Apical aneurysm of Chagas's heart disease★

J SAMUEL M OLIVEIRA, J A MELLO DE OLIVEIRA, ULISSES FREDERIGUE Jr, EUCLYDES C LIMA FILHO

From the Department of Pathology, Faculty of Medicine of Ribeirão Preto, São Paulo University, Brazil

SUMMARY A retrospective study of Chagas's heart disease was carried out by a review of necropsy reports with special reference to the lesion known as the apical aneurysm. It was concluded that this lesion was more frequent in men, was unrelated to age, and was unrelated to heart weight. Patients dying of the cardiac consequences of Chagas's cardiomyopathy were more likely to have an apical aneurysm than those whose death was unrelated to the disease but the mode of death (sudden, or with heart failure) was unconnected with its presence. Transillumination from within the ventricle at necropsy was not only useful in demonstrating the aneurysm but also showed areas of myocardial thinning elsewhere. Thrombosis within the lesion was frequent. The aetiology of the apical aneurysm is discussed and it is concluded that while ischaemia, inflammation, thrombosis, and mechanical factors may produce and localise this lesion, the underlying cause is the basic pathogenetic process—parasympathetic nerve cell destruction.

Chagas's disease is one of the greatest health problems in Latin America.¹ Since its foundation in 1954 the Department of Pathology at Ribeirão Preto, São Paulo, has discovered alarming data about the prevalence of the disease as a cause of death; nearly 35% of deaths in adults can be related to it. The purpose of this paper is to review this experience with regard to the cardiomyopathy, the most frequent manifestation of the disease, present in 1153 (91%) of 1266 cases. Pathologically, many of the cardiac findings are non-specific, for example, hypertrophy, dilatation, or mural thrombosis, but the most conspicuous finding, the apical aneurysm, is now generally accepted as the cardinal sign of cardiac involvement.^{2,3} This odd lesion is caused by a thinning of a localised region of the myocardium, usually at the apex, often to such an extent that only a layer of tissue comprising merely epicardium and endocardium remains (Fig. 1). This was first observed in 1916⁴ but not well described, and it was not until 1938 that the next record was made.⁵ Several papers have been devoted to the study of this lesion.⁶⁻⁸

Material and methods

The diagnosis of apical aneurysm is made chiefly on the basis of the macroscopical findings. The aneurysm usually protrudes at the apex (Fig. 2) or it can be palpated, but thrombosis within it may obscure both

of these features (Fig. 3). When the aneurysm is prominent or when it occurs in the apices of both ventricles the heart may assume a bifid shape (Fig. 4).

The best way to demonstrate an apical aneurysm is to fill the heart with formalin and to open it after 24 to 48 hours by a single cut from apex to base. The size is variable (Fig. 5). There are no specific histological lesions; the two limiting layers of the heart (epicardium and endocardium) sandwich myocardial remains and a greater or lesser amount of fibrous tissue. Elsewhere, the myocardium may show inflammatory reaction as well as microinfarcts or myocytolysis. Thrombus, often organised, sometimes completely fills the aneurysm.

Every necropsy report between June 1954 and December 1968 was examined (a total of 5715). Special attention was devoted to patients known to have had Chagas's disease. One thousand one hundred and fifty-three patients older than 10 years having Chagas's cardiomyopathy were found, but this was not necessarily the direct cause of death. In analysing the data presented in the results, cases with doubtful information about a particular feature were excluded, so that totals vary.

In order to study the pathology of the apical aneurysm further, 18 hearts with the cardiomyopathy were prepared as described above, and after the epicardium had been removed, studied by means of light bulbs of suitable sizes introduced through incisions in both atria into the ventricles. With this internal illumination the hearts were examined and photographed in a darkened room.

★ Research supported by a grant from the World Health Organisation.
Received for publication 28 April 1980

Fig. 1 Chagas's heart disease with apical aneurysm.

Fig. 2 Apical aneurysm bulging at the apex.

Fig. 3 Thrombosis of the apical aneurysm.

Fig. 4 Apical aneurysm in both apices "cor bifidum".

Fig. 5 Apical aneurysm of different sizes (all same enlargement).

Results

Five thousand seven hundred and fifteen reports were examined and, of these, 1153 had chronic Chagas's cardiomyopathy. The incidence of apical aneurysm in 1078 cases studied was 560 (52%). The male to female ratio was 739:339. Four hundred and one of the 739 men (54%) and 159 of the 339 women (47%) had an apical aneurysm ($\chi^2=5.04$ $p<0.05$). The incidence of apical aneurysm related to age in 817 cases is shown in Table 1 and to the heart weight/ body weight ratio in these cases in Table 2. The relation to the cause of death is shown in Table 3 and Fig. 6. Statistical analysis was carried out using an appropriate technique^{9 10} as follows (see Fig. 6):

$$ps = \frac{Xs}{Ns} - \frac{Xo}{No} / 1 - \frac{Xo}{No}$$

ps = 0.39, its SD is 0.037

The incidence of apical aneurysm in patients in whom the cause of death was chronic Chagas's cardiomyopathy is related to the mode of death in 654 cases in Table 4.

The site of the aneurysm in 560 cases was as follows: the left ventricular apex, 460 (82%), the right ventricular apex, 50 (9%), and in both apices, 50

Table 1 Incidence of apical aneurysm (AA) related to age (817 cases studied)

Age (y)	No. of cases	Without AA	With AA
10-19	28	15	13 (46.4%)
20-29	112	44	68 (60.7%)
30-39	154	60	94 (61.0%)
40-49	204	84	120 (58.8%)
50-59	163	55	108 (66.3%)
60-69	110	50	60 (54.5%)
70-79	39	20	19 (48.7%)
80-89	7	3	4 (57.1%)

$\chi^2 = 3.39$, not significant; $p>0.1$.

Table 2 Incidence of apical aneurysm (AA) related to heart weight/body weight ratio multiplied by 100 (817 cases studied)

Ratio	No. of cases	Without AA	With AA
<0.6	111	59	52 (45.8%)
0.6	289	182	107 (37.0%)
0.8	191	109	82 (42.9%)
1.0	144	86	58 (40.3%)
1.2	51	31	20 (39.2%)
1.4	31	16	15 (48.4%)

$\chi^2 = 2.69$, not significant; $p>0.1$

Table 3 Incidence of apical aneurysm (AA) related to cause of death in patients with chronic Chagas's cardiomyopathy (817 cases studied)

Cause of death	Total	Without AA	With AA
Chronic Chagas's cardiomyopathy	654	247	407 (62.2%)
Other than chronic Chagas's cardiomyopathy	163	87	76 (46.6%)

(9%). Of 471 cases studied in this respect, 130 (28%) showed thrombosis. Of the 18 hearts studied, eight showed transillumination of the apical region indicating an aneurysm and all showed transilluminated areas in the right ventricle adjoining the interventricular septum. Areas of transillumination in the posterior walls of the ventricles were also seen (Fig. 7).

Discussion

The apical aneurysm of Chagas's disease is a peculiar lesion. Though our experience of the ventricular aneurysm caused by myocardial infarction is small, others acquainted with this have stressed that it is impossible to confuse the two conditions.¹ The left ventricular thin point recently reported¹¹ cannot be misinterpreted as an apical aneurysm, nor can a subvalvular aneurysm.¹² The incidence of the lesion we found (52%) was similar to that of other studies,

Table 4 Incidence of apical aneurysm (AA) in patients where cause of death was chronic Chagas's cardiomyopathy related to mode of death (654 cases studied)

Mode of death	Total	Without AA	With AA
Death related to cardiac failure (47.2%)	309	123	186 (60.2%)
Sudden death (52.7%)	345	124	221 (64.1%)

$\chi^2 = 1.04$, not significant $p > 0.1$.

though our data are based on a larger number of cases. Thus, the previously reported incidence has been, 61.7%,⁶ 65%,⁷ 58.8%,⁸ 45%,¹³ and 54%.¹⁴ The incidence is higher in men but the reason for this is unknown. Greater physical activity was suggested as the cause of the higher incidence of heart disease in men with *T. cruzi* infection.¹⁵ It is not clear in the published reports when an apical aneurysm develops or how it evolves. Assuming this would take time, the incidence should be higher in older subjects, but this

Fig. 6 X_S , number of cardiac deaths with apical aneurysm. N_S , number of cases with Chagas's cardiomyopathy and cardiac death. X_O , number of non-cardiac deaths with apical aneurysm. N_O , number of cases with chronic Chagas's cardiomyopathy and non-cardiac death. X_A , number of cardiac deaths actually related to apical aneurysm (not observable). X_B , number of cardiac deaths not related to apical aneurysm (not observable). X_A and X_B are estimated from the observed frequencies X_S , X_O , and N_O as $X_B = (X_O \times S_S)/N_O$ and $X_A = X_S - X_B$.

Fig. 7 "Aneurysm" of the posterior wall of left ventricle (transillumination).

was not the case. It is widely accepted that the infection with *T. cruzi* usually occurs in childhood and, since age plays no part, we may assume that the apical aneurysm is an early lesion. Unfortunately we had no data on size, so it is impossible to estimate how much the aneurysm enlarges with time. There was no relation between the presence of an aneurysm and heart weight (see Table 2 and Fig. 5). This observation is important because those not familiar with Chagas's disease tend to assume the apical aneurysm to be a result of cardiac dilatation.

Prognosis is affected by the presence of an apical aneurysm (Table 3 and Fig. 6); it was present more frequently in patients with Chagas's cardiomyopathy dying a cardiac death than in those dying from other causes. The reason is unclear, because the aneurysm itself is not a direct cause of death, as, for example, by rupture—there is only one such published case.¹⁶ Nevertheless, from our data it appears that its presence was linked with 39% of the cardiac deaths and must be regarded as a sign of a poor prognosis.

The exact cause of death in Chagas's heart disease is unknown. Some believe in at least three different types of cardiac involvement.¹⁷ The mode of death in our patients was not influenced by the presence of an apical aneurysm, which was equally common in those who died suddenly and those who died of heart failure. This does not support the idea of different types of Chagas's heart disease. It is widely accepted that apical aneurysms are much more frequent at the left ventricular apex and our results confirm this. Thromboembolism is common³; the atria are often filled in thrombus, as well as the ventricular apices, even when an apical aneurysm is not present.

Transillumination of the hearts we studied showed several areas of thinning of the myocardium. This has been described before.^{18, 19} Dissection of the epicardium is not therefore necessary to disclose such lesions (Fig. 7).

The aetiology of the apical aneurysm is uncertain. It has been called an "apical infarction"⁵ and indeed lesions of the left anterior descending coronary artery described could be responsible for its pathogenesis.¹⁸ On the other hand, apical dilatation could be caused by chronic myocarditis⁶ and an inflammatory process is favoured by others.¹³ Hypokinesia and the pre-existent endocarditis would promote stasis of the blood and thus apical thrombosis. Organisation in the thrombus would seal the communicating vessels between the cardiac chamber and the myocardium, resulting in ischaemia, and finally aneurysm formation.

Dissection of the epicardium and fat of the apical region⁷ has shown a "true herniation" of the endocardium sliding across separated muscle bundles (Fig. 8) and a mechanical factor is likely to play an

Fig. 8 Raso's theory.⁷ Diagram illustrating the apical region after dissection of the pericardium. The endocardium bulges through the space in the left ventricle. (Courtesy of the author, P Raso, Belo Horizonte).

important role, but though this and, in our view, ischaemia are involved, the primary explanation is likely to lie elsewhere.

The "neurogenic" theory states that the cardiac involvement in Chagas's disease has the same

Fig. 9 Heart from normal rat 10 days after two injections (340 mg/kg) of orciprenaline.²⁰

pathogenesis as the other manifestations of the disease,¹⁵ the basic mechanism being a decrease in the number of nerve cells, chiefly of the parasympathetic system, because of the action of *T. cruzi*. The result of this destruction of parasympathetic innervation would be that the heart is subjected to increased sympathetic tone, with consequent microinfarctions and myocytolytic foci and destruction of muscle cells. The sum of all these factors would lead to the formation of the apical aneurysm. With this hypothesis it is possible to explain not only the apical aneurysm proper but also similar lesions elsewhere in the heart as well as all manifestations of the disease, for example mega-oesophagus, megacolon, and the central nervous system lesions. To test the theory we have injected high doses of beta-sympathomimetic agents into normal rats (orcioprenaline or norepinephrine plus an alpha blocker)²⁰ and have shown that they develop cardiac changes similar to those found in human chronic Chagas's cardiomyopathy, including the apical aneurysm (Fig. 9).

Thus, while the formation and localisation of the apical aneurysm of Chagas's cardiomyopathy may be the result of ischaemia, inflammation, thrombosis, and mechanical factors, the basic aetiology is parasympathetic nerve cell destruction.

References

- 1 Davies JNP, Feijfar Z. Chagas' disease in Brazil: a survey of clinical and pathological aspects. *Pan American Health Organisation Document* 1965; RES 4/10: 1-80.
- 2 Moia B, Rosenbaum MB, Hojman D. Aneurismas ventriculares en la miocarditis crónica chagásica. *Rev Argent Cardiol* 1955; 22: 113-50.
- 3 Andrade ZA, Andrade SG. Patologia. In: Brener Z, Andrade ZA, eds. *Trypanosoma cruzi e doença de Chagas*. Rio de Janeiro: Editora Guanabara Koogan SA, 1979: 199-248.
- 4 Chagas C. Processos patogênicos da tripanosomíase americana. *Mem Inst Oswaldo Cruz* 1916; 8(2): 5-36.
- 5 Montes Pereja J, Amargos A, Estable JJ, Berruti PF. Forma cardíaca de la *Trypanosomiasis cruzi*. *Arch Urug Cardiol* 1938; 2: 119-32.
- 6 Andrade ZA. A lesão apical do coração na miocardite crônica chagásica. *Hospital (Rio)* 1956; 50: 803-12.
- 7 Raso P. Contribuição ao estudo da lesão vorticilar na cardite chagásica crônica. Thesis 1964, Belo Horizonte (MG) Universidade Federal de Minas Gerais.
- 8 Oliveira, JAM. Contribuição ao estudo da patogenia do "aneurisma da ponta" na cardiopatia chagásica. Thesis, Ribeirão Preto (SP) Universidade de São Paulo, 1967.
- 9 Sheps MS. An examination of some methods of comparing several rates or proportions. *Biometrics* 1959; 15: 87-97.
- 10 Duarte GG, Haddad N, Fávoro M. Análise do componente etiológico exclusivamente chagásico no estudo da prevalência de cardiopatias. *Rev Inst Med Trop São Paulo* 1967; 9: 327-32.
- 11 Bradfield JWB, Beck G, Vecht RJ. Left ventricular apical thin point. *Br Heart J* 1977; 39: 806-9.
- 12 Abrahams DG, Barton CJ, Cockshott WP, Edington GM, Weaver EJM. Annular subvalvular left ventricular aneurysms. *Q J Med* 1962; 31: 345-60.
- 13 Mignone C. Alguns aspectos da anatomia patológica de cardite chagásica crônica. Thesis, São Paulo (SP) Universidade de São Paulo, 1958.
- 14 Capriles MA, Berrios G, Guevara JM, Gómez E. Complicaciones tromboembólicas en la cardiopatia crônica de Chagas y su correlación anatómico-clínica. *Arch Hosp Vargas* 1962; 4: 293-8.
- 15 Köberle F. Die Chagaskrankheit: ihre Pathogenese und ihre Bedeutung als Volksseuche. *Z Tropenmed Parasit* 1959; 10: 236-68.
- 16 Oliveira JSM, Barbieri Neto J. Cardiopatia chagásica: "aneurisma da ponta" roto. *Arq Bras Cardiol* 1970; 23: 335-8.
- 17 Ramos JA, Carvalho S. Moléstia de Chagas: evolução de conceito. In: Cançado JR, ed. *Doença de Chagas*. Belo Horizonte: Imprensa Oficial do Estado de Minas Gerais, 1968; 401-19.
- 18 Dias E, Laranja FS, Nobrega G. Doença de Chagas. *Mem Inst Oswaldo Cruz* 1945; 43: 495-581.
- 19 Anselmi A, Pifano F, Suarez JA, Gurdíel O. Myocardiopathy in Chagas' disease. I—Comparative study of pathologic findings in chronic and experimental Chagas' myocarditis. *Am Heart J* 1966; 72: 469-81.
- 20 Oliveira JSM. Cardiopatia "chagásica" experimental. Thesis Ribeirão Preto (SP) Universidade de São Paulo, 1968.

Requests for reprints to Dr J Samuel M Oliveira, Department of Pathology, Faculty of Medicine, Universidade de São Paulo, 14100 Ribeirão Preto - SP, Brazil.