

SIX NEW CASES OF CHAGAS' DISEASE IN PANAMA WITH REVIEW OF PREVIOUS CASES¹

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INTRODUCTION

Since the discovery of Chagas' Disease in Panama in 1931, 13 cases have been reported. The only case terminating fatally was reported by DeCoursey (1). This one was not seen by a physician prior to death and the diagnosis was made at autopsy.

Since March 1, 1935, the writers have been able to collect 6 additional cases, including two fatalities. These will be reported in this paper.

A somewhat detailed report of the first case will be given as it is considered to be typical, at least of the fatal cases, while the others will be presented more briefly.

REPORT OF CASES

Case 1. The patient, S. D., three months of age, a resident Panamanian of Chiva Chiva, was admitted to the Santo Tomas Hospital on February 25, 1935, at which time a provisional diagnosis of malaria was made. The day following admission, thick blood film examinations failed to reveal malaria parasites but instead *Trypanosoma cruzi* was found.

The history given by the mother indicated that the patient had been ill eight days prior to admission and that during this time had had fever each day. On the fourth day of the illness he began to refuse nursing and showed signs of restlessness and an increasing pallor. No history of chills, convulsions or vomiting could be elicited.

The past medical history was negative, the boy having been in good health until the onset of the present illness.

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When questioned as to the presence of bugs in the home, the mother stated that in the village there are "big bugs" which bite the children at night and suck blood. From the mother's description they might well have been a species of Reduviidae. She also said that the child had been bitten on one of the toes by a vampire bat about a month before he became ill.

Physical examination showed the patient to be well nourished and well developed. There was a definite paleness of the cheeks and conjunctiva and evident weakness and restlessness. The eyes, ears, mouth and throat showed no abnormalities. The superficial lymph nodes were not palpable and there was no enlargement of the thyroid. The thorax was well formed. The respirations were about forty per minute, and very shallow. There was no indication of any pulmonary lesion. The heart sounds were loud, and there was an accentuation of the first mitral sound as well as a cardiac irregularity in the nature of a sinus arrhythmia. The abdomen was somewhat distended and the liver was palpable. The spleen was not felt. Throughout the illness the patient's temperature fluctuated between 98° and 100.2°F.

The laboratory findings were as follows: The urine was negative. A blood count taken on the second day showed 5,540,000 erythrocytes with a hemoglobin estimation of 70 per cent (Tallquist), and 15,000 white cells of which 85 per cent were neutrophils and 15 per cent lymphocytes. A few basket cells were also seen. A second blood count taken on the fourth day showed an increase of the white cell count to 23,000 with no change in the differential count and no decrease in the erythrocytes or hemoglobin.

On the third day after admission an injection of Neo I. C. I., an Italian arsenical preparation, was administered in the dosage of 0.01 gram, but the patient became progressively worse and died on the fourth day.

Autopsy

The body was that of a well developed, black, male infant, 10 pounds in weight and 22½ inches long, on which superficial examination showed nothing.

Brain. Weight 610 grams. The substance was soft and mushy; congestion and edema were prominent throughout the entire organ. The membranes were also edematous and to such an extent that they appeared as a gelatinous cap covering the brain. The capillaries stood out prominently and here and there small hemorrhages indicated broken vessels. There was a small amount of clear fluid present, which on

examination was found to contain motile trypanosomes. Sections from all parts of the organ showed congestion and a moderate amount of perivascular round cell infiltration. The most prominent lesion was a focal inflammation which could be readily seen with low power magnification. These lesions consisted of collections of mesoglia cells mixed with mononuclear cells. In many instances necrosis of these areas was present. These foci had no relation to the blood vessels and occurred in all portions of the brain examined. The cerebrum was the only part in which the parasites were seen. Here they were present within the focal inflammatory areas just described. They were also seen in protoplasmic astrocytes but no inflammatory reaction was observed around these cells. Some of these astrocytes were so crowded with the parasites that considerable distention had occurred.

Heart. Weight 75 grams. It was definitely enlarged and flabby; the myocardium was pale and contained numerous yellow streaks. The valves were normal. The pericardial sac contained a large amount of a cloudy yellow fluid in which flecks of fibrin were suspended. Microscopically the picture was that of an acute myocarditis, with an extensive infiltration of lymphocytes, plasmocytes, macrophages and few round cells. The muscle cells were widely separated and a large number showed fragmentation and hyaline degeneration. There were large nests of parasites in the interstitial spaces and within the muscle cells, but none were observed in any of the phagocytic cells.

The pleural cavities were clear and the lungs appeared normal. The abdominal cavity contained a large amount of clear straw colored fluid. The liver was enlarged and showed extensive cloudy swelling and fatty degeneration. The kidneys were normal. The spleen was slightly enlarged and showed nothing abnormal. Several giant cells resembling the Dorothy Weed type were seen.

The adrenal glands showed no gross abnormalities and no microscopical lesions were found, but in one section a group of parasites were seen in the medulla, extracellularly and without any inflammatory reaction in the surrounding tissue. It may be noted here that previous workers have always found the parasites in the cortex of the adrenal glands.

The immediate cause of death in this case rests between a myocarditis and an encephalitis, both caused by the invasion of *Trypanosoma cruzi*. We do not feel that the clinical information is sufficient to warrant a decision one way or the other. Certainly from the gross and histopathological findings it might well be either.

Case 2. The patient, E. D., a male three years of age, was admitted to Santo Tomas Hospital in a moribund condition on May 25, 1935, and died within an hour and a half. A tentative diagnosis of bronchopneumonia had been made.

The autopsy revealed an anemic looking child with some edema of the extremities. The chest contained a considerable amount of fluid and the lungs were markedly congested and edematous.

The heart was about normal in size and somewhat flabby. On section the myocardium appeared pale and showed considerable degeneration. In the liver and kidneys some cloudy swelling and fatty degeneration were noticed.

A heavy infestation of *Ascaris lumbricoides* was found as well as a concomitant hookworm infestation.

On the basis of the gross findings at autopsy, the cause of death was given as secondary anemia due to intestinal parasitism with a resulting myocardial degeneration and eventual heart failure. This is a rather common finding in small children in this locality.

Microscopical examination of the various organs showed no important pathological changes, except in the heart. Scattered throughout the heart muscle were numerous cysts containing the *Leishmania* forms of *Trypanosoma cruzi* accompanied by an advanced degree of myocardial degeneration with round cell infiltration and fragmentation of the muscle cells. In fact the histological picture of this heart differed in no essential particulars from that described in the previous case.

Case 3. P. G., a girl fourteen suffering from lobar pneumonia was found, on examination of the blood, to harbor *Trypanosoma cruzi*. The patient was also suffering from quartan and estivoautumnal malaria. She died on September 9, 1935.

This case was encountered during a malaria survey and although there was a fatal termination, it is not considered among the fatal cases of Chagas' Disease, since death was obviously due to the pneumonia. The malaria and trypanosomiasis were considered as contributory factors.

Case 4. The patient, I. M., a male one year and four months of age, was admitted to the Santo Tomas Hospital on September 18, 1935. On admission he was suffering from some elevation of temperature, 98° to 100.8°F., evident abdominal distress with distension, a moderate anemia and a rather advanced degree of malnutrition. *Trypanosoma cruzi*

was found in the blood the day following admission; they have not only persisted but have increased in numbers since that time. At the first examination only one parasite was found per thick drop smear, while at the time of writing, fifteen days later, a total of nine parasites have been found. This despite the administration of Neo I. C. I., an Italian arsenical, which has been given empirically as a possible specific. Since admission, in spite of the increase in numbers of trypanosomes in the blood, the patient has shown a steady improvement under a proper dietary régime. Of two guinea pigs inoculated from this patient one became positive on the third day, while the other has remained negative.

Cases 5 and 6. These two, aged 28 and 14 respectively, were diagnosed on finding the trypanosomes in blood smears taken during a malarial survey. Neither of these cases showed any symptoms or abnormal physical findings.

Electrocardiographic studies have been and are still being carried out on the three cases that are living, but as yet no results conclusive enough to warrant a report have been found.

RESULTS OF ANIMAL INOCULATION

According to the literature, young dogs are very susceptible to this disease, dying soon after inoculation, while other experimental animals show varying degrees of resistance. At the time the trypanosomes were found in the blood of the infant, reported as case 1, 1 dog and 3 guinea pigs were given intraperitoneal inoculations.

Blood smears from the guinea pigs became positive 18 and 20 days after inoculation. Two of the pigs died, one 32 days and the other 65 days after they were infected. The third pig is still alive and has shown the trypanosomes in the peripheral blood continuously since it first became positive. The trypanosomes appeared in the peripheral circulation of the dog on the day following the inoculation and they were never absent from that time until its death 36 days later. During this time the animal became less and less playful, preferring to be by itself. No apparent external edema, no enlargement of the thyroid or lymph glands, as described by Chagas and others, were present. The autopsy showed that the animal had died of cardiac failure.

There was fluid in all cavities, edema and congestion of the lungs and a typical nut-meg liver. The microscopic examination of the heart showed an abundance of parasites and an advanced

TABLE 1

SYMPTOMS	RESIDENCE	AGE	DATE	ANIMAL INOCULATIONS
1. Acutely ill. Fever, gastro-enteritis.....	Aguas Buenas	18 mos.	12/ 1/30	Pos. guinea pigs
2. Occasional fever, not acutely ill.....	Aguas Buenas	2 yrs.	3/ 1/31	Neg. guinea pigs
3. Occasional fever in past. Not ill on admission.....	Aguas Buenas	6 mos.	2/ /31	Neg. guinea pigs
4. Not ill.....	Aguas Buenas	?	3/ 2/31	No inoculations
5. Fever, skin eruptions for 3 days.....	Chiva Chiva	10 yrs.	8/20/31	Pos. guinea pigs
6. No symptoms.....	Madd. Dam Highway	6 yrs.	2/ /31	No inoculations
7. No symptoms.....	Madden Dam	36 yrs.	12/18/31	Neg. guinea pigs
8. No symptoms.....	New San Juan	10 yrs.	1/ /31	No inoculations
9. No symptoms.....	Madden Dam	25 yrs.	8/ /32	No inoculations
10. No symptoms.....	La Chorrera	50 yrs.	10/ 7/32	No inoculations
11. No symptoms.....	Santa Rosa	18 yrs.	7/18/33	Neg. guinea pigs
12. No symptoms.....	Santa Rosa	74 yrs.	9/19/33	Neg. guinea pigs
13. Fatal. Not seen before death.....	Chiva Chiva	3 mos.	8/ 6/33	No inoculations
14. Fatal.....	Chiva Chiva	3 mos.	2/25/35	Pos. guinea pigs
15. Fatal. Diagnosis histologically.....	La Chorrera	3 yrs.	5/25/35	No inoculations
16. Died of lobar pneumonia.....	Guayabalito	14 yrs.	9/ 9/35	No inoculations
17. Fever and malaise....	Aguas Buenas	15 mos.	8/18/35	Pos. guinea pigs
18. No symptoms.....	Las Guacas	28 yrs.	9/ 9/35	Pos. guinea pigs and dog
19. No symptoms.....	Chilibre	14 yrs.	9/ 9/35	No inoculations

Cases 1 to 3 reported by Miller (2). Cases 4 and 5 reported by Clark and Dunn (3). Cases 6 to 12 reported by Clark (4). Case 13 reported by DeCoursey (1). Cases 14 to 19, Johnson and De Rivas.

Note. Cases 1 to 6 as reported in this paper correspond to cases 14 to 19 respectively of the table.

degree of myocardial degeneration. In contrast to the human case from which the dog was inoculated, the parasites were found only in the heart.

COMMENTS

This brings the total number of cases of American trypanosomiasis in Panama to 19. A summary of these cases appears in table 1.

While it is of course impossible to draw any definite conclusions from such a short series of cases, it is evident that certain trends or tendencies are discernible. It will be noted that no age is exempt. The disease has been found in patients ranging from three months to 74 years of age. However, 7 out of the 19 occurred in children under three years of age, and among these 7 cases there were three fatalities, a mortality rate of 42.8 per cent. Of the non-fatal cases all but the first and the seventeenth were picked up as an incidental finding during malaria surveys carried out by the Gorgas Memorial Laboratory.

In this group it was found that the symptoms and physical signs of Chagas' Disease were practically absent, and such signs and symptoms as were encountered were mild and indefinite, or usually there was a history of general malaise accompanied by a few paroxysms of fever, while in some cases even these were absent. In several of the cases there was a concomitant intestinal parasitism, malarial infection or other complicating factor to make the symptomatology and physical findings still more obscure. Case 1 of the table, as reported by Miller (2), will serve to illustrate this point adequately. This patient was more acutely ill than any of the others.

Case 1. E. B., the patient, a poorly developed, poorly nourished apathetic infant of 18 months was admitted with a diagnosis of gastroenteritis. Her head was covered with crusts and pustules and her body with scars from insect bites. The temperature ranged between 96.4° and 100.0°F., the pulse between 100 and 130 while respirations were 20 or 30. The laboratory reported heavy infestation with *Ascaris lumbricoides* and trichocephalus on stool examination. The blood examination showed a marked anemia, slight leucocytosis, an estivoautumnal gamete and *Tropanosoma cruzi*. *Two hundred and sixty-nine parasites were found per thick drop film.* Treatment directed against the helminthiasis resulted in a gradual and steady improvement. The trypanosomes disappeared from the blood after four weeks.

The absence of symptoms definitely referable to the trypanosome infection and the mildness of such symptoms as do exist in most of these cases is in rather striking contrast to the description of the disease as reported by workers from other localities. In fact, if the clinical picture as it is described by Chagas and others is to be taken as being requisite to the diagnosis of Chagas' disease it might well be argued that we are not dealing with Chagas' disease at all. What is certain, however, is that the cases presented were patients harboring the *Trypanosoma cruzi* and are therefore cases of American trypanosomiasis. The possibility that we are dealing here with a different or less virulent strain of the trypanosome, suggests itself, and there would seem to be some justification for at least entertaining this possibility.

In the 3 fatal cases, those reported in this paper, as well as the one reported by DeCoursey, the outstanding lesion in the heart was of the diffuse inflammatory type associated with a considerable degree of damage to the muscle fibers themselves. In the brain, on the other hand, the lesions were focal, consisting of collections of nests of cells in which occasionally were seen clumps of the parasites. In this situation the neuroglia cells were the elements invaded. In both the heart and brain the various developmental stages of the parasite were seen, i.e., the crithidial forms and dividing *Leishmania* forms, etc.

Since the discovery of the *Trypanosoma cruzi* in 1909 (5) there has been a steady increase in the number of cases reported as well as a widening of the geographic distribution. Whether this is due to a spread of the disease or a more ready recognition of the same, is difficult to say. The situation in Panama is such, that, since the disease has been so rarely encountered, the index of suspicion for it is extremely low, while the index of suspicion for malaria, with which it is most likely to be confused, is high. This holds not only for the clinical diagnosis but for the laboratory diagnosis as well. Cases are liable to be overlooked, since, when the examination of the blood reveals malaria parasites, the diagnosis of malaria is made and no further examination for other parasites is undertaken. The case with which the diagnosis in these cases can be missed is specially well illustrated in

case 2 of the present report. In this case it will be remembered that the diagnosis was not made before death and was missed at the time of the autopsy; it was only through the routine histological examination of the organs that the infection was recognized. Another source of error is, undoubtedly, the scarcity of the parasites in the peripheral blood. In order to hope for any success at all, thick drop blood preparations must be examined and even in these, frequent negative results can be expected in patients known to harbor the trypanosome. As a rule but one or two parasites have been found per preparation in most of these cases. It is obvious therefore that the thin film preparation is of little diagnostic value.

In view of the foregoing, it would not seem unlikely that in the past some cases of Chagas' disease have been regarded as cases of malaria. This seems likely considering that 13 cases have been reported from Panama since 1931 when the disease was first recognized, and that 6 additional cases have been discovered within the past seven months.

From the distribution of the cases, thus far reported, it is reasonable to believe that, if Chagas' disease is at all prevalent, it is to be looked for in the more out-lying districts of the interior of the Republic where the vectors and animal reservoirs are found. Here medical service is either absent or inadequate, and the lack of laboratory facilities makes a definite diagnosis impossible, except in the somewhat rare instances where the patient is brought to the hospital, as in the cases reported from the Santo Tomas Hospital, or where the laboratory is taken to the patient, as in those discovered by the workers of the Gorgas Memorial Laboratory. It is also significant that practically all of the cases were found in the Chagres River Basin, which is the only territory where extensive malarial surveys have been made.

It has been pointed out that *Trypanosoma cruzi* in Panama can give rise to grave symptoms and may terminate fatally in infants or young children, but seems to have no very marked or recognizable effect on the adult, so that a considerable percentage of the population may unsuspectingly harbor the parasite. Also, it is evident that this parasite is distinctly cosmopolitan in its

preferences, since it is infective, not only for man, but also for numerous wild and domestic animals. Insect vectors, of which there are three, *Triatoma geniculata* (3) *Rhodnius pallescens* (6) and *Eratyrus cuspidatus* (7), show quite promiscuous tendencies, being equally partial to infants and armadillos, as well as many other susceptible animal species. Besides these, there are several insects, such as the tick (8), which stand accused and while they have not been authoritatively convicted, neither have they been definitely acquitted.

All the above mentioned factors tend to favor a wide distribution. In Panama there is an ample supply of the various species of armadillos, opossums, and other animals serving as wild reservoirs, together with three distinct insect vectors. It seems reasonable, therefore, to infer that we are likely to encounter an increase in the number of cases of Chagas' disease in this country, coincident with a further and more extensive study of the interior population.

And if it be remembered, in addition, that as far as present studies go, the symptomatology here in Panama is vague and atypical and that the infant mortality of the disease is high, a careful investigation for the presence of trypanosomes in all doubtful cases would seem to be indicated.

SUMMARY

1. Six additional cases of Chagas' disease have been discovered in Panama since March 1, 1935, including 2 which terminated fatally.

2. In Panama the disease is probably fatal in a high percentage of cases in the very young, but seems to have few or no effects on adults.

3. The disease as it has thus far been encountered in Panama does not present the clinical picture as it has been described from other localities.

4. There is probably a higher incidence of Chagas' disease on the Isthmus of Panama than has been heretofore suspected.

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