Journal of Cardiovascular Magnetic Resonance (2005) **7,** 685–688

ISSN: 1097-6647 print / 1532-429X online
DOI: 10.1081/JCMR-200065627

Taylor & Francis
Taylor & Francis Group

MYOCARDITIS AND CARDIOMYOPATHY

Chagas myocarditis and syncope

RAJAN A. G. PATEL, M.D.,[1] JOHN P. DIMARCO, M.D., PH.D.,[1] JOSEPH G. AKAR, M.D., PH.D.,[1] SZILARD VOROS, M.D.,[1] and CHRISTOPHER M. KRAMER, M.D.[1,2,*]

[1]*Cardiovascular Division, Department of Medicine, University of Virginia Health System, Charlottesville, Virginia, USA*
[2]*Department of Radiology, University of Virginia Health System, Charlottesville, Virginia, USA*

This case report describes the diagnosis of Chagas myocarditis in a patient from Honduras who presented with syncope. The discussion summarizes the pathophysiology of cardiac Chagas disease. Acute, latent, and chronic Chagas myocarditis are described. The role of CMR in diagnosing Chagas myocarditis is discussed.

Key Words: Chagas disease; Myocarditis; MRI

1. Case report

A 37-year-old gentleman was transferred to the University of Virginia Health System for cardiac evaluation after presenting to an outside hospital following a syncopal event. The patient immigrated from Honduras 6 years ago. Witnesses at the patient's workplace report that he dropped suddenly to the floor and was unconscious for approximately 30 seconds without tonic-clonic seizure activity. The patient had full recollection of events preceding and following his syncopal event. He denied angina or palpitations. Upon regaining consciousness, blood pressure was normal. The patient had no known past medical history. He was raised on a farm in Honduras. He denied tobacco, alcohol, or recreational drug use. His sister had died suddenly at age 32 during exercise.

Physical exam included normal vital signs and was remarkable only for a 2/6 holosystolic murmur loudest at the left lower sternal border. EKG was remarkable for right bundle branch block (RBBB) with left anterior fascicular block (LAFB) and frequent premature ventricular contractions (PVC's) (Fig. 1). Transthoracic echocardiogram at the referring hospital was remarkable for LV dilatation and biventricular dysfunction with a LV ejection fraction of 30%. The patient underwent an exercise sestamibi stress test prior to transfer. He reached a workload of 13.5 mets without chest pain. The patient experienced multiple PVC's during exercise, but no VT nor ST or T wave changes. Perfusion imaging did not demonstrate ischemia. After transfer, an electrophysiologic study was performed. Sinus node function was normal. The atrial-His (AH) interval was 70 msec and the His-ventricular (HV) interval was slightly prolonged at 38 msec. No ventricular tachycardia was inducible with programmed stimulation. The diagnosis of Chagas cardiomyopathy was entertained and a CMR was ordered.

CMR images are shown in Figs. 2–4. Steady state free precession cine images (repetition time [TR] 3.1 ms; echo time [TE] 1.6 ms; flip angle 60°, field of view [FOV] 315–400 mm; matrix 164 × 256, slice thickness 8 mm) demonstrated severe right ventricular dysfunction and moderate global left ventricular dysfunction (Figs. 2A, 3A, 4A). Late contrast enhanced gradient echo inversion recovery images (TR 8.0 ms, TE 4.3 ms, flip angle 30°, FOV 315–400 mm, matrix 148 × 256, slice thickness 8 mm) 20 minutes after infusion of 0.15 mM/kg Gd-DTPA were obtained. (Figs. 2B, 3B, 4B) These images demonstrate enhancement in the basal anterior and basal lateral walls consistent with scar in a non-coronary distribution as can be seen with chronic Chagas myocarditis.

The diagnosis of Chagas disease was confirmed with a T. cruzi antibody titer of 1:64 (high normal 1:16) which returned several weeks later. As ventricular tachycardia was not inducible during electrophysiologic study, the patient was discharged on amiodarone 400 mg oraly daily for 1 week, followed by 200 mg oraly daily. To date, he has experienced no further syncopal events.

2. Discussion

Chagas disease, also known as American trypanosomiasis was first described in 1909 by Dr. Carlos Chagas. The disease is common in parts Central and South America. The prevalence is approximately 20 million (1). Cardiac disease is one

Received 23 September 2004; accepted 27 February 2005.
*Address correspondence to Christopher M. Kramer, M.D., Departments of Medicine and Radiology, University of Virginia Health System, Lee St., Box 800170, Charlottesville, VA 22908, USA; Fax: (434) 982-1618; E-mail: ckramer@virginia.edu

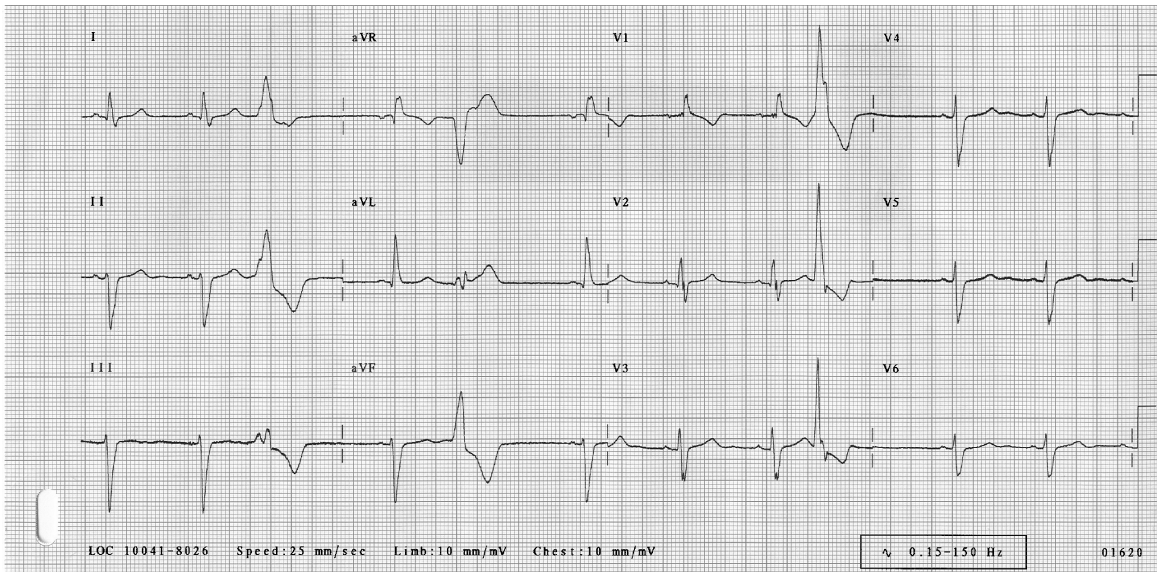

Figure 1. 12-lead ECG demonstrating frequent PVC's and RBBB and LAFB.

of the most prominent manifestations of the disease. In fact, in endemic areas, Chagas disease in the leading cause of cardiovascular morbidity. Transmission is usually via the bite of a vector carrying the responsible parasite. In recent years, transmission via blood transfusions and organ transplantation has been described as well as maternal fetal transmission (1, 2).

Chagas disease manifests in 3 phases: acute, latent, and chronic. The parasite responsible for Chagas disease is Trypanosoma cruzi. The vector of transmission is Triatoma infestans also known as the reduviid bug. The Triatoma ingests trypomastigotes of T. cruzi. When the Triatoma takes a blood meal, the metacyclic trypomasticgotes in the feces of the Triatoma enter the human host via the bite wound or via exposed mucous membranes such as the conjuctiva. Local skin swelling at the bite wound produces the classic skin finding of the acute phase known as Chagoma symptoms including fever, sweats, myalgia, hepatosplenomegaly, periorbital edema, and, to a variable degree, symptoms of congestive heart failure (CHF) as a consequence of myocarditis.

The diagnosis of Chagas disease may be easily missed in the acute phase due to nonspecific symptoms or may be mistaken for other infections. The latent phase may last 10 to 30 years. During this phase, patients are asymptomatic but have positive serology. However, data from Barreto et al. suggests myocardial disease may be present during this phase (3). Approximately 20 years after the acute phase, 30% of patients progress to the chronic phase which is heralded by symptoms of cardiac and GI disease. The chronic phase of cardiac Chagas disease manifests as three syndromes: congestive heart failure, thromboembolic disease, and arrhythmias. In a study by Salles et al. 738 patients with chronic Chagas disease were followed for an average of almost five years. Of the sixty-two deaths in this population, fifty-four were attributed to Chagas disease of the cardiovascular system. Forty were from sudden death, twelve were from progressive heart failure, and two were from embolic stroke (4).

The diagnosis of acute Chagas disease is based on history and detection of parasites. The diagnosis of chronic Chagas

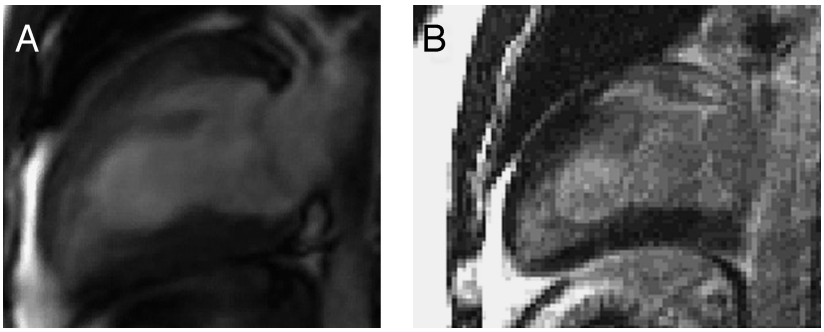

Figure 2. A. Steady state free precession end-systolic cine image in a 2-chamber long axis orientation demonstrating LV systolic dysfunction, more pronounced in the basal segments. B. Late contrast-enhanced inversion recovery gradient echo image in the same orientation demonstrating contrast enhancement in the basal anterior wall, not in a coronary distribution.

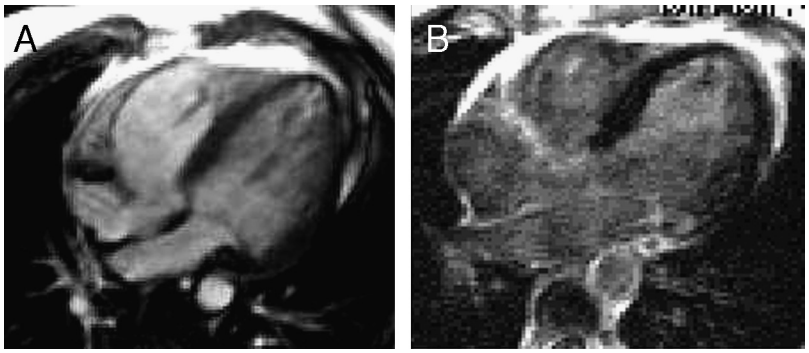

Figure 3. A. Steady state free precession end-systolic cine MRI in a 4-chamber long axis orientation demonstrating RV dilatation and dysfunction and regional LV systolic dysfunction, worse in the basal segments. B. Late contrast-enhanced inversion recovery gradient echo image in the same orientation demonstrating a small region of contrast enhancement in the basal lateral wall.

disease is made using complement fixation assays or ELISA to detect IgG antibodies that bind T. Cruzi antigens. A potential problem with these assays is a false positive result in patients who have other parasitic infections (5).

The most common EKG findings among patients with Chagas' myocarditis include RBBB, LAFB, PVC's, and atrial fibrillation (6, 7). Ventricular arrhythmias are a prominent feature of this disease. In fact, sudden death or syncope from VT or VF may develop before symptoms of CHF (7, 8). In patients prone to ventricular arrhythmias, VT can often be evoked by exercise (6). In one small series, the presence of an apical aneursym and an increased left ventricular end diastolic diameter correlated with the development of sudden death (9). The QT interval dispersion may be useful for predicting sudden death (4). At present, data supporting the role of AICD's in preventing sudden cardiac death among patients with Chagas cardiomyopathy is limited (10, 11). However, the GESICA study demonstrated that low dose amiodarone conferred a survival benefit in patients with Chagas cardiomyopathy (12).

Structural changes that occur within the heart include dilatation of all four chambers. The left ventricle is particular prone to becoming thin with an aneursymal appearance (13). Sections of affected hearts demonstrate extensive fibrosis of the left ventricle with an infiltrate of lymphocytes, macrophages, and mast cells (14). Myocytes, vascular smooth muscle, and capillary basement membranes all appear thickened in affected regions. Interestingly, parasites are rarely found in affected myocardial sections (13). Cardiac autonomic dysfunction may also play a role in the development of Chagas myocarditis (15). Among the causes for the pathology seen in Chagas cardiomyopathy are microvascular spasm and matrix dissolution. Endothelin-1 may be partly responsible for these changes. Jelicks et al. infected C57BL16x129sv mice with a Brazilian strain of T. cruzii. An experimental group also received phosphoramidon, a nonspecific metalloprotease inhibitor that also inhibits endothelin-converting enzyme. The control and experimental groups both experienced similar levels of parasitemia. However, CMR demonstrated less severe cardiac pathology in the phosphoramidon group (16). This group later showed that cine CMR was useful in the serial evaluation of the heart in murine Chagas disease. They were able to demonstrate an increase in right ventricular internal diameter between baseline, acute infection, and chronic infection (17).

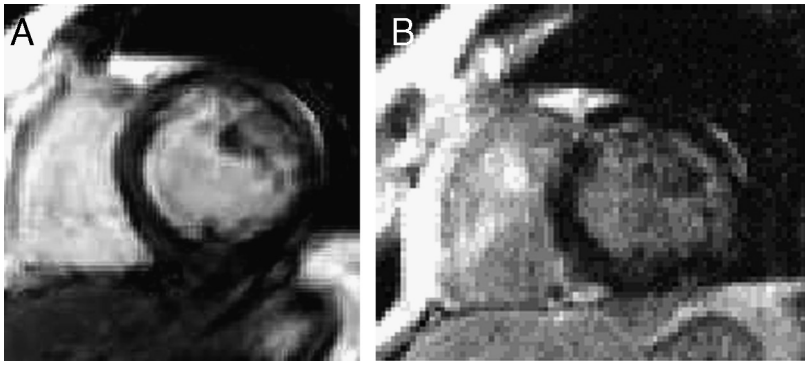

Figure 4. A. Steady state free precession end-systolic cine MRI in a basal short axis orientation demonstrating global LV systolic dysfunction in this slice. B. Late contrast-enhanced inversion recovery gradient echo image in the same orientation demonstrating contrast enhancement in the basal anterior wall, not in a coronary distribution.

In an early study using CMR in humans with Chagas cardiomyopathy, both CMR and right ventricle endomyocardial biopsy were performed on 10 patients with Chagas disease and class II–IV CHF in addition to 10 patients with idiopathic dilated cardiomyopathy. All patients with biopsy proven Chagas heart disease had an increase in septal signal after gadolinium infusion (18). The same group later demonstrated that these 10 patients also had increased gallium 67 uptake relative to controls. This correlation suggests that increased CMR signal after gadolinium infusion is associated with myocardial inflammation (19).

A recent study using techniques similar to those used in the present patient demonstrated a correlation between areas of contrast enhancement and endomyocardial biopsy specimens suggestive of myocarditis in patients who had clinically diagnosed viral myocarditis. The authors proposed several mechanisms for the contrast enhancement seen in myocarditis. Necrosis occurs in small focal areas of the heart as a consequence of the pathologic insult that results in myocarditis. This results in increased extracellular space between damaged myocytes. Additionally, myocyte cell membranes rupture. These two processes allow gadolinium contrast to diffuse between and into myocytes. As healing occurs necrotic myocytes are replaced by fibrous tissue so chronic contrast enhancement may persist. As the scar shrinks, the contrast enhancement will decrease and may disappear (20). Given the present patient's history, CMR clearly demonstrated the anatomic and functional aspects of Chagas.

In conclusion, this case highlights the added anatomic and functional assessment of the heart that CMR can provide in the patient with suspected Chagas' cardiomyopathy. CMR, specifically late gadolinium enhancement techniques, provided important information regarding structural abnormalities in this patient's heart that was not readily obtained from other cardiac imaging modalities. This information was valuable as it supported the working diagnosis while an ELISA for IgG against T Cruzi antigens was performed at an outside laboratory.

References

1. Kirchhoff LV. American trypanosomiasis (Chagas Disease)—a tropical disease now in the United States. N Engl J Med 1993; 329:639–644.
2. Grant IH, Gold JW, Wittner M, Tanowitz HB, Nathan C, Mayer K, Reich L, Wollner N, Steinherz L, Ghavimi F. Transfusion-associated acute Chagas disease acquired in the United States. Ann Intern Med 1989; 111:849–851.
3. Barreto ACP, Ianni BM. The undetermined form of Chagas' heart disease: concept and forensic implications. Sao Paulo Med J 1995; 113:797.
4. Salles G, Xavier S, Sousa A, Hasslocher-Moreno A, Cardoso C. Prognostic value of QT interval parameters for mortality and risk stratification in Chagas' disease: results of a long term follow-up study. Circulation 2003; 108:305–312.
5. Kirchhoff LV, Gamm AA, Gusmao A, Goldsmith RS, Rezende M, Rassi A, et al. Increased specificity of serodiagnosis of Chagas disease by detection of antibody to the 72- and 90-kilodalton glycoproteins of Trypanosoma cruzi. J Infect Dis 1987; 155:561–564.
6. Hager JM, Rahimtoola SH. Chagas Heart Disease. Curr Probl Cardiol 1995; 20:825–924.
7. Bestetti RB, Dalbo CM, Freitas OC, Teno LA, Castilho OT, Oliviera JS. Non-invasive predictors of mortality for patients with Chagas heart disease—a multivariate stepwise logistic regression study. Cardiology 1994; 84:261–267.
8. de Paola AAV, Melo WDS, Tavora MZP, Martinez EE. Transcoronary chemical ablation of VT in chronic chagasic myocarditis. J Am Coll Cardiol 1992; 20:480.
9. Bestteti RB, Dalbo CM, Arruda CA, Correia Filho D, Freitas OC. Predictors of sudden cardiac death for patients with Chagas disease: a hospital-derived cohort study. Cardiology 1996; 87:481–487.
10. de Paulo AA, Horowitz LN, Miyamoto MH, Pinheiro R, Ferriera DF, Terzian AB, Circenza C, Guiguer N Jr, Andrade JC, Fo EE. Automatic implantable defibrillator with VVI pacemaker in a patient with chronic Chagas myocarditis and total AV block. Am Heart J 1989; 118:415–417.
11. Muratore C, Rabinovich R, Iglesias R, Gonzalez M, Daru V, Liprandi AS. Implantable cardioverter defibrillator in patients with Chagas disease: are they different from patients with coronary disease. Pacing Clin Electrophysiol 1997; 20:194–197.
12. Curiel R, GESICA investigators. Randomized trial of low dose amiodarone in severe congestive heart failure. Lancet 1994; 344:993–998.
13. Bellotti G, Bocchi EA, de Moraes AV, Higuchi ML, Barbero-Marcial M, Sosa E, Esteves-Filho A, Kalil R, Weiss R, Jatene A, Pileggi F. In vivo detection of Trypanosoma cruzi antigens in hearts of patients with chronic Chagas disease. Am Heart J 1996; 131:301–307.
14. Rossi MA, Bestetti RB. The challenge of chagasic cardiomyopathy: the pathologic role of autonomic abnormalities, autoimmune mechanisms and microvascular changes, and therapeutic implications. Cardiology 1995; 86:1.
15. Soares Barreto-Filho JA, Consolim-Colombo FM, Lopes Ferreira H, Sobrinho Martins CR, Guerra-Riccio GM, Krieger EM. Dysregulation of peripheral and central chemoreflex responses in Chagas' heart disease patients without heart failure. Circulation 2001; 104:1792–1798.
16. Jelicks LA, Chandra M, Shtutin V, Petkova SB, Tang B, Christ GJ, Factor SM, Wittner M, Huang H, Douglas SA, Weiss LM, Orleans-Juste PD, Shirani J, Tanowitz HB. Phosphoramidon treatment improves the consequences of chagasic heart disease in mice. Clin Sci 2002; 103:267S–271S.
17. Jelicks LA, Shirani J, Wittner M, Chandra M, Weiss LM, Factor SM, Bekirov I, Braunstein VL, Chan J, Huang H, Tanowitz HB. Application of cardiac gated magnetic resonance imaging in murine Chagas' disease. Am J Trop Med Hyg 1999; 61:207–214.
18. Kalil R, Bocchi EA, Ferrerira BM, de Lourdes Higuchi M, Lopes NH, Magalhaes AC, Mady C, Pereira Barretto AC, Albuquerque CP, Bellotti G. Magnetic resonance imaging in chronic Chagas cardiopathy. Correlation with endomyocardial biopsy findings. Arq Bras Cardiol 1995; 65:413–416.
19. Bocchi EA, Kalil R, Bacal F, de Lourdes Higuchi M, Meneghetti C, Magalhaes A, Belotti G, Ramires JA. Magnetic resonace imaging in chronic Chagas' disease: correlation with endomyocardial biopy findings and gallium 67 cardiac uptake. Echocardiography 1998; 15:279–288.
20. Mahrholdt H, Goedecke C, Wagner A, Meinhardt G, Athanasiadis A, Vogelsberg H, Fritz P, Klingel K, Kandolf R, Sechtem U. Cardiovascular magnetic resonace assessment of human myocarditis: a comparison to histology and molecular pathology. Circulation 2004; 109:1250–1258.