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Chagas Disease in Latin American Immigrants With Dilated Cardiomyopathy in New York City

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Abstract

Chagas disease–associated cardiomyopathy is clinically similar to other causes of cardiomyopathy and, therefore, the diagnosis can be easily overlooked. We found a 13% point prevalence of Chagas disease in a sample of New York City immigrants with dilated cardiomyopathy.

Keywords

Chagas disease; *Trypanosoma cruzi* ; cardiomyopathy; United States

Approximately one-third of people infected with Chagas disease (CD) experience cardiac involvement, including life-threatening dilated cardiomyopathy (CM) [1]. CD-associated dilated CM can lead to heart failure, malignant arrhythmias, and death [1]. Because there has been an increase in immigration of persons from CD-endemic countries [2], CD may now be an important cause of dilated CM in the United States. However, many US physicians are not familiar with CD and may not consider this as a cause of CM in their patients. Confirming that CD is the cause of CM may have implications for patient treatment and prognosis and for possible testing and treatment of family members.

CD is endemic in North, Central, and South America, from Mexico to Argentina. Infection with *Trypanosoma cruzi*, the parasite that causes CD, usually occurs in early childhood. If not treated in the acute phase, CD becomes chronic. The chronic phase begins

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with an asymptomatic or “indeterminate” form. Approximately two-thirds of the patients remain asymptomatic throughout life [3], and one-third develop cardiac or gastrointestinal symptoms decades after infection, the determinate form of chronic CD [4]. Treatment with antiparasitic drugs during the chronic phase may prevent the progression to clinical disease [5]. Because of the long latency between infection and development of symptoms, infected immigrants from CD-endemic countries may arrive in the United States while asymptomatic, and may develop symptomatic CD-associated CM while here.

Because CD-associated CM is clinically similar to other causes of CM, and no sign or symptom is pathognomonic, the etiologic diagnosis may not be considered, appropriate diagnostic testing might not be requested or performed, and, therefore, the diagnosis might be often missed. We hypothesized that a significant number of patients in New York City with dilated CM, who have come from CD-endemic areas, have CD-associated CM. We conducted a cross-sectional study of patients from at-risk countries diagnosed with dilated CM to determine the prevalence of CD in this population and to identify risk factors associated with CD-associated CM.

METHODS

Study Sites

The study was conducted at the Cardiology Clinics of Mount Sinai Medical Center, a 1171-bed tertiary-care teaching facility, and Elmhurst Hospital Center, a 525-bed community hospital.

Study Population and Data Collection

Participants were recruited from July 2009 to December 2011, and were eligible for inclusion if they were aged ≥18 years, had a left-ventricular ejection fraction (LVEF) <45% without evidence of ischemic CM, and were born and lived for ≥12 months in a CD-endemic country. LVEF was determined by echocardiograms, ventriculograms, and/or multigated acquisition scans. Ischemic CM was defined as evidence of significant coronary artery disease: either >50% coronary obstruction by cardiac angiography, history of coronary artery bypass grafting, receipt of 1 or more coronary stents, history of myocardial infarction, evidence of moderate or severe ischemia on nuclear stress testing, or ST segment depressions of at least 2 mm in ≥2 consecutive leads on exercise stress testing.

Persons were considered to come from a CD-endemic country if they were from the continental Americas, with the exception of the United States and Canada. Persons from the Caribbean islands were also excluded, as these are not considered CD-endemic countries.

Eligible persons were identified via medical records review. Once identified, patients were offered participation at their next regularly scheduled medical appointment by a research assistant. Patients who did not have a scheduled appointment within 3 months were contacted via mail.

After obtaining informed consent, a standardized, closed-answer questionnaire was administered to collect data on demographics and medical history. Past laboratory,

radiologic, and echocardiographic test results were obtained from the medical record. Electrocardiographic data were recorded, including information on dysrhythmias known to be associated with CD, such as right bundle branch block (RBBB) and left anterior fascicular block (LAFB). Twenty milliliters of blood was collected through standard venipuncture. Eligible subjects were given US$15 after participating in the study.

Blood samples were centrifuged and separated serum was frozen at −57°C. Batched serum samples were sent to the Parasitic Diseases Branch of the Centers for Disease Control and Prevention for *T. cruzi* immunoglobulin G antibody testing. Enzyme immunoassay (EIA; Chagatest enzyme-linked immunosorbent assay recombinante v.3.0, Wiener Laboratorios, Argentina) and an in-house indirect immunofluorescence assay (IFA) were performed on all samples. Samples were considered positive if both EIA and IFA results were positive, indicating the presence of *T. cruzi* antibodies, negative if both EIA and IFA results were negative, and indeterminate if only either EIA or IFA result was positive. Indeterminate samples were then tested by an immunoblot assay using trypomastigote excreted-secreted antigens (TESA) [6], and the sample was considered positive if results of TESA were positive, meaning that results of testing with 2 of the 3 assays were positive.

Participants who tested positive were offered a free-of-charge clinical visit with a physician (D.C.) to answer any questions about the disease or the test, and to provide referrals for follow-up care.

Statistical Methods

Demographic and clinical characteristics of persons infected with CD were compared to persons uninfected with CD in univariate analysis, using Fisher exact test or Student *t* test as appropriate. A *P* value of ≤.05 was considered significant.

This study was approved by the institutional review boards of the Mount Sinai School of Medicine and Elmhurst Hospital Center.

RESULTS

Forty-four eligible persons were identified, of whom 39 (88%) consented to participate. Reasons for declining participation included lack of time to complete the survey (n = 2), no desire to donate extra blood (n = 2), and no specific reason (n = 1). Participants' mean age was 62.2 ± 13.6 years and 25 (64%) were men. Subjects came from Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, El Salvador, Honduras, Mexico, Peru, Paraguay, and Venezuela. Of 39 patients, 5 (13%) were infected with *T. cruzi*, and none had prior knowledge of their infection. Countries of origin for the infected patients were Bolivia, Brazil, Ecuador, El Salvador, and Venezuela.

Persons with CD were more likely to have a family member with CD (40% vs 0%, $P = .01$), to complain of chest pain (80% vs 24%, $P = .02$), and to have premature ventricular contractions (PVCs) on routine electrocardiography (40% vs 3%, $P = .04$; Table 1). No differences were observed in the prevalence of RBBB ($P = .21$), and there were no episodes of LAFB in either group.

DISCUSSION

Our study demonstrates a 13% point prevalence of CD in a sample of Latin American immigrants with dilated CM. These data are consistent with a study in Los Angeles, which included a predominantly Mexican and El Salvadoran population with dilated CM and found a CD infection rate of 15% [7]. The correct identification of CD-associated CM is important for prognosis. Mortality is 2–3 times higher in patients with CD-associated CM compared those with idiopathic dilated CM [8–10]. More importantly, persons with CD-associated dilated CM have longer-term survival after cardiac transplantation than persons with idiopathic dilated CM [11]. In addition, because CD can reactivate in immunocompromised persons, knowing the *T. cruzi* serostatus before initiating transplant in patients from endemic countries can guide the posttransplant follow-up strategy [12].

Findings traditionally associated with CD, including the presence of RBBB and LAFB, were not helpful in identifying persons with CD compared to those without CD in this study. However, having chest pain was 80% sensitive and 76% specific in diagnosing CD-associated CM. In addition, our study showed that all participants who reported a family member with CD were ultimately diagnosed with CD (positive predictive value, 100%). However, the report of an infected family member had low sensitivity for screening. We also found that PVCs were more common in patients with CD. PVCs have been reported to occur in up to 85% of patients with CD-associated CM and can be associated with risk of sudden death [13].

A major limitation of our study was the small number of patients, which may limit the representativeness of our sample, and thus bias our estimated seroprevalence. Because our study confirms a previous study in a similar patient population [7], we believe our estimates to be accurate. This study assumes a causal relationship between *T. cruzi* infection and dilated CM, but it is possible that 1 or more patients were coincidentally infected with CD and had a different etiology for their CM. In clinical practice, however, patients who have CM and positive *T. cruzi* antibody serology are considered to have CD-associated CM and rarely receive additional testing to validate the diagnosis.

CD is an important cause of CM in Latin American immigrants, and although this study was small, it suggests that there is an unrecognized burden of CD in the United States. Further studies are needed to find out if this high prevalence exists in other Latin American immigration hubs, and to delineate the most cost-effective strategy to screen patients at risk for CD who might benefit from treatment. At present, a large randomized placebo-controlled trial is evaluating the use of benznidazole in patients with compensated Chagas heart disease [14]; if the use of benznidazole in this population proves beneficial, it will reinforce the need to correctly diagnose all patients with CD CM.

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Table 1.

Baseline Characteristics of Study Participants

Characteristic	Chagas Disease (n = 5)	No Chagas Disease (n = 34)	*P* Value
Age, y, mean ± SD	65.8 ± 8.98	61.7 ± 14.1	.54
Male sex	4 (80)	21 (62)	.64
Years in the United States, mean ± SD	22.6 ± 13.9	26.6 ± 12.7	.51
Finished high school	2 (40)	23 (74)	.15
History			
Seen triatomine insect before	3 (60)	12 (35)	.36
Bitten by the triatomine insect	2 (40)	9 (26)	.61
Family member with Chagas	2 (40)	0	.01
Lived in a mud house	4 (80)	17 (50)	.35
Cardiac symptoms			
Chest pain	4 (80)	8 (24)	.02
Shortness of breath	4 (80)	20 (59)	.63
Electrocardiographic results			
QRS, msec, mean ± SD	139 ± 56.8	129.9 ± 33.8	.61
QTc, msec, mean ± SD	464.8 ± 30.9	462.7 ± 36.0	.9
PVC	2 (40)	1 (3)	.04
RBBB	2 (40)	5 (15)	.21
LAFB	0	0	…
Any heart block	2 (40)	5 (15)	.21
Cardiac pacemaker	2 (40)	2 (6)	.08
ICD	3 (60)	11 (32)	.33
CXR with cardiothoracic ratio >0.5	2 (40)	12 (35)	1
Systolic BP, mm Hg, mean ± SD	120.8 ± 18.1	126.4 ± 19.5	.55
Diastolic BP, mm Hg, mean ± SD	72.8 (7.0)	74.8 (9.2)	.65
LVEF, %, mean ± SD	33.0 ± 9.7	36.5 ± 8.8	.41

Data are presented as No. (%) unless otherwise specified.

Abbreviations: BP, blood pressure; CXR, chest radiograph; ICD, implantable cardioverter defibrillator; LAFB, left anterior fascicular block; LVEF, left-ventricular ejection fraction; PVC, premature ventricular contraction; RBBB, right bundle branch block; SD, standard deviation.