hernia, inflammatory infiltrate, unlike the fibrosis, it was almost always discreet. The vascular lesions were minimum or practically nonexistent".

According to OLIVEIRA (1969), "the aneurysm of the apex is fundamentally constituted of a zone of myocardium thinning and destruction of the musculature, in different intensities. In the most typical cases the myocardium disappears completely, remaining only the epicardium and the endocardium. The most frequent site of the lesion is the apex of the left ventricle, occurring very rarely on the right side and occasionally in both sides or still in another areas of the myocardium".

PUPO JR (1969) studied the "apex fibrotic lesion, describing it macroscopically as "a whitish and irregular area in the apex of the heart, whose thickness varies from 2 to 3mm", presented in 90.9% of the cases on the left vortex and 18.8% on the right one.

OLIVEIRA & BARBIERI NETO (1970), when presenting a case of chronic chagasic cardiopathy with rupture of the aneurysm of the apex, they affirmed that: "this lesion is fundamentally constituted of myocardium thinning, reaching areas of variable dimensions, and in the most typical cases it just remains the apposition of the endocardium onto the epicardium. This layer is so thin that it can be also transparent to the light. Not so rare, the aneurysm is filled by thrombus, when then it presents fibroblastic reaction, sometimes accentuated, more frequent on the left ventricle than on the right one, although could occur in both".

CARVALHAL (1972) has argued that the apex lesion in the chagasic cardiopathy presents, in its histological aspect, a picture of myocardium degenerative lesions, interfibrillar mononuclear infiltrate, capillary hemorrhages and variable degrees of fibrosis, mainly endocardial. Such finding suggests a progressive installation of the endo for the epicardium until converting the wall, per times, in a thin fibrous lamina.

LOPES *et al* (1975), when studying the vortex lesion by Mall's technique (1911) in 37 hearts of chagasic subjects suddenly died and 89 hearts of chagasic subjects with congestive heart insufficiency, they observed this lesion on the left vortex in 56.7% of the cases of chagasic subjects with sudden death and in 59.5% with congestive heart insufficiency. Microscopically, the referred authors affirmed that "regressive phenomena of the fibrocytes are frequent, especially translated for hyaline, hydropic degeneration, myocitolisis and fragmentation. The remaining fibrocytes are morphologically entire. In some cases, discreet to moderate increase of volume is noted in some of them; and the intensity of this hypertrophy is very larger in the chagasic group with congestive heart insufficiency than in the cases of sudden death".

Of the 148 hearts of chronic chagasic subjects examined by ALMEIDA (1976), 53.2% presented the left vortex lesion. From these, in 29% there was removal of the muscular bundles that form the vortex. Microscopically, ALMEIDA (1976) describes the vortex lesion with removal of the muscular bundles, in the following way: "the myocardium of the area, always scarce, it is highly committed by chronic inflammation, characterized by serious intra and interfascicular fibrosis and cellular infiltrate of variable degree. The remaining muscular cells, partly, are isolated in the stroma of the fibrous conjunctive or form thin fascicles interrupted by the fibrosis in its majority. Regressive phenomena as hypotrophy, swelling or citoplasmatic hyalinization, myocitolisis, are observed in some myocytes; another have normal aspect or are hypertrophic. The **carneous** trabecules that emerge of the wall show similar inflammatory involvement".

Material and Methods

We used in the present work 20 human hearts of adult individuals (aged 23 to 84 years) coming from the Laboratory of Pathological Anatomy of the Federal University of Uberlândia, Minas Gerais, which were divided in 2 groups:

Group A – It was constituted of hearts from individuals who had negative serological reactions for Chagas' disease and have not presented signs of cardiovascular diseases at necropsy. These were used as control.

Group B – It was constituted of hearts from chronic chagasic individuals.

Histological Assay

Once having been collected, the hearts were fixed "in totum" in 10% formol solution and fragments of the left ventricle apex of each specimen, with approximately 2mm of thickness, were removed and submitted to common histological technical of inclusion in paraffin, according to MASSON (1956).

Twelve seriated sections, 7 μm thick, were obtained from each paraffin block; thus 140 slides were prepared. From each 12 sections, 3 were used for immunohistochemical studies and the remnants 9 were submitted to staining with hematoxylin and eosin (HE), **Massom tricrome** and silver impregnation.

Immunohistochemical assay

Each fragment was treated with **monoclonal** antibody against the clotting VIII factor. It was used as primary antibody, anti-factor VIII obtained from the immunization of rabbits with human antigen (polyclonal rabbit anti-human Von Willebrand factor, Dako, Stª Bárbara, California - Lot 128, code A 082).

After deparaffinization with xylol, rehydration, blockade of activity of the endogenous peroxidase and washing with PBS, the sections were incubated with primary antibody, secondary antibody (biotinylated anti-rabbit IgG) and ABC complex (avidin-biotin peroxidase).

After revelation with DAB (3,3'-diaminobenzidine tetrahydrochloride), it was carried out counterstaining with Harris' hematoxylin, dehydration and assembly of the slides with Canada balsam.

Simultaneously, another histological section was destined to "negative control", where only the primary antibody was not added, thus allowing that any technique artefact was not confused with vessel.

Histometric Assay

After the histopathological and immunohistochemical materials have been processed, morphologic and morphometric studies were carried out for quantitative verification of previously established parameters: cardiomyocytes (heart

striated muscular fiber), capillaries, collagen fibers and residues (other structures) according to the method of CHALKLEY *et al.* (1949) modified by HENNING, WEIBEL, (1963); DIAS *et al* (1975).

Using an ocular KF10X/18 (Zeiss) with reticule, containing 100 points, adapted to a microscope (Zeiss) using X40 objective with X400 final magnification carried out the histometry.

In the microscopic field in focus, cardiomyocytes, capillaries, collagen fibers and the another elements that coincided with each one of the points of the ocular, denominated hits, were noted.

For each studied slide, four randomly chosen fields were counted by the horizontal sweeping system, in a total of 400 hits. This number of points is enough to obtain an absolute error less than 1% (DIAS et al., 1975).

Statistical Assay

At the morphometry assay, for the comparison of the groups with regard to the cardiomyocyte, capillary and collagen fiber proportions, the qui-square test was used, according to Fischer's restrictions, with the value equal or less than 5% (p 0.05) for rejection level of the validity hypothesis (HOLLANDER & WOLFE, 1973).

In all the used tests, when the values were statistically significant, we used an asterisk (*) for their characterization.

Results

Morphologic Assay

Control group – By the microscopic observation of the lateral portion of the left ventricle apex (Fig. 1), we noticed that the myocardium is basically constituted of great concentration of cardiomyocytes, which form bundles oriented in several directions. At transversal section, the cardiomyocytes show an 11μm average diameter. The muscular fibers of each bundle are approximately parallel, but each bundle runs in different direction, so that it one can notice groups of fibers that were cut at longitudinal, transversal senses and, at variable degrees of obliquity. The nuclei generally are oval-shaped, too large and are located in the central portion of the cell, sometimes occupying half of the cell diameter. We still observed a clear area around the nucleus. Each cardiomyocyte is well defined, showing around reticular fibers. It is also possible to visualize among the cardiomyocytes, blood capillaries and some collagen fibers.

Chagasic group – From ten analyzed hearts, eight presented aneurysm with thinning on the left side, while in the two remaining hearts, such thinning was associated to another on the right side. The myocardium of the lateral portion of the heart apex (left ventricle), carrier of Chagas' disease, was shown be constituted of cardiomyocytes involved by connective tissue and blood vessels. The cardiomyocytes join

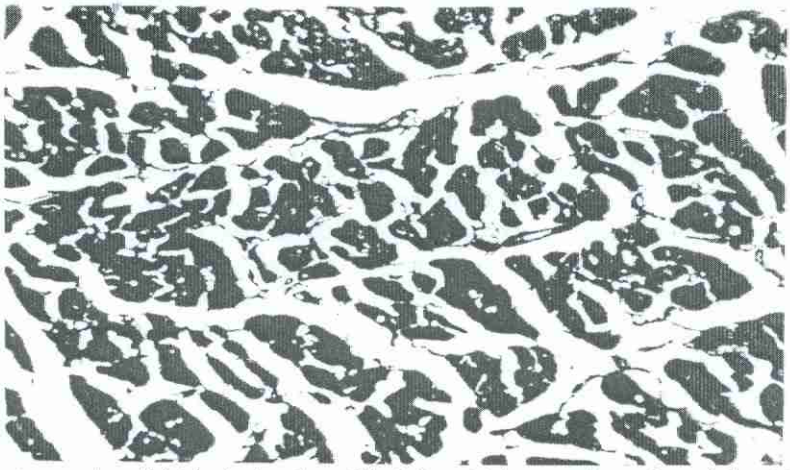

FIGURE 1 – Photomicrography of histological section of the left ventricle apex of non-chagasic heart. Note clear prevalence

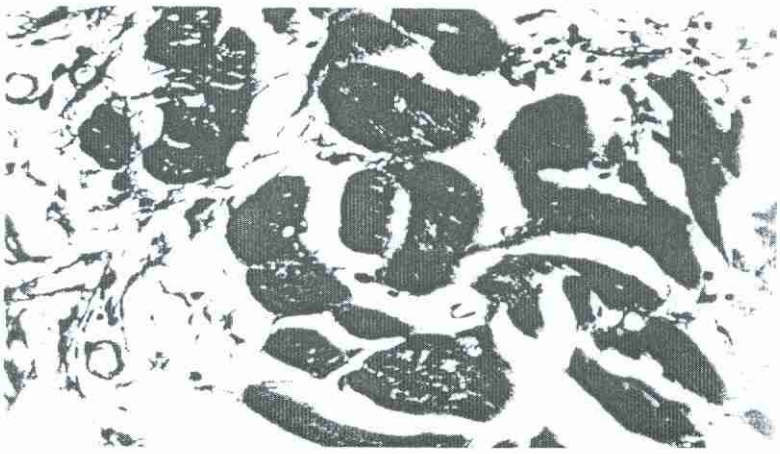

FIGURE 2 – Photomicrography of histological section of the left ventricle apex of chagasic heart. Note clear prevalence of collagen fibers and small concentration of heart muscular fibers. Masson x400.

in an irregular way, forming bundles similarly to the previous group. These run in different directions. In this group, we noticed that besides the cardiomyocytes are larger, they are more separate than in the control group. Around the cardiomyocytes, scarce reticular fibers and great concentration of collagen fibers are noted. We also observed reduced number of vessels with severe caliber variability.

Immunohistochemical Assay

In this preparation the endothelial cells are shown brown, thus evidencing the blood capillaries (Fig.3)

Morphometric Assay

The proportional values of cardiomyocytes, collagen fibers, capillaries and residues observed in the myocardium of the left ventricle apex of hearts both control and chagasic groups are expressed in the table 1. Below the results of the statistical analysis are expressed.

Discussion

The chagasic cardiopathy still constitutes a considerable cause of fatal prognostics in our region, mainly in the patients over the middle age.

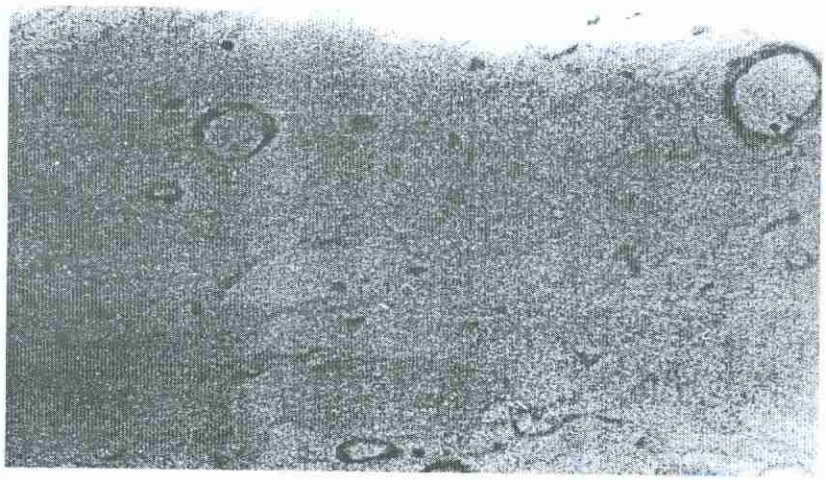

FIGURE 3 – Photomicrography of histological section of the left ventricle apex of chagasic heart. Note the quantitative decrease and the extremely variable caliber of the capillaries with irregular wall. Anti-factor VIII x400.

TABELA I - Proportional values of cardiomyocytes, collagen fibers, capillaries and residues observed in the myocardium

Cases	Cardiomyocytes		Collagen Fibers		Capillaries		Residues	
	Control	Chagasic	Control	Chagasic	Control	Chagasic	Control	Chagasic
01	200	123	20	139	16	13	104	62
02	213	119	35	60	19	9	76	114
03	230	91	27	98	36	11	67	135
04	240	117	23	124	20	6	71	73
05	200	104	43	129	13	10	81	91
06	227	110	47	131	13	9	50	83
07	211	134	34	115	15	11	79	76
08	187	146	31	118	23	11	102	60
09	186	147	63	118	29	13	75	59
10	224	125	39	142	17	11	60	57
Total	2118	1216	362	1174	201	104	765	810
	$X^2 = 409,32$		$X^2 = 599,67$		$X^2 = 27,57$			
	$5\% = 2,73$		$5\% = 0,21$		$5\% = 1,90$			

Among the predisponent factors to morbidity of the chagasic subject, the aneurysm of the apex occupies prominence place. According to our data, besides other alterations, it is noticed a decrease of the muscular cell number with increase of collagen fibers in the affected area. This is the main cause of the myocardium thinning in the site. Many works have been published on the matter, although not always with concordant opinions. Thus, CHAGAS (1916) already had described the aneurysm of the apex, characterizing it as a localized thinning of the right ventricle comparable to a paper

leaf, without however to make any consideration on the causes of such lesion. In our study, we verified greater frequency of the aneurysm on the side left (eight isolated cases and two associated to right vortex aneurysm), in agreement with the data of ROMAÑA & COSSIO (1944), LARANJA *et al.* (1956), MIGNONE (1958), KOBERLE (1958), CAPRILES *et al.* (1962), RASO (1964), ANSELMI *et al.* (1966), OLIVEIRA (1969), OLIVEIRA & BARBIERI NETO (1970), FONTES *et al.* (1972), LOPES *et al.* (1975), ALMEIDA (1976) and FERREIRA (1978). In addition, other authors have described macroscopically the lesion of the apex, denominating it by different nouns: MONTES-PEREJA et al. (1938) called it infarct of the apex; ROMAÑA & COSSIO (1944) characterized a dilation of the ventricular wall with a thrombi adhered to its internal face, while FERREIRA BERRUTI (1947) mentioned a fibrous nodule of the left ventricle apex. CARVALHAL *et al.* (1954), ANDRADE (1956), CAPRILES *et al.* (1962), OLIVEIRA and BARBIERI NETO (1970) also described the presence of thrombus inside the aneurysm. We found thrombus inside the aneurysm in 60% of the cases.

Although it is possible to identify similarities among the authors' citations that describe the apex lesion, divergences also exist. ROMAÑA & COSSIO (1944) just observed a rounded saliency with 0.5 cm in diameter and wall thinning, whose thickness was not superior to 1 mm; LARANJA *et al.* (1951) mentioned a fibrosis of the left ventricle apex; CARVALHAL *et al.* (1954) suggested predilection of the lesion for the apex of the left ventricle. MOIA *et al.* (1955) just mentioned a circumscribed thinning of the apex; LARANJA et al. (1956) considered a necrotic lesion of the apex; MIGNONE (1958) commented about atrophic lesion of the vortex; KOBERLE (1958) just mentioned an apex alteration; CAPRILES *et al.* (1962) described thinning of the apex whose vortex thickness was not superior to 3 mm in 54% of the examined cases. VELOSO *et al.* (1964) commented the difficulty for defining the apex lesion clearly; ANSELMI *et al.* (1966) found six aneurysms in the left apex and two in the submitral area in 29 examined hearts, finding nothing on the right side; OLIVEIRA (1967) commented about the apex lesion in 30% of the studied cases; PUPO JR. (1969) described the apex lesion as a whitish and irregular area whose wall varies among 2 and 3 mm in thickness, presented in 90.9% on the left side and 18.8% on the right side; OLIVEIRA & BARBIERI NETO (1970) characterized the lesion as a thinning of the muscular wall, where the myocardium totally disappears, in the most serious cases, just remaining the endocardium under the epicardium. In our study, we did not find any case with these characteristics; FONTES *et al.* (1972) found apex lesion in 76% of the examined cases, which was characterized as an area of apex rarefaction with mamilar or glove-finger shape; LOPES *et al.* (1975) observed left apex lesion in 56.7% of the chagasic individuals with sudden death and 59.5% of those with congestive heart insufficiency. According to these authors, regardless of the group, the lesions could be seen now as a simple rift crossing all the myocardium thickness, now in V shape occupying a wider area, now in discoid shape. ALMEIDA (1976) found left vortex lesion in 39.5% of the cases, while FERREIRA (1978) described the same lesion in 53.2% of the cases.

Our research did not have as objective to verify the presence or absence of the apex lesion, but to study morphometric aspects of the own lesion; however when analyzing the pertinent literature, we verified that the frequency of such lesion has showed great variation, with descriptions of the apex lesion since inferior limits of 30% (OLIVEIRA, 1967) until 76% of the studied cases (FONTES *et al.*, 1972).

It is possible that the great difference of frequency found by the authors above mentioned is due to different used methodologies, or even the difficulties in characterizing, with clarity, the apex lesion in its several phases of evolution.

As regards the microscopic alterations of the apex lesion, ROMAÑA & COSSIO (1944) have described a reaction with diffuse cellular infiltrate with predominant lymphocytes and macrophages. After ROMANÃ & CASSIO, many authors mentioned or described the chagasic myocarditis; thus, in one way or another, LARANJA *et al.* (1951), MIGNONE (1958), RASO (1964), ANSELMI *et al.* (1966), PUPO JR (1969), CARVALHAL (1972), LOPES *et al.* (1975) & ALMEIDA (1976) referred to inflammatory reactions located at the level of the aneurysmatic lesion of the apex. We also found, in 100% of the cases, intense reaction with cellular infiltrate in the area of the lesion.

When still analyzing the microscopic alterations of the atrophic lesion of the apex, we found descriptions on the degeneration or necrosis of the heart muscular cells, in the majority of the authors; thus, the first authors who characterized the vortex lesion, denominating it of aneurysm of the apex were ROMAÑA & COSSIO (1944), when observing very accentuated myofibrillar degenerative processes, reduction of the number of muscular fibers, hypertrophy of the remaining fibers and invasion by fibrous tissue.

After these pioneer authors, others came and brought valuable contributions, in the same way. For LARANJA *et al.* (1951), PUPO JR. (1969), it occurs destruction of the heart myocytes in the most serious cases; according to OLIVEIRA (1969) & OLIVEIRA *et al.* (1970), the destruction can lead to the total disappearance of the myocardium in the affected area, remaining so only the endocardium in apposition to the epicardium. In our observations, we did not verify any case in which there was total destruction of the muscular cells of the apex. For ANDRADE (1956), it is frequent the installation of a fibrous thickness located in the injured area, finding not detected in our material as well. Still in agreement with ANDRADE, it is frequent the presence of necrosed and/or atrophic heart fibers, findings also found by ALMEIDA (1976) and by us.

MIGNONE's reports (1958) have identified a deep disarrange in the architecture of the vortex myocardium: diffuse sclerosis, drastic reduction of the cardiomyocyte number and grouping of the remaining fibers in thin bundles dispersed in the fibrous tissue. RASO (1964) has also described the decrease of the number of muscular cells, in certain cases until its disappearance and substitution for fibrous tissue. CARVALHAL (1972) commented about degenerative lesions of the myocardium, while LOPES *et al.* (1975) affirmed that the degenerative lesions of the myocardium are frequent, however the remaining cells stay entire and just in some cases it occurs discreet hypertrophy. ALMEIDA (1976) described a removal of the muscular bundles of the apex caused by intense inflammatory infiltration and also for proliferation of the fibrous tissue. Although ALMEIDA has

nothing mentioned about myocells destruction, we believed that the removal detected by him is due to the cardiomyocyte degeneration.

Other authors have also verified rarefaction or removal of cardiomyocyte bundles, but they described it as destruction or degeneration (ROMAÑA & COSSIO, 1944; LARANJA *et al.*, 1951; MIGNONE, 1958; ANDRADE, 1956; RASO, 1964; ANSELMI *et al.*, 1966; PUPO Jr., 1969; OLIVEIRA, 1969; OLIVEIRA *et al.*, 1970; CARVALHAL, 1972; LOPES *et al.*, 1975; ALMEIDA, 1976).

Our results show agreement with the authors above mentioned because we equally observed accentuated removal of the cardiomyocyte bundles, as well as inflammatory infiltration and proliferation of fibrous tissue (fig 2).

When proceeding the histometric evaluation of the cardiomyocytes, we detected severe decrease of the number of these cells in the area of the apex lesion, as compared to the non-chagasic control group (table 1-3). According to OLIVEIRA (1969), RASO (1964) and OLIVEIRA *et al.* (1970), the destruction of the fibers can be total in the most serious cases; in our observations, however, the greater destruction of cardiomyocytes reached 60.5% of the fibers (table 1-3, case 03).

The used statistical analysis showed significance with regards to the reduction of the cardiomyocyte number in the aneurysm of the apex, since for a nullity hypothesis established at 5%, we had a critical $X^2 = 2.73$, while the calculated X^2 was 409.32.

As regards the proliferation of the fibrous tissue in replacement for degenerated muscular fibers, ROMANA & COSSIO (1944) have affirmed that there is substitution of contractile tissue for an intense proliferation of fibrous tissue. In addition, LARANJA *et al.* (1951), MOIA *et al.* (1955), ANSELMI *et al.* (1966), OLIVEIRA (1969), OLIVEIRA *et al.* (1970) and ALMEIDA (1976) have also reported an intense fibrosis located in the lesion area. MOIA *et al.* (1955) has still affirmed that the fibrous proliferation is fundamental component to determine the lesion of the vortex. On the other hand, ANDRADE (1956) and MIGNONE (1958) have mentioned a fibrous thickness of the apex. While RASO (1964) has affirmed that it may occur total substitution of the muscle for fibrous tissue, CARVALHAL (1972) has appointed variable degrees of fibrous involvement mainly endocardial and PUPO Jr. (1969) has described the fibrous proliferation as an early form of diagnosing the vortex lesion. This latter author refers that the fibrosis begins at the endocardium, progressing for the subendocardial areas and later for the myocardium.

The analysis of our observations revealed an intense fibrous proliferation in the lesion area similar to that described by ROMANA and COSSIO (1944), LARANJA *et al.* (1951), MOIA *et al.* (1955), ANSELMI *et al.* (1966), OLIVEIRA (1969), OLIVEIRA *et al.* (1970) and ALMEIDA (1976) (fig.2). The histometry of the collagen fibers showed a highly significant degree of variability between the chagasic and control groups (table 4), what was confirmed by the statistical analysis (calculated $X^2 = 599.67$ and critical $X^2 = 0.21$).

As regards the vascular lesions, LARANJA *et al.* (1951) have instituted the ischemic theory to explain the appearance of the fibrosis of the left ventricle apex, to which it is attributed the circulatory deficiency caused by intimal hyperplasia, medial hypertrophy and fragmentation of the elastic limiting, the destruction of the heart muscular fibers. CARVALHAL *et al.* (1954) has commented about circulatory deficit caused by vascular lesions. MOIA *et al.* (1955) has admitted "anatomical reasons" and "circulatory regimen" for the apex lesions. LARANJA *et al.* (1956) has admitted that the ischemic factor, though important in the genesis of the lesion, it would not only be consequence of vascular lesions, but also of dynamic lesions.

ANDRADE (1956) has observed, in the middle of the fibrous tissue, blood vessels of very thin walls and dilated lumen full of blood, and some of those vessels exhibiting thrombosis in varied degrees of organization.

RASO (1964) has described the vascular lesions as minimum or practically non-existent. ANSELMI *et al.* (1966) has not evidenced vascular lesions. OLIVEIRA (1967) has found vortex lesions in 20% of the hearts with good vascular conditions and in 90% of the hearts with bad circulatory conditions, thus concluding that circulatory factors are important for genesis of the apex lesion. FERREIRA (1978) has mentioned vascular alterations of variable intensity.

Although none of the compiled authors have presented quantification about the vascular lesions, many have admitted the vascular lesion presented in a decisive way in the genesis of the aneurysm of the apex. It was verified in the reports of LARANJA *et al.* (1951), CARVALHAL *et al.* (1954), MOIA *et al.* (1955), LARANJA *et al.* (1956), ANDRADE (1956), RASO (1964), ANSELMI *et al.* (1966), OLIVEIRA (1967) and FERREIRA (1978). In our observations, we detected severe vascular alterations with degeneration and significant reduction of the number of vessels in the area of the apex lesion; thus, by histometry, we identified a 52% reduction of the capillaries in the chagasic group in relation to control group. When statistically analyzing the results, we found a calculated $X^2 = 27.57$ for a critical $X^2 = 1.90$.

For these and possible other reasons, we believed that the vascular lesion is important factor for the genesis of the left vortex lesion.

We believed that the matter still deserves studies of greater depth, for example by using electronic microscopy for a demonstration of correlation more exact between the cardiomyocytes and the proportion of capillaries.

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