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Case Report

Aleatory *Trypanosoma cruzi* Vertical Transmission in Chiapas, Mexico: A Case Report

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Abstract

Congenital Chagas disease is considered a form of dispersion of *Trypanosoma cruzi* related to human migration from endemic, often rural to previously non-endemic urban areas. This fact increases the Chagas disease establishment risk inside of family members by vertical transmission pathway. Congenital Chagas disease cases in newborns could not identified by the health professional even in endemic regions. Here we present the first family cluster of Chagas disease cases from Chiapas: one of the most important endemic areas in South of Mexico, where vertical *T. cruzi* transmission incidence rate is ranged between 2% to 22% revealing an important public health problem. Two cases inside a family from Chiapas, México with positive antibodies against *T. cruzi* detected by ELISA are presented; one of them got the infection through vertical pathway. We think that congenital Chagas disease should not be ignored in a newborn born from an asymptomatic Chagas disease mother, who may transmit the parasite infection randomly.

Introduction

Chagas disease (CD) also known as American trypanosomiasis, is a parasitic zoonotic disease caused by *Trypanosoma cruzi,* recognized as one of the 20 Neglected Tropical Diseases (NTDs) listed by the WHO (1). Around the world, this illness affects about 7 million people, but CD is found mainly in endemic areas of 21 continental countries of the Region of the Americas reaching from the southern United States of America all the way to South America (2), where the main transmission pathway to human is during defecation after blood feeding hematophagous insect species (vector-borne transmission) (3), further the parasite can also be acquired through other pathways (4), one of them is the vertical transmission (5). This can occur from childbearing age women themselves infected congenitally, perpetuating the disease in the absence of the infected blood-sucking triatomine bugs (6), and contributing in the disease spread patterns (7), mainly due to population mobility, urbanization and emigration changed from a rural to a mostly urban disease (8).

In an urban domestic cycle setting, the vertical transmission of *T. cruzi* can occur from one asymptomatic infected mother to child from one generation to another (5). The mother to child *T. cruzi* infection can occur during pregnancy, delivery, or lactation (6). Congenital *T. cruzi* infection in newborns frequently are asymptomatic too, while clinical manifestations of congenital CD are non-specific, the newborns can manifest signs of edema, fever, preterm birth (born before 37 weeks of pregnancy) and low birth weight (<2,500 g), cardiomegaly and myocarditis, hepatosplenomegaly, respiratory distress syndromes, and pneumonitis, even stillbirth during pregnancy (9).

México is one of three countries who concentrate more than 60% of CD cases in Latin America (10). According to the Pan American Health Organization (PAHO), Congenital CD represents more than 25% of the new cases of CD worldwide (11). The first report of a congenitally transmitted case of CD occurring in Mexico was in 1998 (12). The congenital CD epidemiology in Chiapas is estimated from 7% to 22% in urban settlements (there are not estimations for congenital CD to rural areas) (13).

In this study, we pretend to present a childbearing age female case diagnosed positive for CD and her child boy diagnosed as a congenital CD case.

Case presentation 1

A 29 yr-old female, from San Juán Cancuc, a small autochthonous Mayan settlement in Chiapas, México a region whit an unknown *T. cruzi* transmission rate. The patient at the age of 15 moved to Tuxtla Gutiérrez, the Chiapas´ Capital city. During an interview the patient refers never have had exposure to infection sources or blood transfusion, but her childhood had lived in a rural and sub-standard housing (mud floors, adobe walls and thatched roof) in San Juán Cancuc, also she had contact whit potential wild and domestic reservoirs (opossums, dogs, cats, goats and sheep). The case recognizes does not know the *T. cruzi* vector *T. dimidiata.*

In 2017 the patient was diagnosed positive for CD after a voluntary blood donation and confirmed by two ELISA Tests by Public Health Statal Laboratory (PHSL) and Children's Hospital of Mexico "Federico Gómez" (CHM-FG), where sera samples were analyzed by conventional serology through an indirect immunoenzymatic ELISA with *T. cruzi* total antigen and a recombinant Micro ELISA (ACCUTRACK CHAGAS ®), following the manufacturer's guidelines, also a rapid immunochromatographic test (Chagas Stat Pak ®)

to identify *T. cruzi* antibodies was developed, as well as a conventional PCR was carried out for diagnosis in all family members.

A clinical evaluation of the patient was performed following medical standards for chronic infection of CD, including anamnesis and physical examination. No one clinical signs related whit chronic CD was found; also, the basic blood laboratory test revealed normal red (6,860 cells/µL), hemoglobin of 13 g/dL, and platelet count of 238,000 cells/µL. The white blood cells count showed absolute lymphocyte count of 4,680 cells/µL. Chemistry panel was normal, with a blood urea nitrogen (7.7 mg/dL) and creatinine (0.6 mg/dL) and urine normal, VDRL and HIV negative. Related to her obstetric history she had two normal previous pregnancies and deliveries; abortions were denied.

The patient was treated orally according to the WHO criteria, with nifurtimox at 9 mg/kg/day divided into three doses, but the treatment was interrupted at fourth day due to the developing adverse side effects presumably (vomiting impulses, dizzy and apathy), clinically related with an early pregnancy and threatened abortion whit a slight vaginal bleeding off. A blood test was taken, and the outcomes reported five weeks of pregnancy. This one corresponds to her third pregnancy. A second event of threatened abortion at four months of pregnancy (second trimester of pregnancy) was diagnosed. The patient was hospitalized and stabilized, the rest of pregnancy no more uneventful was detected, and finally a male infant by vaginal delivery was born in 2019 in Pascacio Gamboa Hospital in Tuxtla Gutiérrez, Chiapas.

Case presentation 2

The case was a 9-month-old boy infant born to a seropositive mother to chronic CD in October 2019 (Case presentation 1). After birth weight (3,565 grams) and height (50 cm) were according to gestational age, Apgar test was normal (8/9). The patient did not show complications during and birth, neither congenital CD signs nor symptoms were detected during birth medical history. The systematic clinical evaluation carried out at nine months after birth, showing the infant had been asymptomatic, but the ELISA test showed positive reaction against *T. cruzi* antibodies.

Nowadays all family members live in Tuxtla Gutiérrez, Chiapas. An epidemiological extension survey was made in the family house, the results revealed no risk factors related with vector borne or food transmission. The Chagas antibodies screening gave negative results to *T. cruzi* infection in siblings even father (Table 1).

Table 1: Characterization of familial Chagas disease cases (mother and son 3) and no cases (Son 1 and 2), and *T. cruzi* infection diagnostic tests results for each one

Variable	*Mother (Case 1)*	*Son 1*	*Son 2*	*Son 3 (Case 2)*
Gender	Female	Male	Male	Male
Age	31	3 years	2 years	9 Months
T. cruzi Infection	Positive	Negative	Negative	Positive
Evolution time	Unknown	NC	NC	9 months
Clinical signs CD*	Negative	NC	NC	Negative
Basic Laboratory Test	Normal	Normal	Normal	Normal
Chagas ELISA§	Positive	Negative	Negative	Positive
Chagas StatPak ®	Positive	Negative	Negative	Positive
PCR ɵ	Positive	Negative	Negative	Positive

Abbreviations: List all abbreviations and full terms

* Chagas Disease

§ Enzyme-Linked Immunosorbent Assay

ϴ Polymerase Chain Reaction
NC Not a case

This report does not contain any personnel information that could be used to compromise patient confidentiality. Informed consent was taken from the parents before the study

Discussion

These patients represent the first CD familiar cases registered in Mexico, for our knowledge. These cases suggest the possible and potential urbanization of asymptomatic CD, randomly transmitted through vertical pathway inside a nuclear autochthonous Mayan family in Chiapas in absence of the vector. This fact could be supported by previous evidence, have demonstrated a vertical transmission incidence ranged between 7 to 22% in two different areas from Chiapas, Mexico, where the mother and newborn were asymptomatic (13-15).

It is important how the mother (Case presentation 1) transmitted the parasite only to the third son (Case presentation 2) but not to the two previous pregnancies and deliveries. Is documented those infected mothers may transmit the parasite, in one, some, or all their gestations, even infect some or all the siblings in multiple deliveries (16), the reason is not known, but increasing the possibility to generate familial clustering cases. The threatened abortion at 4 months of pregnancy in case presentation 1, could be related whit an increasing of parasitemia (Not information available), and a probable transmission of blood parasites could occur during the second trimester of pregnancy (5).

Many serologic assays have been used for *T. cruzi* infection; the most extensively used method is ELISA (14, 15, 19). In this study, we used two serological ELISA tests. An indirect immunoenzymatic ELISA with *T. cruzi* total antigen and a Micro ELISA (ACCUTRACK CHAGAS ELISA ® Laboratorio Lemos S.R.L. Santiago del Estero, Buenos Aires, Argentina) based on recombinant antigen of *T. cruzi*. The manufacturer reports a sensitivity of 100% and a specificity of 99%, in the diagnosis of CD. Positive results were considered at a cut-off value of 0.453 ±2 nm of optical density (OD), ranged at 0.431 to 0.475 OD ("gray zone") following the manufacturer instructions. For positive control, CD positive patient será was employed. Both serological test and rapid immunochromatographic assay (Chagas Statpak ®) were used to identify *T. cruzi* antibodies. To ensure the specificity and avoid crossreaction whit other trypanosomatides, positive control sera from chagasic patient was used. While, for molecular test by PCR assay, the set of primers proposed TCZ1 and TCZ2 nuclear primers were used. For positive control DNA from *T. cruzi* tripomastygotes cultures of CL Brener strain and gDNA from Chagas disease patient was employed. To demonstrate vertical transmission of CD means an opportunity to estimate the parasite contact frequency inside an urban population, even related whit dispersion dynamic through internal migration. As a relevant reference, Chiapas State is considered an endemic region not only for the CD prevalence, but also the presence of *Triatoma dimidiate* bugs one of main important *T. cruzi* vector in Southeast of Mexico (17) even South American Countries as Guatemala, Honduras and Nicaragua (18).

This first CD familiar cases remark the importance of tight surveillance in all asymptomatic CD cases in childbearing age woman during pregnancy and their newborns in endemic regions as Chiapas. We propose, standardize the screening using at least standard diagnostic methods in all pregnant woman (ELISA) and their newborns by in situ *T. cruzi* direct observation or looking for parasite´s DNA in cord blood (9,19). In fact, we consider important the constant training of all atten-

tion health teams to improve the systematic surveillance for congenital CD.

Conclusion

The asymptomatic cases of CD and the aleatory occurrence of congenital CD in newborns are closely linked to the generation of family cases and the modification of the distribution patterns of the CD. The establishment of a *T. cruzi* infection-screening program in all childbearing age pregnant women and their offspring remark the importance to reduce the gap in treatment allocation and limiting of the disease progression at individual and populational level.

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Conflict of interest

The authors declare that there is no conflict of interest.

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