ABSTRACT

A family of four, including a 24-year-old female, presented to our laboratory in December 2006 with a prolonged febrile syndrome of unknown etiology. After extensive laboratory screening, acute Chagas disease was confirmed by positive T. cruzi blood culture, combined with clinical, epidemiological and serological findings. The young female, her parents and husband received a daily dose of benznidazole, but she developed serious drug intolerance and amenorrhea. Her treatment was interrupted by a confirmed pregnancy of about 12 weeks of gestational age. The child was born prematurely on April 18, 2007 with low weight and signs of respiratory distress syndrome. Diagnostic screening tests for congenital infections, including Chagas disease, were negative during the perinatal period. About four months after birth, clinical findings generated the following clinical indicators of congenital disease: convergent strabismus, microcephaly and delayed psychomotor development. Serological tests confirmed seroconversion, and magnetic resonance findings included cystic lesions and intracranial calcifications. The authors discuss the critical nature of this serious public health problem in the region and suggest necessary revisions to the recommended treatment for pregnant patients with acute Chagas disease.

Keywords: Chagas disease; Infectious disease Transmission, Vertical; Trypanocidal Agents.

INTRODUCTION

Brazil has been certified as free of Triatoma infestans, the major vector of Chagas disease. The last seroprevalence survey of Chagas disease made in rural areas from Brazil shows low infection rates among children up to five years of age and demonstrated 0.025% of congenital transmission. Despite this achievement, continuous entomological surveillance should not be halted. Indeed, this paper presents evidence that direct or indirect transmission by other non-domiciliated vectors could be improved, mainly in the Amazon region. This region has well-established T. cruzi enzootic cycles and has suffered ecological imbalance as a result of major anthropogenic changes in the nineties. These multifactorial influences increase the focal risk of Chagas disease in the Amazon region, as previously described. This is the first report of congenital Chagas disease autochthonous from Amazon region, resulting from maternal acute infection acquired during a family-centered outbreak of oral transmission.

CASE PRESENTATION

A family of four, including a young couple (male, 26 years old, and female, 24 years old) and her parents (52 and 56 years old) presented to Instituto Evandro Chagas

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(IEC), seeking a cure for their prolonged febrile illness. This disease appeared simultaneously in all four family members and was of approximately 18 days’ duration. Diagnostics were conducted by two sequential and three parasitological tests. Parasitological (positive T. cruzi blood culture in two of the patients), clinical and serological findings confirmed an acute Chagas disease (ACD) outbreak in this family (Table 1).

Epidemiologic investigation did not find vectors associated with transmission in this family outbreak. In addition, the occurrence in an urban area and the almost simultaneous onset of symptoms in all four patients suggest an association between illness and a food (açaí juice) ingested by all four family members, which is not further discussed in this paper.

All patients received daily doses of benznidazole in January of 2007. The young woman showed serious drug intolerance with nausea, vomiting, abdominal pain and dizziness. Therefore, her treatment was interrupted due to suspected pregnancy (amenorrhea) and she experienced a spontaneous remission of symptoms. A pregnancy of 12 weeks’ gestational age was confirmed, and the patient was followed clinically throughout the pregnancy. The patient’s IgG anti-T. cruzi tests were consistently positive by Indirect Hemagglutination assay (IHA) and Indirect Immunofluorescent Assay Test (IFAT). Her serial parasitological tests (3) showed negative results. Throughout the pregnancy, the patient had no symptoms of Chagas disease. A morphological ultrasonograph from the 29th week of pregnancy showed no abnormalities.

The female child was born prematurely (34 weeks) on Apr. 18 2007, by cesarean section, with a low birth weight (1850 grs), jaundice and signs of Respiratory Distress Syndrome (RDS), requiring intensive care. While in intensive care, she was diagnosed with bacterial Pneumonia. Two days after birth, the newborn was submitted to parasitological and serological exams to detect T. cruzi infection by thick blood film, IFAT and IH. All of these test results were negative (Table 1).

The newborn recovered after three weeks and showed no alterations up to the fourth month of life. During a routine visit to our laboratory when the child had reached four months of age, we observed convergent strabismus and delayed psychomotor development (the child could not support her head). On physical examination, microcephaly and closed bregmatic suture were observed. Hematological parameters showed hemoglobin levels of 9.7 g%.

During this period, results of the search for T. cruzi in peripheral blood by the microhematocrit method, blood culture for T. cruzi, and indirect xenodiagnosis remained negative; however, we observed serological positive conversion by IH and IFAT (IgG anti – T. cruzi: 80). Table 1 shows all results from the mother and child at different times and the results from all persons studied in the course of this outbreak during the acute phase of Chagas disease. In order to evaluate other possible agents of congenital infection, a serologic study was conducted to detect the following: toxoplasmosis (IFAT); cytomegalovirus by the ELISA method; syphilis by the VDRL and FTA-Ab's methods and rubella by the ELISA method. The results for all of these tests were negative in both mother and child, except for the test for IgG antibodies to cytomegalovirus, which was positive in the mother.

Magnetic resonance imaging showed abnormalities in the brain with atrophic lesions characterized by dilated ventricles and encephalomalacia areas, suggesting intracranial calcifications as well as cystic lesions (Figure 1).

Table 1 – Parasitological and serological findings in all family members and in child.

<table>
<thead>
<tr>
<th></th>
<th><strong>Child</strong></th>
<th><em>Mother</em></th>
<th>Family members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2 days</td>
<td>4 months</td>
<td>12 months</td>
</tr>
<tr>
<td>Microhematocrit</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Indirect</td>
<td>Negative</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Hemagglutination</td>
<td>Negative</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>IgM antibodies</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>anti- T. cruzi</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>IgG antibodies</td>
<td>Negative</td>
<td>80</td>
<td>320</td>
</tr>
<tr>
<td>anti- T. cruzi</td>
<td></td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>Xenodiagnosis</td>
<td>Non realized</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Blood Culture</td>
<td>Non realized</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

* Tests on the mother conducted at least twice: before treatment attempt and post delivery
** Tests on the child conducted at least three times post birth

Source: Chagas Disease Laboratory/Instituto Evandro Chagas/SVS - Ananindeua
The child was treated with benznidazole for 45 days and the case was reported to the Ananindeua Municipality Health Department. At 12 months of age, she remains under clinical observation. Her mother was treated, and the side effects of this treatment were rigorously controlled. The serological exams of both mother and daughter remained positive.

**DISCUSSION**

Studies conducted in T. cruzi-endemic areas found a Chagas disease prevalence of about 1% in pregnant women from Brazil, 4% to 6% in pregnant women from Argentina, 2% to 3% in pregnant women from Chile and 12% in pregnant women from Bolivia. These rates are related to chronic maternal infection, in which the blood levels of parasites are low (1 to 10%). In contrast, during the acute phase, the blood parasite levels are high and induce the host immunological response. This state increases the risk of congenital infection. However, the Brazilian Amazon is an area with active transmission of ACD and underestimated rates of chagasic infection.

These occurrences of ACD outbreaks in urban areas probably free of vectors and transmission by unusual form bring forward new epidemiological approaches to the control strategies of this ancient disease.

Moretti et al. (2005) described three pregnant women with ACD in Argentina. Two of them were infected during the third trimester and had uninfected newborns. One of the women became infected during the second trimester and gave birth to a sick child with hepatosplenomegaly. As with any infection with the potential for vertical transmission, early pregnancy is associated with a high risk of infection. In this case, the mother’s infection during the first trimester may have been a determinant of the child’s infection and serious neurological involvement.

Studies carried out in Argentina, Bolivia, Paraguay and Brazil describe clinical spectra of congenital infection as well as asymptomatic to symptomatic forms. In asymptomatic forms the clinical signs vary from mild to severe symptoms: premature births, low birth weight, hepatomegaly, splenomegaly, neurologic signs, jaundice, anemia, anasarca and RDS are commonly described. In the...
Doença de Chagas congênita por infecção aguda maternal por Trypanosoma cruzi transmitida via oral

RESUMO

Uma família de quatro pessoas, incluindo uma mulher de 24 anos de idade, apresentou-se em nosso laboratório em dezembro de 2006 com uma síndrome febril prolongada de etiologia desconhecida. Após uma triagem laboratorial extensa, foi confirmada, por meio de hemocultura positiva para T. cruzi, combinada com achados clínicos, epidemiológicos e sorológicos, a ocorrência de doença de Chagas aguda. A paciente, seus pais e marido receberam uma dose diária de Benznidazol, porém ela desenvolveu intolerância severa à droga e amenorreia. Seu tratamento foi interrompido devido à confirmação de gravidez de cerca de 12 semanas de idade gestacional. A criança nasceu prematuramente em 18 de abril de 2007 com baixo peso e sinais de síndrome do desconforto respiratório. Testes de triagem diagnóstica para infecções congênitas, incluindo a doença de Chagas, resultaram negativos durante o período prenatal e perinatal. Aproximadamente quatro meses após o nascimento, os achados clínicos forneceram os seguintes indicadores de diagnóstico: esotropia, microcefalia e atraso no desenvolvimento psicomotor. Testes sorológicos perinatais resultaram em séroconversão e a ressonância magnética apresentou lesões císticas e calcificações intracranianas. Os especialistas discutem a natureza crítica deste grave problema de saúde pública na região e sugerem revisão de protocolos de tratamento para pacientes grávidas com a doença de Chagas aguda.

Palavras-chaves: Doença de Chagas; Transmissão Vertical de Doença Infecciosa; Tripanossomicidas.
Enfermedad de Chagas congénita por infección aguda maternal por Trypanosoma cruzi transmitida vía oral

RESUMEN
Una familia de cuatro personas, incluyendo a una mujer de 24 años de edad, se presentó en nuestro laboratorio en diciembre de 2006 con un síndrome febril prolongado de etiología desconocida. Luego de una extensa selección y análisis de laboratorio, se confirmó, por medio de hemocultivo positivo para T. cruzi, combinado con hallazgos clínicos, epidemiológicos y serológicos, la ocurrencia de la enfermedad de Chagas aguda. La paciente, sus padres y marido recibieron una dosis diaria de benzonidazol, pero ella desarrolló intolerancia severa a la droga y amenorrea. Su tratamiento fue interrumpido debido a la confirmación del embarazo con cerca de 12 semanas de edad gestacional. El niño nació prematuramente el 18 de abril de 2007 con bajo peso y señales de síndrome de dificultad respiratoria. Pruebas de selección diagnóstica para infecciones congénitas, incluyendo la enfermedad de Chagas, resultaron negativas durante el período perinatal. Aproximadamente cuatro meses después del nacimiento, los hallazgos clínicos suministraron los siguientes indicadores clínicos de enfermedad congénita: esotropia, microcefalia y retraso en el desarrollo psicomotor. Pruebas serológicas confirmaron la seroconversión y la resonancia magnética presentó lesiones císticas y calcificaciones intracraneanas. Los autores discuten la naturaleza crítica de este grave problema de salud pública en la región y sugieren revisiones necesarias al tratamiento recomendado para pacientes embarazadas con la enfermedad de Chagas aguda.

Palabras clave: Enfermedad de Chagas; Transmisión Vertical de Enfermedad Infecciosa; Agentes Tripanocidas.

REFERÉNCIAS


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