Further evidence of spontaneous cure in human Chagas disease

Uma nova evidência de cura espontânea em doença de Chagas humana

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ABSTRACT

An acute case of Chagas disease was studied in 1944, with clinical and laboratory follow-up until 2007, in Bambuí, Minas Gerais, Brazil. A five-year-old girl living in a rural hut that was highly infested with *Triatoma infestans* presented a febrile clinical condition compatible with the acute form of trypanosomiasis. She presented a positive thick blood smear, but never again showed serological and/or parasitological evidence of *Trypanosoma cruzi* infection, on several occasions. This patient never received any specific treatment and, to this day, she remains completely asymptomatic, with normal findings from clinical, electrocardiographic, X-ray and echocardiographic examinations.

Key-words: Chagas disease. Spontaneous cure. Longitudinal study.

RESUMO

Um caso agudo de doença de Chagas foi estudado em 1944, com seguimento clínico e laboratorial até 2007, em Bambuí, Minas Gerais, Brasil. Vivendo em rancho rural altamente infestado por *Triatoma infestans*, e apresentando um quadro clínico febril compatível com forma aguda da tripanossomíase, uma menina de cinco anos teve gota espessa positiva, nunca mais apresentando evidências sorológicas ou parasitológicas de infecção pelo *Trypanosoma cruzi*, em variadas oportunidades. A paciente nunca foi tratada especificamente e permanece, até o presente, completamente assintomática, com exames clínicos eletrocardiográficos, radiológicos e ecocardiográficos normais.

Palavras-chaves: Doença de Chagas. Cura espontânea. Estudo longitudinal.

Untreated human Chagas disease normally evolves in such a way that the parasitic infection persists and is maintained throughout the host's life, independent of clinical features, both in the acute and in the chronic phase. Nevertheless, in some experimental models and even in some very exceptional human cases, spontaneous cure has been demonstrated, in terms of parasite and antibody elimination. The complete meaning of such events is not yet understood, and it is important to record possible occurrences, in order to evaluate the dimensions of this phenomenon.

CASE REPORT

The subject (L.A.B.) is a 68-year-old woman of white skin color, who was born and still lives in the municipality of Bambui, State of Minas Gerais, Brazil. In February 1944, at the age of five years, she presented a febrile and edematous clinical condition that had started 23 days earlier. At that time, she was living in the rural zone of the municipality, at the locality of Sapé, in a poorly constructed mud hut that was highly infested with *Triatoma infestans* (data from the local healthcare post of the Oswaldo Cruz Institute, file card number 070).

The initial examination revealed that she was febrile (37.7°C), with generalized edema and lymph node enlargement. A red papillomatous skin lesion on the posterior face of her left leg, of diameter 2cm, was interpreted as an entry portal for *Trypanosoma cruzi*. Clinical examination revealed tachycardia, rough systolic murmur and very slight splenomegaly. There were no signs of heart failure or acute meningoencephalitis. Direct fresh investigation for *Trypanosoma cruzi* was negative, but a thick drop preparation of peripheral blood was clearly positive. Electrocardiogram (EKG) showed only sinusal tachycardia, and the chest X-ray was normal. Furthermore, a complement fixation test (CFT) at that time was negative.

No specific treatment for Chagas disease has been provided for this patient at any time during her life. Her fever and edema of 1944 disappeared after about three weeks. No xenodiagnosis was performed during the acute period.

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Another CFT for *Trypanosoma cruzi* antibodies was negative in 1947. Other conventional serological tests have been performed on several occasions since then: CFT in 1949, 1951, 1955, 1963, 1964, 1965 and 1969; indirect hemagglutination in 1984, 2002 and 2004; immunofluorescence test in 1984, 2002 and 2006; and enzyme-linked immunosorbent assay (ELISA) test in 2002, 2003, 2004 and 2006. All of these tests produced negative results. In 2004, flow cytometry and polymerase chain reaction (PCR) were also negative, as was another PCR in 2006. Xenodiagnosis (1949, 1954 and 1964) and blood culturing using the Chiari method[4] (1984 and 2003) were also negative. Clinically, the patient has had very satisfactory evolution, never presenting symptoms or signs of chronic cardiac and/or digestive Chagas disease (medical assessments in 1947, 1949, 1951, 1955, 1963, 1964, 1969, 1984, 1990. 2002, 2003 and 2005). The EKGs were normal at all these assessments, with only one record of atrioventricular space enlargement (at the upper limit), in 1964. The chest X-ray result was normal (heart shadow) in 1949, 1964, 2002 and 2003. In 2006, a complete review of the case was performed in Bambuí and Uberaba (Medical School), and showed normal results in the physical examination and complementary clinical tests: EKG, echocardiogram, X-ray (heart, esophagus and colon), ergometric test and electrocardiographic test for cardiac dysautonomy.

DISCUSSION AND CONCLUSIONS

The present case can be interpreted as a further report of spontaneous cure of human Chagas disease. Like the cases described by Zeledón et al[15] and Francolino et al[7], it was registered in an endemic area and presented a typical and well-established acute onset, which was diagnosed by the direct parasitological test. In all the previous reports, the basic argument for claiming that disease cure had occurred was the continuing, consistently negative conventional IgG serology findings, along with the lack of positive indirect parasitological test results (xenodiagnosis and blood culturing), a concept that is well established in the literature[1]. In the present case, the PCR technique also gave negative results, as did flow cytometry, similarly to the Uruguayan observations[8]. In all these cases, the clinical evolution was very good, thus suggesting that the histological and neuronal damage that may have been produced in the acute phase did not result in apparent chronic lesions over a long time, as observed in experimental models and longitudinal studies[2 3 6 7 8 9 10 13 14 15]. A single transient EKG abnormality (enlargement of the PR interval) was observed twenty years after the acute phase, and this disappeared completely in subsequent EKGs. According to several authors, this is a common occurrence among young patients following the acute phase, and it does not have any clinical significance when it is unconnected with any other heart abnormalities[5 9 12 14]. No clinical and/or epidemiological factors were identified in this or in the previous reports that would explain the spontaneous cure[7 15]. The infection route in all of these cases was certainly vectorial (*Triatoma dimidiata* in Costa Rica and *Triatoma infestans* in Uruguay and Brazil) and an apparent acute form was presented, with local and general reactions (fever, adenomegaly and skin lesions). The single common factor among these cases might be the patients' ages at the beginning of the infection, which was over five years old in all cases. This could at least be a factor involving better immunological defenses, since the acute disease is usually less aggressive in older individuals[5 7 8 9 10 13 14 15]. Spontaneous cure from *Trypanosoma cruzi* infection can be observed in cases of experimental Chagas disease, for instance in goats and larger mammals[6 13]. Nevertheless, in spite of its so far unquestionable occurrence in human beings, spontaneous cure remains a very rare and exceptional event. Taking into account the regions where this phenomenon has been described (Bambuí, Costa Rica and Uruguay), hundreds of untreated chronic cases remain infected throughout the remainder of these individuals' lives, independent of the clinical evolution. The same can be observed with regard to well-conducted longitudinal studies in other endemic and nonendemic areas[2 3 5 11 12 14].

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