

Chagas' disease: study of congenital transmission in cases of acute maternal infection

Doença de Chagas: estudo da transmissão congênita nos casos da infecção materna aguda

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ABSTRACT

We studied three pregnant women with acute chagasic infection. Two patients, infected in the third trimester of pregnancy, had uninfected children. The third patient, infected earlier, had an infected newborn. These results encourage research on risk factors of transmission and on medical decisions concerning pregnant women with acute Chagas' disease.

Key-words: Chagas' disease. *Trypanosoma cruzi*. Congenital infection. Acute maternal *Trypanosoma cruzi* infection.

RESUMO

Se descrevem 3 gestantes com a doença de Chagas aguda. Duas gestantes infetadas no 3º trimestre de gestação não tiveram crianças infetadas. O 3º filho, daquela mãe foi infetado no 1º trimestre, nasceu com doença de Chagas congênita. Estes resultados induzem a investigação sobre os fatores de riscos da transmissão e sobre as decisões médicas na condução dos casos de gestantes com a doença de Chagas aguda.

Palavras-chaves: Doença de Chagas. *Trypanosoma cruzi*. Infecção congênita. Infecção materna aguda.

Chagas' disease is one of the most important parasitic endemic diseases in Latin America, where near 20 million people are infected and 60 million are at risk of infection. Due to the efforts to carry out vector control in several countries, the transmission through the insect bite, the main epidemiological way of infection, is decreasing, at least in Brazil, Uruguay, Chile and Argentina. Indeed, some of these countries, and some provinces of other countries have been declared free of vector transmission by the Pan American Health Organization. Therefore, nowadays congenital transmission has become more important. In fact, it is estimated that in Argentina the congenital cases are at least 10 times more frequent than the acute cases by vector transmission⁵. Because of migration of people from endemic countries, in the United States there were reported cases of infection, probably by blood transfusion or congenital transmission⁶.

Our group has performed several studies on congenital Chagas' disease, and has proposed a protocol for diagnosis and treatment^{8,9}. Moreover, several experimental studies have been done in an attempt to determine the possible mechanisms involved in congenital transmission, taking into account that only 2 to 10% of infected mothers transmitted the infection to their babies^{4,11}. Nevertheless, to date little is known about the factors involved in vertical transmission in humans. There has been speculation about parasitic factors, such as the strain of *T. cruzi* or the parasitic load, and about host factors, such as immunological or nutritional status of pregnant women, obstetrical history and maternal stage of disease² but none of these factor have been conclusively demonstrated yet. Epidemiological surveys and studies about possible mechanisms of congenital Chagas' disease have been conducted in mothers in the indeterminate or chronic period of infection.

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In this communication, we report clinical, parasitological and serological patterns of three cases of mother-child in which acute Chagas' infection during pregnancy was detected, as well as the presence or absence of infection among the newborns.

CASE REPORTS

The study group included three pregnant women infected during pregnancy and their babies. Diagnosis of the maternal infection was made by clinical, epidemiological and parasitological parameters. The parasitological methods used were the microhematocrit centrifuge technique, as described by Woo¹², Strout and hemocultures, essentially performed as previously described in our laboratory¹. The classical serological methods (ELISA, Indirect Immunofluorescence and Indirect Hemagglutination) were performed for immunodiagnosis. For histological examination, the placenta was fixed with 10% formaldehyde for 24h, dehydrated with alcohol/xylool, embedded in paraffin and stained with hematoxylin-eosin.

Case 1. A 30-year-old pregnant woman, accidentally infected while manipulating *T. cruzi* in a research laboratory. She was at the 32nd week of pregnancy when she became infected, and developed severe acute Chagas' disease, with fever, hepatosplenomegaly and schizotrypanids. Parasitemia was high, detectable through direct blood examination. Due to the severity of the clinical course, the patient required hospitalisation in the intensive care unit and it was necessary to anticipate parturition. Cesarean delivery was indicated at 35 weeks of pregnancy according to clinical, obstetric, and therapeutic criteria. Therapy with benznidazole was successfully applied to the mother immediately after delivery.

In spite of the high parasitemia and the severe clinical course presented by the mother, the newborn - a male infant weighing 3.7kg - was not infected, as demonstrated by the absence of circulating parasites and antibodies at birth and until the twelfth month of life. The parasitemia was serially studied by hemoculture, a methodology that previously proved to have near 100% sensitivity in congenital and acute cases. All the serology tests were negative up to 12 months.

Case 2. A 17-year-old woman, infected by vector transmission, in whom the acute infection was clinically diagnosed by ophthalmic ganglionar complex (Figure 1A), and was parasitologically confirmed by the detection of circulating parasites by microhematocrit technique at the 28th week of pregnancy. The clinical course of the disease was mild, and the patient was controlled on an outpatient basis. The delivery took place at 38 weeks of pregnancy, by cesarean section. In this case, histological studies of the placenta were performed, and amastigote forms of *T. cruzi* were detected in the free chorionic villi (Figure 1B), as well as along the decidua plate. The following microscopic alterations were observed in the placenta: granulomatous changes, inflammatory infiltrates and focal necrosis in the

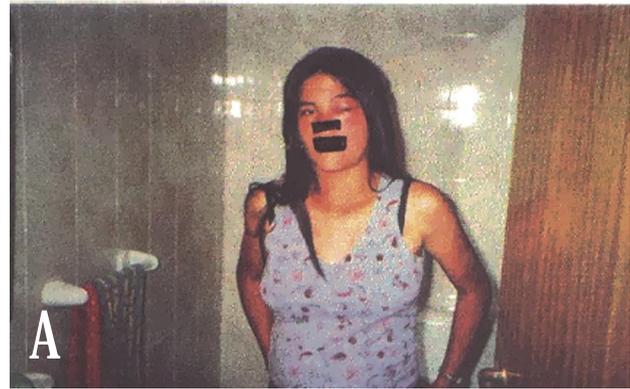


Figure 1A - Pregnant woman (case 2) at 28 weeks of pregnancy, showing ophthalmic ganglionar complex, typical sign of acute Chagas disease.

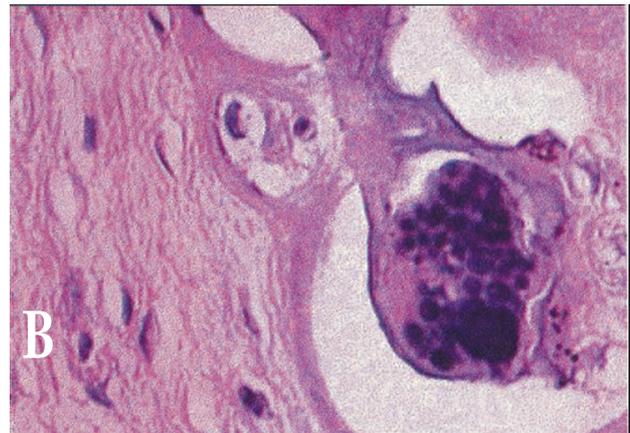


Figure 1B - Histological section of placenta (case 2), stained with hematoxylin-eosin, showing amastigote forms of *Trypanosoma cruzi* (400x).

chorionic villi. The fibrinoid layer was thicker in some modified villi in which syncytial modifications such as edema and calcification foci were present. Vascular thromboses were also seen.

The newborn was a female infant weighing 3.4kg, and did not present clinical symptoms of Chagas' infection. The absence of infection was confirmed by the fact that the parasitological examinations of cord blood - both by microstrout and hemoculture methods - were negative at birth, and also at the 6th month of life. The infant also have negative serology during the first year of life. Treatment with benznidazole was administrated to the mother after delivery.

Case 3. A 19-year-old woman, in whom the acute infection was clinically and parasitologically diagnosed by ophthalmic ganglionar complex and circulating parasites detected during the 20th week of pregnancy. The maternal infection occurred by vector inoculation. The clinical course of disease was mild, and the patient was controlled on an outpatient basis. The baby was born by vaginal delivery at 38 weeks of gestation, with a weight of 3.1kg, with hepatosplenomegaly, and positive parasitemia and serology. Both, the mother and the newborn were treated with Benznidazole immediately after delivery, and examined through parasitological and serological methods. Sera collected during the longitudinal follow-up of the baby

Table 1 - Clinical, parasitological and serological results of infected mothers and newborns.

Case	Age	Week of infection	Week of delivery	Clinical symptoms	Type of delivery	Mother			Newborn	
						parasitology	serology	placenta	parasitology	serology
1	30	32	35	severe	cesarea	positive	doubtful	ND*	negative	negative
2	17	28	38	mild	cesarea	positive	doubtful	positive	negative	negative
3	19	20	38	mild	vaginal	positive	positive	ND	positive	positive

* Not done

became negative for *Trypanosoma cruzi* as determined by the same serological tests, at 7 months of age. The parasitological test for parasites was negative, as well.

Table 1 summarizes the main clinical, parasitological and serological findings in the three infected mothers and their babies.

DISCUSSION

The incidence of congenital transmission has always been determined in women during the indeterminate or chronic period of infection^{2,7}. During these phases of the disease, the parasitemia is low and recurrent, undetectable by direct parasitological methods and only detectable in some cases by xenodiagnosis or hemoculture. There are few previous reports on acute infection of pregnant woman. In fact, Rassi et al¹⁰ in 1958 in Brazil, reported a case, then reviewed by Brabin³. In the present work we studied three acute cases in pregnant women, with high parasitemia and, at least in one of those cases, placental infection and severe histological changes. Taken together, the lack of congenital infection in two of the three studied cases, suggests that the parasitic load does not seem to be a main factor involved in the maternal-fetal transmission of *T. cruzi*, at least during acute infection of the mother. Moreover, in case 2, the only one in which it was possible to study the placenta, the presence of amastigotes and the severe histological changes were not associated with fetal infection, results that are in agreement with Rassi et al¹⁰ and Moya et al⁷, who reported that placental infection is not synonymous with fetal infection. Even though we studied only three cases, it is interesting to note that in both non-infected cases the maternal infection took place during the third trimester of pregnancy, while in the case in which the newborn was infected, the infection occurred in the earlier period of pregnancy. This finding suggests that the time of infection could be a risk factor for *T. cruzi* transmission, in the acute infection of the mother. On the other hand, it should not be discarded that, as in other bacterial or viral infections, the transmission could also take place at the moment of delivery. In this sense, in our previous experience⁸ we have found babies who were parasitologically negative at birth and who became positive at 10-15 days of life; with no possibility of other possible forms of transmission.

Finally, as specific antiparasite therapy can not be administrated during pregnancy with the available drugs, it will be necessary to discuss possible medical and therapeutic decisions in pregnant women with acute chagasic infection.

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