



Case Report

Chagas disease across pregnancy and early infancy: Leukoencephalomalacia and achondroplasia in two unusual cases

Wilmer E. Villamil-Gómez^{1,14,*}, Guillermo Edgardo Barahona-Escobar²,
 Melvin Antonio Moisa-Martínez³, Diana Peña-Navarro^{4,5}, Lorena Vanessa Paniagua-Rojas⁶,
 Dainer Elías Rincones-Soto⁷, María Leonor Barcha⁸, Ángel Ochoa-Salcedo⁹,
 Melchor Álvarez-Mon Soto¹⁰, Melisa Eyes-Escalante¹¹, Juan Venegas-Hermosilla¹²,
 Alfonso J. Rodríguez-Morales^{13,*}

¹ Centro de Investigación en Ciencias de la Vida, Universidad Simón Bolívar, Barranquilla, Colombia

² Pediatric Infectious Diseases Department, Hospital Nacional de Niños Benjamin Bloom, San Salvador, El Salvador

³ Pediatric Intensive Care Department, Hospital Nacional de Niños Benjamin Bloom, San Salvador, El Salvador

⁴ Pediatrics Department, Hospital de la Orinoquia (HORO), Yopal, Casanare, Colombia

⁵ Grupo de Investigación Parasitología Veterinaria, Laboratorio de Parasitología Veterinaria, Universidad Nacional de Colombia (UNAL), Bogotá, Distrito Capital, Colombia

⁶ Universidad Cristiana de Bolivia (UCEBOL), Santa Cruz de la Sierra, Bolivia

⁷ Medical Network, Health Secretary, Barranquilla, Atlántico, Colombia

⁸ Hospital Universitario de Sincelajo, Sincelajo, Sucre, Colombia

⁹ Clínica La Concepción, Sincelajo, Sucre, Colombia

¹⁰ Hospital Universitario Príncipe de Asturias, Universidad de Alcalá, Instituto Ramón y Cajal de Investigaciones Sanitarias-IRYCIS, Alcalá de Henares, Spain

¹¹ Programa del Doctorado de Medicina Tropical, SUE Caribe, Universidad del Atlántico, Barranquilla, Colombia

¹² Programa de Biología Celular y Molecular, Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile, Santiago de Chile, Chile

¹³ Faculty of Health Sciences, Universidad Científica del Sur, Lima, Peru

¹⁴ Committee of Tropical Diseases, Asociación Panamericana de Infectología, Lima, Peru

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ABSTRACT

Background: Congenital Chagas disease remains an underdiagnosed cause of neonatal morbidity and mortality in endemic regions. Although most infected neonates are asymptomatic or present with nonspecific findings, severe and atypical manifestations involving the central nervous system or coexistence with genetic disorders are rarely reported. The full spectrum of neurologic injury and potential interactions between *Trypanosoma cruzi* infection and fetal developmental conditions remain poorly characterized.

Cases: We report two unusual clinical presentations of *T. cruzi* infection during early infancy and pregnancy from El Salvador and Colombia. The first case involved a 2-month-old female infant who presented with septic shock, acute kidney injury, coagulopathy, and respiratory failure. Direct parasitological examination revealed circulating *T. cruzi* trypomastigotes, confirming acute Chagas disease; however, the route of transmission could not be definitively established. Despite a favorable parasitological response to nifurtimox, brain magnetic resonance imaging subsequently demonstrated bilateral cystic leukoencephalomalacia and widespread ischemic sequelae, which were interpreted as secondary hypoxic-ischemic injury after the severe systemic illness. The second case involved a pregnant woman with confirmed *T. cruzi* infection whose fetus was prenatally diagnosed with achondroplasia. The neonate developed severe respiratory failure and died 10 days after birth. No alternative infectious or metabolic causes that explained the skeletal dysplasia or fatal outcome were identified.

Conclusion: These cases highlight unusual presentations of *T. cruzi* infection during early infancy and pregnancy, including severe systemic disease followed by hypoxic-ischemic neurologic sequelae and coexistence with fetal achondroplasia. They underscore the importance of maternal screening and systematic evaluation of exposed neonates.

* Corresponding authors.

E-mail addresses: wilmer.villamil@unisimon.edu.co (W.E. Villamil-Gómez), arodriguezmo@cientifica.edu.pe, alfonso.rodriguez@uam.edu.co (A.J. Rodríguez-Morales).

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Introduction

Chagas disease, caused by *Trypanosoma cruzi*, remains an important public health problem in Latin America and increasingly affects non-endemic regions through population mobility [1,2]. Although vector-borne transmission predominates, congenital transmission is increasingly relevant and may occur during any stage of maternal infection [3]. Most congenitally infected neonates are asymptomatic, contributing to underdiagnosis, whereas symptomatic disease may include prematurity, hepatosplenomegaly, cytopenias, respiratory distress, myocarditis, meningoencephalitis, and multiorgan failure [4,5]. Early diagnosis is critical because antiparasitic treatment during infancy is highly effective [5].

Neurologic involvement and neurologic sequelae after severe Chagas disease in early infancy remain incompletely characterized [6]. In critically ill infants, distinguishing direct central nervous system (CNS) involvement from secondary hypoxic-ischemic injury is particularly important. Moreover, the interaction between maternal *T. cruzi* infection, fetal development, and coexisting genetic disorders is poorly understood [7]. Achondroplasia, the most common skeletal dysplasia, is associated with respiratory complications and increased early-life mortality [8].

We report two unusual clinical presentations: acute Chagas disease in early infancy, with the route of transmission remaining uncertain, followed by extensive cystic leukoencephalomalacia; and maternal *T. cruzi* infection during pregnancy coexisting with fetal achondroplasia and fatal neonatal respiratory failure. These cases illustrate uncommon clinical scenarios and highlight unresolved questions concerning neurologic injury and developmental vulnerability in the context of *T. cruzi* infection.

Cases

Case 1

A 2-month-old female infant from El Salvador presented with diarrhea, vomiting, respiratory distress, hypotonia, abnormal sucking movements, gaze deviation, cyanosis, and poor peripheral perfusion. Oxygen saturation was 63% on room air, requiring intubation and mechanical ventilation for 7 days (Figure 1). On admission, she was hypothermic (35°C), hypotensive (53/31 mmHg), and bradycardic (72 beats/min). She developed refractory shock requiring dobutamine, acute kidney injury requiring peritoneal dialysis, severe metabolic abnormalities, and coagulopathy and had an 8-day intensive care stay (Supplementary Table S1).

The infant had been born at term after a pregnancy with limited prenatal care. Maternal screening for human immunodeficiency virus and toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex virus infections was negative; however, the mother was not tested for *T. cruzi* infection during pregnancy, and maternal Chagas disease was, therefore, not diagnosed at that time. The initial diagnosis was acute gastroenteritis with severe dehydration, metabolic acidosis, and septic shock. Examination showed pallor, hepatomegaly, and impaired peripheral perfusion.

Peripheral blood smear showed *T. cruzi* trypomastigotes, confirming acute infection (Figure 1), although the initial Strout test was negative. We initiated nifurtimox (20 mg/kg/day for 60 days). During hospitalization, necrotic lesions compatible with thrombotic complications developed in the extremities, together with diffuse petechiae, and enoxaparin was administered. Given the absence of maternal *T. cruzi* testing and entomological investigation, the route of transmission could not be definitively established, and congenital and early postnatal vector-borne transmission remained possible.

Clinical and parasitological improvement occurred during the first week of treatment. At 6 months, the Strout test remained negative. Cardiac evaluation showed no structural or functional abnormalities. However, brain magnetic resonance imaging demonstrated bilateral frontal

cystic leukoencephalomalacia and symmetric ischemic lesions involving the parietal, occipital, and temporal lobes.

Case 2

A 23-year-old pregnant woman from a rural Chagas-endemic area of Sucre Department, Colombia presented with pelvic pain, headache with visual aura, bilateral eyelid edema, and palpitations. She lived in housing favorable to triatomine infestation and reported frequent exposure to wild animals. Tests for dengue, Zika, chikungunya, and syphilis, toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex virus infections were negative. There was no known family history of achondroplasia or other skeletal dysplasias.

At 32 weeks gestation, ultrasonography demonstrated findings consistent with achondrodysplasia (Figure 1). At 39 weeks and 2 days, examination showed bipalpebral edema, mild jaundice, cervical lymphadenopathy, rash, and hepatomegaly. Electrocardiography demonstrated ventricular extrasystoles and left anterior fascicular block (Figure 1). *T. cruzi* immunoglobulin G was positive by enzyme-linked immunosorbent assay and indirect immunofluorescence. Blood smears were negative, whereas polymerase chain reaction was positive, confirming maternal infection. She had not received specific treatment for Chagas disease before pregnancy, and no trypanocidal treatment was administered during pregnancy.

The neonate had achondroplasia, developed severe respiratory distress, and died 10 days after birth despite supportive care. We identified no alternative infectious or metabolic explanation for the fatal respiratory course. Neonatal testing for *T. cruzi* infection and genetic confirmation of an *FGFR3* mutation were unavailable. Consequently, we could not confirm congenital *T. cruzi* transmission.

Discussion

These cases illustrate two uncommon clinical scenarios involving *T. cruzi*: severe acute infection in early infancy with an undetermined route of transmission, followed by extensive ischemic neurological sequelae, and maternal infection during pregnancy coexisting with fetal achondroplasia and fatal neonatal respiratory failure (Figure 1). Together, they highlight the clinical heterogeneity of *T. cruzi* infection during pregnancy and early life and the challenges of interpreting complex outcomes when infection coexists with developmental abnormalities [3,5,7]. Despite the absence of detectable cardiac abnormalities, the infant developed profound shock and hypoperfusion, respiratory failure, renal failure, metabolic abnormalities, and severe coagulopathy. In this context, the subsequent leukoencephalomalacia and ischemic lesions are most consistent with secondary hypoxic-ischemic brain injury resulting from systemic critical illness rather than primary *T. cruzi*-associated encephalitis or direct CNS parasitic invasion. This interpretation is further supported by the relatively unremarkable cerebrospinal fluid findings on day 14 and the absence of direct parasitological or molecular evidence of CNS infection. Accordingly, although acute *T. cruzi* infection contributed to the severe systemic illness, a direct neurologic effect of the parasite cannot be established. Nevertheless, the case highlights severe neurologic sequelae occurring after acute Chagas disease in early infancy [5,9].

Case 2 raises a different clinical question. Achondroplasia is primarily caused by activating *FGFR3* variants that impair endochondral ossification and can be complicated by respiratory insufficiency and early mortality [8]. Because neonatal *T. cruzi* infection was not confirmed and molecular testing for *FGFR3* was unavailable, no causal relationship between maternal infection, skeletal dysplasia, and neonatal death can be inferred. The coexistence is nevertheless noteworthy because pregnancy-associated immunologic changes can influence maternal parasitemia and congenital transmission, whereas *T. cruzi* infection can alter host cell signaling and inflammatory pathways [7,10].

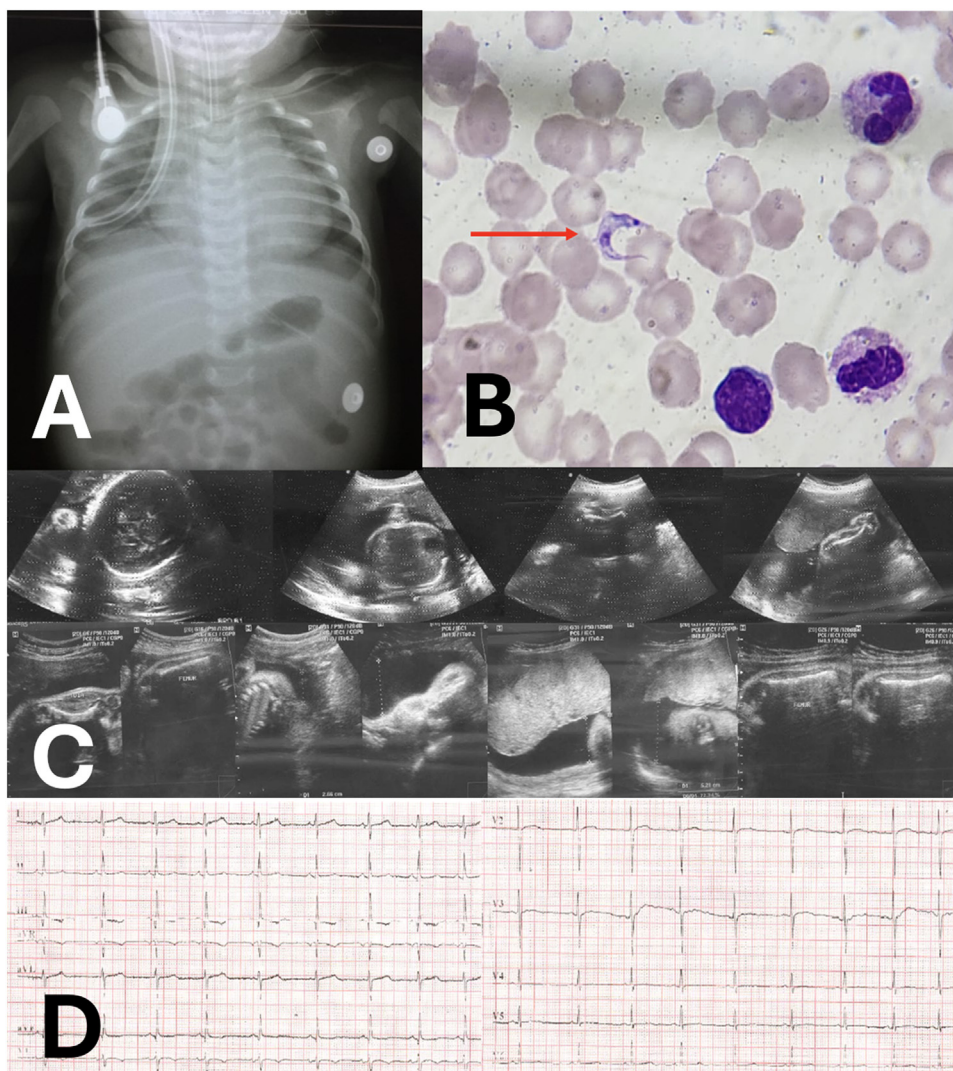


Figure 1. a. Chest radiograph of the newborn from case 1 during intensive care management. An endotracheal tube and a left subclavian venous catheter are identified. Moderate cardiomegaly with left hilar consolidation is present. Small amounts of pleural fluid are present in both costophrenic angles. Bilateral chest wall edema is evident. No abdominal abnormalities are detected. b. Peripheral blood smear from a 2-month-old infant from rural El Salvador demonstrating *Trypanosoma cruzi* trypomastigotes (red arrow). Giemsa stain, $\times 1000$ magnification (oil immersion). c. Prenatal ultrasound findings consistent with achondroplasia in a fetus born to a mother with *Trypanosoma cruzi* infection. The composite grayscale obstetric ultrasound image shows multiple prenatal sonographic views obtained during the third trimester. The upper panels include standard fetal biometric and anatomical planes (head, thorax, and abdomen). The lower panels focus on long-bone assessment, with labeled views of the femur demonstrating marked shortening and abnormal morphology relative to gestational age. The constellation of findings is consistent with skeletal dysplasia, specifically achondroplasia, as identified during prenatal evaluation. No obvious visceral malformations are highlighted in the image set. d. Electrocardiogram showing ventricular extrasystoles and left anterior fascicular block in the mother. The image shows a standard 12-lead electrocardiogram recorded from the pregnant woman in case 2. The tracing demonstrates ventricular premature beats within an otherwise regular rhythm, along with left axis deviation and characteristic QRS morphology in the limb leads. No acute ischemic ST-segment changes are evident.

Experimental observations indicate that *T. cruzi* can modulate growth-factor and tyrosine-kinase signaling. Whether gestational infection could interact with pathways relevant to fetal growth or modify the severity of an underlying skeletal dysplasia remains unknown. The present observation should, therefore, be considered hypothesis-generating rather than evidence that *T. cruzi* causes or modifies achondroplasia.

These cases reinforce two practical messages. First, acute Chagas disease, including possible congenital transmission, should be considered in critically ill infants from epidemiologically relevant settings, particularly those presenting with extracardiac manifestations. Second, screening pregnant women at risk and ensuring neonatal parasitological follow-up remain essential because maternal infection alone does not establish congenital transmission [5,11]. Rapid, accessible, and reliable diagnostic tools for congenital *T. cruzi* infection are also needed, particularly in resource-limited settings where conventional parasitological or molecular testing may not be readily available [12–15]. Recent advances in point-of-care molecular approaches, including loop-mediated isothermal amplification, are promising but require further validation and implementation studies [16].

Limitations

The principal limitations are the descriptive nature of two cases and incomplete diagnostic characterization. Parasite genotyping, ma-

ternal parasite load quantification, and placental studies were unavailable. In case 1, maternal *T. cruzi* testing and entomological investigation were unavailable; therefore, although the infant had parasitologically confirmed acute Chagas disease, congenital transmission could not be demonstrated, and early postnatal vector-borne transmission could not be excluded. Moreover, neuroimaging was performed 6 months after the acute illness, preventing determination of the timing and mechanism of cerebral injury. In case 2, neonatal *T. cruzi* testing and *FGFR3* molecular confirmation were unavailable; therefore, congenital transmission and any mechanistic relationship between maternal infection and achondroplasia cannot be established. Limited long-term follow-up further restricts interpretation.

Conclusions

Severe *T. cruzi* infection during early infancy may present with multisystem critical illness followed by neurologic sequelae secondary to hypoxic-ischemic injury, even without evident cardiac involvement. Maternal *T. cruzi* infection may also coexist with complex fetal disorders whose relationship to infection remains uncertain. These cases support systematic screening of at-risk pregnant women, timely parasitological evaluation and follow-up of exposed neonates, and cautious investigation of atypical developmental outcomes associated with maternal infection.

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Ethics approval and informed consent

The patients' parents gave informed consent for publication. We followed the Nuremberg Code, the Declaration of Helsinki, the Belmont Report, and Resolution 8430 of 1993 for research in Colombia.

Written informed consent to take part in the study and publish the article was obtained from all participants or their legal representatives. The privacy rights of participants were observed.

This study was performed in compliance with the relevant laws, regulatory frameworks, and guidelines where the research took place. Ethics committee approval was not required under the relevant laws and institutional guidelines.

This research follows the CARE guidelines (CAsE REport guidelines) and the CARE checklist.

Declaration of competing interests

The authors have no competing interests to declare.

CRediT authorship contribution statement

Wilmer E. Villamil-Gómez: Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Guillermo Edgardo Barahona-Escobar:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Formal analysis, Data curation. **Melvin Antonio Moisa-Martínez:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis. **Diana Peña-Navarro:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Investigation, Data curation. **Lorena Vanessa Paniagua-Rojas:** Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Investigation, Formal analysis. **Dainer Elías Rincones-Soto:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Data curation. **María Leonor Barcha:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Investigation, Data curation. **Ángel Ochoa-Salcedo:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Resources, Investigation. **Melchor Álvarez-Mon Soto:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Investigation. **Melisa Eyes-Escalante:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation. **Juan Venegas-Hermosilla:** Writing – review & editing, Writing – original draft, Visualization, Software, Investigation, Data curation. **Alfonso J. Rodríguez-Morales:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ijregi.2026.101017](https://doi.org/10.1016/j.ijregi.2026.101017).

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