Sustained monomorphic ventricular tachycardia as the presenting sign of Chagas’ cardiomyopathy in a low prevalence setting, diagnosis and management challenges. A case report

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Abstract: Approximately 300,000 people in the United States are estimated to have Chagas’ disease, with cardiac manifestations including arrhythmias occurring in 20%–30% of patients. We report a patient diagnosed with Chagas’ cardiomyopathy after presenting in ventricular tachycardia. This patient was asymptomatic before her presentation with recurrent episodes of ventricular tachycardia, which motivated us to screen her since she was an immigrant from an endemic Chagas region. This manuscript highlights some of the characteristic cardiac magnetic resonance imaging (MRI) and electrophysiology findings present in patients with Chagas’ cardiomyopathy. We also detail the management of patients with Chagas’ cardiomyopathy who have suffered from ventricular tachycardia.

Keywords: cardiac MRI, Chagas’ cardiomyopathy, Chagas’ disease, ventricular tachycardia

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Introduction
Sudden cardiac death (SCD) including ventricular tachycardia (VT) and ventricular fibrillation (VF), constitute 15%–20% of all deaths.1 In Western countries, 75% of SCD is due to coronary heart disease.1 However, 10%–15% of SCD are caused by non-ischemic cardiomyopathies unrelated to coronary heart disease.1 Caused by Trypanosoma cruzi parasitic infection, Chagas’ disease is one important infectious cause of non-ischemic dilated cardiomyopathy. Of patients who have chronic Chagas’ disease, 20%–40% are affected by cardiomyopathy.2,3 SCD claims the lives of 55%–65% of patients with Chagas’ cardiomyopathy (CM).3 Chagas’ disease is endemic to Latin America, with prevalence ranging from >3% in Bolivia and Argentina to 0.1%–0.9% in Mexico.4 Due to immigration from Latin America, this disease now affects the American patient population. By a screening study from 2008 to 2014, the disease was found in 1.24% of Latin American-born Los Angeles County residents.5 Once established, chronic Chagas cardiomyopathy carries a staggering annual mortality of 8%, higher than AIDS.6

With the increasing awareness that Chagas’ disease affects the lives of Latin American-born patients in the United States, optimal screening and management strategies remain under active investigation. As illustrated in this case report, SCD can infrequently be the initial manifestation of Chagas’ cardiomyopathy in an otherwise asymptomatic individual.3 The incorporation of advanced cardiac imaging modalities such as cardiac magnetic resonance imaging (MRI) and electrophysiology mapping now presents a way to evaluate the consequences of Chagas’ cardiomyopathy carefully.
We aim to increase awareness of VT as a presenting sign of Chagas’ cardiomyopathy. We will also discuss cardiac magnetic resonance imaging (CMR) and electrophysiology (EP) findings in Chagas’ CM and VT management in Chagas’ CM.

**Case report**

A 55-year-old woman with a history of hypertension, type 2 diabetes mellitus, and stroke presented with recurrent palpitations. She had been in her usual state of health until 6 months prior to admission to our hospital. At that time, she developed acute left arm discomfort, malaise, palpitations, and shortness of breath while on a plane to Mexico. Upon landing, she underwent electrical cardioversion for hemodynamically unstable wide-complex tachycardia (WCT). Cardiac catheterization at that hospital demonstrated no coronary artery obstruction. She also underwent an electrophysiology (EP) study, which reportedly showed atrial flutter with 2:1 conduction, which was ablated. She was then started on amiodarone and remained asymptomatic for about a month when she again experienced similar symptoms requiring electrical cardioversion. A repeat EP study was done, but no ectopic rhythm could be entrained. Diltiazem was then started. She then remained asymptomatic for approximately 5 months before presenting to our hospital. She was again found to be in an unstable WCT at 240 beats per minute, requiring electrical cardioversion. Her symptoms resolved. She denied orthopnea, leg swelling, dyspnea on exertion, or unexpected weight gain. She had no difficulty swallowing, nausea, vomiting, constipation, or diarrhea.

The patient’s medications included aspirin, irbesartan, metformin, and atorvastatin. Her diabetes and hypertension were controlled with these medications. She denied alcohol, tobacco, or drug use. She was originally from a rural city in southern Mexico but had not lived there for 20 years. She did not have a family history of heart disease or sudden cardiac death.

The initial differential for the patient’s initial WCT was VT, supraventricular tachycardia with aberrancy, or pre-excited supraventricular tachycardia. The patient’s initial electrocardiogram (EKG) demonstrated possible atrioventricular association with intermittent p waves that did not correspond with QRS complexes, raising suspicion for monomorphic VT [Figure 1(a)].

Following cardioversion, the patient was in sinus rhythm with a first-degree atrioventricular (AV) block [Figure 1(b)]. As with all VT, we considered scar-related VT due to ischemic heart disease given her risk factors at the top of our differential diagnosis. However, the patient’s prior cardiac catheterization demonstrated no obstructive coronary artery disease making this diagnosis less likely. Inflammatory cardiomyopathies, including cardiac sarcoidosis and Chagas’ cardiomyopathy (CM) were thus considered more likely. To further evaluate for the presence of structural heart disease, the patient underwent a transthoracic echocardiogram (TTE), which demonstrated no aneurysms, no thrombi, and normal left and right ventricular function. The left ventricular ejection fraction was estimated to be 50%–55%. Given the lack of remarkable positive findings, we pursued cardiac MRI (CMR) to evaluate for inflammatory cardiomyopathy.

On CMR cine images, the basal to the mid inferolateral wall was thinned, aneurysmal, and dyskinetic [Figure 2(a) and (b)]. Global systolic function was mildly reduced with an ejection fraction of 50%. Increased signal intensity on T2-weighed imaging [short tau inversion recovery (STIR) imaging] and transmural late gadolinium enhancement (LGE) in the inferolateral wall consistent with myocardial edema/inflammation and replacement fibrosis, respectively. These CMR findings were consistent with inflammatory cardiomyopathy and highly suggestive of Chagas’ CM given her social history. The patient’s *Trypanosoma cruzi* IgG antibody was sent for evaluation of Chagas’ CM and was positive on the initial assay. Confirmatory *T. cruzi* IgG was also positive by both enzyme immunoassay (EIA) and *T. cruzi* excreted-secreted antigen blotting [TESA-blot] at the Centers for Disease Control, establishing the diagnosis of chronic Chagas’ CM stage B2. This stage of chronic Chagas’ CM is defined by the presence of global ventricular dysfunction without heart failure symptoms, as described by Nunes *et al.*

An electrophysiology study (EPS) was then performed to localize the origin of the patient’s VT and to guide catheter ablation of this locus. The patient’s monomorphic VT was easily induced
during the infusion of isoproterenol, and it was not hemodynamically tolerated. Sinus rhythm voltage mapping of the left ventricle (LV) demonstrated a small area of reduced bipolar voltage in the basal inferolateral LV, corresponding to the aneurysmal region on CMR [red/green region, Figure 3(a)]. Unipolar mapping of this area revealed a larger region of reduced voltage (< 8.27 mV) [green region, Figure 3(b)], corroborating the epicardial substrate seen on CMR.

Pacemapping over the abnormal region in the basal lateral wall resulted in an excellent match to the clinical VT. Endocardial radiofrequency ablation (RFA) was performed, followed by epicardial mapping (Figure 4) and epicardial RFA, resulting in both core isolation and VT non-inducibility.9

A single-chamber ICD was placed for secondary prevention. Metoprolol and rivaroxaban were started for VT suppression and anticoagulation given the presence of a left ventricular aneurysm, respectively. The patient was subsequently treated with the antiparasitic medication benzimidazole. Our patient has had no episodes of sustained VT detected over one year of ICD.
follow-up. She also has no heart failure symptoms such as shortness of breath, edema, or orthopnea at follow-up.

Discussion
In this case, the patient presented with the isolated life-threatening finding of hemodynamically unstable VT in the absence of heart failure symptoms or other manifestations of Chagas’ disease. Chagas’ disease is caused by the parasite *Trypanosoma cruzi*, transmitted by feces of triatomine insects as they feed on blood. Human-to-human bloodborne transmission, vertical transmission from infected mothers to fetuses, transmission via solid organ transplantation from infected donors, and transmission via contaminated food or beverages are also possible.

Chagas’ disease begins as a brief 8- to 12-week acute phase, in which a patient can be asymptomatic or can develop a chagoma (local edema) at the inoculation site, as well as possible fever, malaise, or body aches. Afterward, patients typically become asymptomatic and enter an indeterminate chronic phase that can last for decades without clinically significant gastrointestinal or cardiac manifestations. These patients develop chronic Chagas’ cardiomyopathy at a 2% annual rate. As described by Nunes et al., chronic Chagas’ CM is differentiated into stages B1, B2, C, and D depending on ventricular dysfunction and heart failure symptoms.

Chagas’ CM is a chronic myocarditis due to tissue parasitism and exacerbated inflammatory response. Characteristically, wall motion abnormalities and aneurysms develop within coronary watershed regions in the basal inferolateral wall and apex. Aneurysms are believed to occur due to endothelial dysfunction within the coronary microcirculation through the formation of microthrombi or vasospasms from the chronic inflammatory response to the parasitic infection. As illustrated by this report, CMR is useful for a more sensitive evaluation of regional wall motion and structural abnormalities than an echocardiogram, which was normal in this case. CMR aids in the staging and management of the disease.

Myocardial edema, suggestive of myocarditis, is detected on T2-weighted imaging and often overlaps with areas of replacement fibrosis identified on LGE imaging. Torreão et al. found that 100% of patients with the cardiac phase of Chagas’ disease with left ventricular dysfunction had increased signal intensity on T2-weighted imaging and LGE.

In addition to structural abnormalities, Chagas’ CM may cause sinus node dysfunction or cardiac conduction abnormalities, including right bundle branch block, left anterior fascicular block, atrioventricular block, or sinus bradycardia. Our patient had a first-degree atrioventricular block. Arrhythmias are also common, including atrial fibrillation, premature ventricular complexes, and predominantly epicardial non-sustained VT.
Our patient presented with monomorphic VT involving the epicardium caused by reentry within areas of fibrosis.

The need for epicardial ablation for VT in Chagas’ cardiomyopathy is well-established. Performing both endocardial and epicardial ablation as we pursued is supported by a wealth of observational data as well as a recent randomized control trial. Pisani et al. found that combined endocardial and epicardial ablation significantly decreased VT recurrence versus endocardial ablation alone. In addition to single-chamber ICD placement for prevention of SCD, metoprolol was started due to left ventricular dysfunction and to suppress VT that could trigger ICD shocks, which are higher in Chagas’ CM patients due to intense ventricular arrhythmic activity. Amiodarone is often used in

Figure 3. (a) Sinus rhythm voltage map of the LV with bipolar voltage demonstrating a small area of reduced voltage [red/green] in the basal inferolateral wall, corresponding with the aneurysm. [b] Sinus rhythm voltage map of the LV with unipolar voltage demonstrating a larger area of reduced voltage [green] in the basal inferolateral wall, corresponding with the aneurysm. [CARTO, Biosense Webster, Inc.].
Chagas’ CM to reduce the risk of ICD shocks as it is in other cardiomyopathies, but this drug was not initiated in this patient’s case due to her relatively young age, concern for long-term toxicities, and successful ablation. The absence of significant bradycardia associated with the patient’s Chagas’ cardiomyopathy was also critical in this decision. The CHAGASIC trial is underway to compare ICD to amiodarone therapy in primary prevention of overall mortality in high-risk patients, which should help begin to clarify the role of amiodarone in the management of Chagas’ related VT.

Traditionally, the Rassi et al. score has been used to prognosticate patients with Chagas’ CM since its validation in 2006. However, it is important to note that it does not apply to this patient because the presence of sustained VT was an exclusion criterion for the study of Rassi et al., along with VF, implanted cardiac pacemaker, and another associated heart disease. With the advent of more advanced endocardial and epicardial ablation strategies, it may be reasonable to revisit this scoring system.

Due to the presence of left ventricular aneurysms in Chagas’ CM, patients are at risk of stroke. The Chagas’ cardioembolism risk score was used to assess this patient’s risk. Based on a cardioembolism risk score of 3, the patient has an annualized risk of stroke of 2.1%. Based on the work of Sousa et al., warfarin or aspirin would be indicated. Rivaroxaban was initiated for convenience.

In order to manage this patient’s Trypanosoma cruzi infection, benznidazole antitrypanosomal therapy was initiated based on her early phase of Chagas’ CM (stage B2) following a risk-benefit discussion with the patient, acknowledging that there would likely be little to no benefit of treatment based on the BENEFIT trial. The BENEFIT randomized control trial found that in patients with established Chagas’ cardiomyopathy, benznidazole therapy did not significantly reduce a composite primary outcome including death, VT, ICD placement, or hospitalization. The trial was performed in Latin America, which may hinder applicability to this patient, partly because this patient is unlikely to be reinfected with T. cruzi in the United States, unlike many of the patients in the BENEFIT trial. The patient was closely monitored for benznidazole side effects including dermatitis, leukopenia, weight loss, nausea, vomiting, and peripheral neuropathy. She had complete blood counts, basic metabolic panel, and liver function tests every 2–4 weeks for monitoring. The patient did not develop significant side effects or lab abnormalities. The authors note that the American Heart Association (AHA) does not recommend routine use of benznidazole.
However, the AHA does suggest that treatment could be offered to those patients such as the one presented in this report, who have chronic cardiomyopathy but not dilated cardiomyopathy, following shared decision making with the attending physician. In our treatment, the authors followed the AHA guidance proposed by Nunes et al. in prescribing benznidazole. Unfortunately, there remains no antiparasitic treatment that has been proven to be effective in halting progression of Chagas’ cardiomyopathy.

Conclusions
We describe a patient presenting with VT as the initial sign of Chagas’ CM. This report demonstrates the limitations of the American healthcare system’s ability to identify patients with this disease. There is currently no guideline for Chagas’ disease screening in patients who immigrate from endemic regions. Patients such as ours may develop unstable arrhythmias before developing any other symptoms. Although this patient survived and underwent ablation, ICD placement, and beta blocker therapy as demonstrated, antiparasitic therapy is of unclear benefit in such patients who have already developed features of Chagas’ cardiomyopathy. Such screening efforts have recently been described in Los Angeles County and at our institution in Colorado. There is a lack of randomized controlled trial data regarding the optimal treatment or monitoring of these patients. Such investigations should be paired with novel screening efforts.

Cardiac MRI (CMR) also played an important role in the management of this patient’s case, demonstrating subtle findings of Chagas’ CM that were initially missed on the echocardiogram. As illustrated in this report, typical CMR findings of Chagas’ CM include regional wall motion abnormalities, left ventricular aneurysms, and overlapping regions of edema and replacement fibrosis. Chagas’ CM should be considered in all patients presenting with VT who have lived in endemic regions, and testing for T cruzi IgG should be strongly considered in all such patients.

Declarations

Ethics approval and consent to participate
The use of the clinical data has been performed under an approved protocol by the Colorado Multiple Institutional Review Board (COMIRB Protocol 19-2011) and an exemption of informed consent was granted. All identifying details of the patient have been removed in accordance with our institutional policy (COMIRB) and the World Medical Association Declaration of Helsinki.

Consent for publication
An exemption of informed consent was granted as per the above protocol.

Author contributions
Devang R. Amin: Conceptualization; Data curation; Investigation; Writing – original draft; Writing – review & editing.
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Daniel W. Groves: Conceptualization; Data curation; Formal analysis; Investigation; Supervision; Visualization; Writing – original draft; Writing – review.

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There are no additional data for this article.

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