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Pathological Features of *Trypanosoma cruzi* Infections of *Rattus rattus*

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Naturally acquired *Trypanosoma cruzi* infections were studied in *Rattus rattus* kept in the laboratory for intervals from one day to 33 months. *Trypanosoma cruzi* was found at necropsy in the tissues of 85 (51%) of 167 rats kept three months or less, 7 (50%) of 14 rats kept 3 to 12 months, and 5 (24%) of 21 rats kept 12 to 33 months.

Myocarditis and meningoencephalitis were the principal pathological lesions present. The pathological lesions of naturally acquired *T cruzi* infections in *R rattus* resemble the lesions of Chagas disease, as it is seen in Panamanians.

Rattus rattus has been found[1] to be an important mammalian reservoir of *Trypanosoma cruzi* in the central Panamanian villages of Bonguito, Mendoza, Santa Rita, and Caimito de Capira where Chagas disease is endemic. Of 100 rats examined, *T cruzi* was found in 55 by microscopic identification of parasites in tissues obtained at necropsy.

Although De Alencar et al[2-4] and Ferriolli and Barretto[5] have identified *T cruzi* in the tissues of naturally infected *R rattus* at necropsy, descriptions of the pathological lesions of natural *T cruzi* infections of *R rattus* were limited to a few observations on a few animals.

The purpose of this paper is to describe and illustrate the pathological lesions of naturally acquired *T cruzi* infections of Panamanian *R rattus*.

Materials and Methods

Live-trapped *R rattus* from Bonguito, Santa Rita, Mendoza, Caimito de Capira, Chepo, and Chilibre were maintained singly in cages in the laboratory for periods of time ranging from one day to 33 months. Under these conditions, reinfection does not occur.

The rats were examined periodically by thick smear, blood culture, and complement-fixation test for evidence of *T cruzi*. When they died or were killed, necropsies were performed. Blocks of heart, lungs, brain, intestine, stomach, salivary glands, kidneys, liver, spleen, and skeletal muscle were fixed in 4% formaldehyde, solution, embedded in paraffin, and were sectioned at 8μ. Sections stained with hematoxylin-eosin were examined microscopically.

In all, 202 rats were necropsied. Of these, 167 were in the laboratory for three months or less, 14 were in the laboratory 3 to 12 months, and 21 were in the laboratory 12 to 33 months.

Results

Prevalence of *T cruzi* Infection.—Of 167 rats kept in the laboratory less than three months, 85 (51%) were found to be infected with *T cruzi*; 7 (50%) of 14 rats kept in the laboratory 3 to 12 months, and 5 (24%) of 21 rats kept in the laboratory 12 to 33 months were found to be infected with *T cruzi*.

No significant differences in the prevalence of infection by sex were found. Almost all rats examined were adults (males: 225 to 300 gm, females: 125 to 200 gm).

Distribution of Lesions and Parasites.—Parasites were found in 97 (49%) of 202 rats. The distribution of the parasites in the infected rats was heart, 96 (99%); brain, 25 (27%); lungs, 15 (15%); kidneys, 4 (4%); liver, adipose tissue, and skeletal muscle, 1 (1%). Chronic, inflammatory infiltrates of plasma cells, lymphocytes, and monocytes were present in the myocardium, cerebellum, skeletal muscle, visceral muscle, and adipose tissue.

Description of Pathological Lesions.—In the hearts of three rats necropsied within a week of arrival at the laboratory, numerous parasitized muscle fibers (10 to 12 per microscopic section) were present (Fig 1); more parasitized fibers were observed in the walls of the ventricles than of the atria. In these hearts, inflammation

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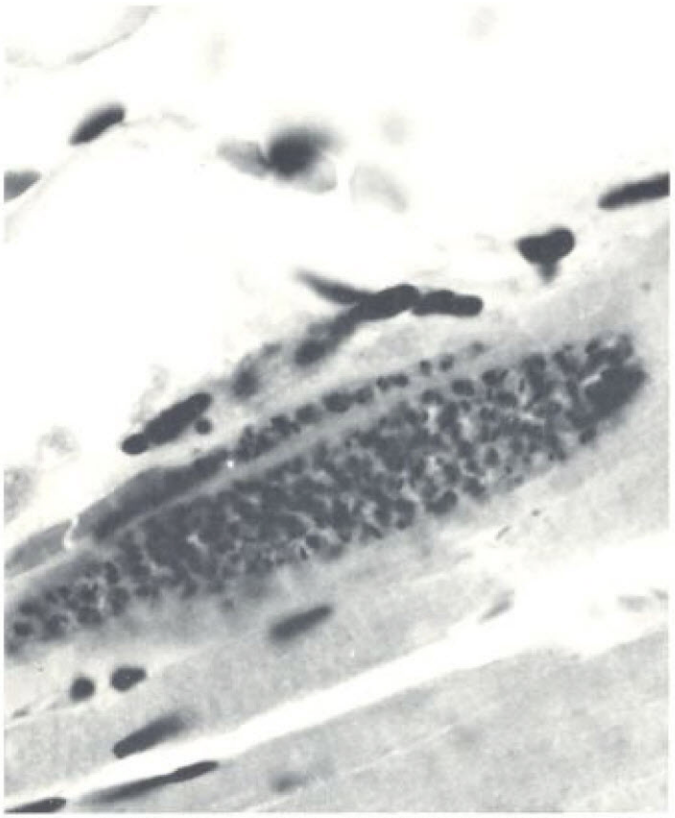

Fig 1.—Myocardial fiber filled with leishmanial (amastigote) forms of *Trypanosoma cruzi* (hematoxylin-eosin, original magnification × 1,000).

Fig 2.—Chronic myocarditis, interventricular septum, showing multiple foci of dense mononuclear inflammation (hematoxylin-eosin, original magnification × 100).

was minimal. Most *T cruzi* had well-developed rod-shaped blepharoplasts characteristic of amastigote forms, but some muscle fibers contained organisms with dot-like blepharoplasts and other organisms that were lanceolate in shape. With increased time in the laboratory, myocarditis appeared and became more severe as the number of parasites in the heart diminished. At 10 to 11 weeks, the degree of myocarditis reached a peak. It regularly consisted of scattered foci of lymphocytes, plasma cells, and macrophages, associated with loss of individual muscle fibers (Fig 2). In this material, parasites were not identified in inflammatory foci, but parasites could be found in small numbers in uninflamed areas of the heart. Parasites were found in the heart of one rat that had been in the laboratory 20 months and in the hearts of four rats that had been there 19 months. Myocarditis in the absence of identifiable *T cruzi* was present in one rat that had been in the laboratory 28 months. In another rat with positive findings necropsied after 34 days in the laboratory, the heart was dilated, and there was an apical lesion similar to the lesions found in chronic chagasic myocardiopathy in man. In some rats with chronic myocarditis and rare parasitized muscle fibers, interstitial fibrosis of the myocardium was present.

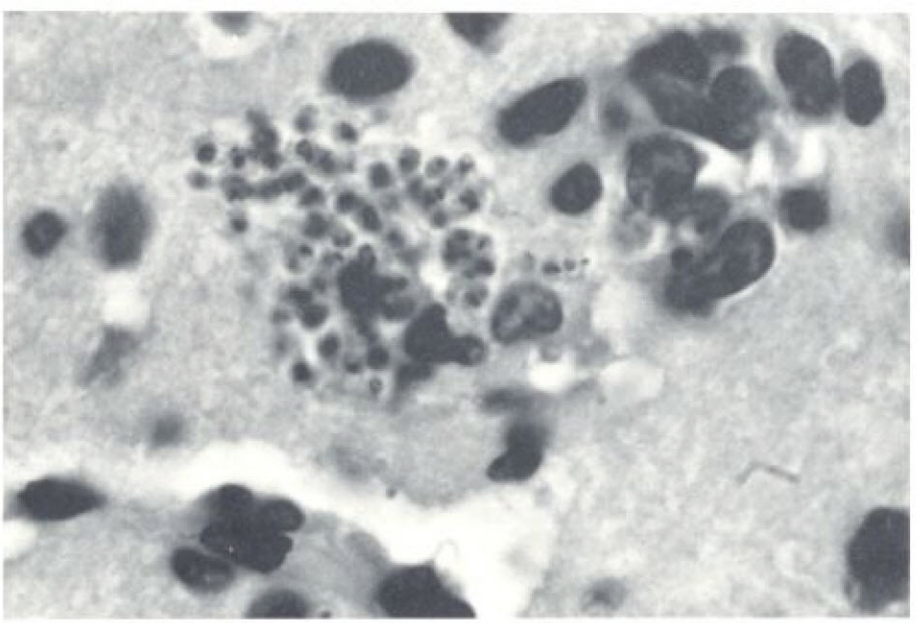

Fig 3.—Leishmanial (amastigote) forms of *T cruzi* surrounded by astroglia and lymphocytes in the cerebellum (hematoxylin-eosin, original magnification × 1,000).

In the brain, parasites were found

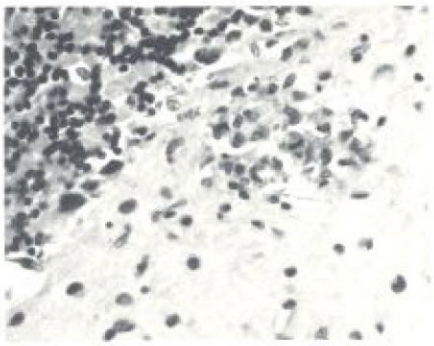

Fig 4.—Granuloma consisting of astroglia, microglia and lymphocytes, in the molecular layer of the cerebellum (hematoxylin-eosin, original magnification × 400).

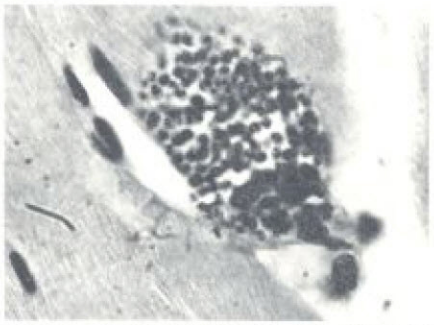

Fig 5.—Leishmanial (amastigote) forms of *T cruzi* in skeletal muscle (hematoxylin-eosin, original magnification × 1,000).

in the astroglia (Fig 3), pericapillary space, subarachnoid space, and the Purkinje cells of the cerebellum. Parasites were most frequently seen in the molecular layer of the cerebellum. In the brain, parasites were regularly associated with inflammation: some parasites were intracellular, and some were extracellular. In the meninges, the inflammatory reaction consisted of dense, focal infiltrates of lymphocytes and macrophages. In the substance of the brain, both perivascular cuffing and granulomas (Fig 4) were present. The cells in the perivascular cuffs were lymphocytes. The granulomas consisted of astrocytes, microglia, and mononuclear cells. In the rat, meningoencephalitis caused by *T cruzi* can be strikingly localized to the cerebellum.

In the gastrointestinal tract, no parasites were identified. Chronic inflammation unassociated with organisms was seen in the smooth muscle of the stomachs of five rats with *T cruzi* elsewhere in their bodies.

Parasites were seen in association with inflammation in the cardiac muscle of the large pulmonary veins. This was the only site in the lungs in which *T cruzi* was identified.

Parasites were found in skeletal muscle (Fig 5) near the thyroid gland in one rat. Focal myositis and evidence of regeneration of muscle were noted in four other rats.

In four rats, parasites were found in the smooth muscle of the renal pelvis, where they were associated with chronic inflammation of visceral muscle and adjacent adipose tissue. In one rat with parasites in the renal pelvis, parasites were also seen in the adjacent adipose tissue.

In one rat with parasites in its heart, a few parasites were seen in reticuloendothelial cells in the liver.

Comment

These observations on wild *R rattus* maintained in the labratory show that under circumstances of no reinfection, limited exercise, and adequate nutrition, infections with *T cruzi* follow chronic courses with persistence of parasites in the tissues for many months. Such a host-parasite relationship is consistent with *R rattus* being a good reservoir for *T cruzi*.

Parasites were most consistently found in the hearts of infected animals, and they were present in the heart of one rat 20 months after its arrival in the laboratory. Parasites were not uncommonly found in the cerebellum and pulmonary veins but were relatively uncommon elsewhere.

Trypanosoma cruzi infections in Panamanian *R rattus* resemble *T cruzi* infections (Chagas disease) in Panamanians. In both hosts, myocarditis is the principal feature and acute fatal infections are uncommon. Chronic trypanosomiasis is common to both. In Panama, neither man[6,7] nor rat with *T cruzi* infection has been seen with megaesophagus or megacolon.

Our study of Panamanian *R rattus* has revealed diseases which must be distinguished from *T cruzi* infection. Fleas on the rats are exceedingly rare, and *T lewisi* has not been seen directly or by culture. *Trypanosoma rangeli* has been seen in cultures of the blood but not on direct examination. It has not been possible to ascribe histological changes to *T rangeli*, for the trypanosome has not been seen in sections. In the myocardium, adrenal gland, and brain of one rat kept eight months in the laboratory, *Toxoplasma gondii* was identified. *Toxoplasma* might be confused with *T cruzi* at low magnifications, but under higher magnifications the presence of blepharoplasts in *T cruzi* is diagnostic. Other inflammatory diseases of Panamanian *R rattus* include chronic bronchiectasis, chronic pyelonephritis, chronic sialadenitis and nephritis associated with cytomegalovirus, nonspecific hepatic granulomas, hepatic cysticercosis, and parasitosis by tapeworms, roundworms, and filaria. In the rats examined, there was no correlation of these diseases with *T cruzi* infection.

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