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Sustained Ventricular Tachycardia as a Harbinger of Cardiac Amyloidosis

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Patient: Male, 71-year-old
Final Diagnosis: Cardiac amyloidosis
Symptoms: Diaphoresis • presyncope • shortness of breath
Medication: —
Clinical Procedure: Electrical cardioversion
Specialty: Cardiology

Objective: Rare co-existence of disease or pathology

Background: Cardiac amyloidosis is an infiltrative cardiomyopathy caused by the extracellular deposition of insoluble precursor protein amyloid fibrils. These depositions of protein amyloid fibrils are found on the atria and ventricles and can cause a wide array of arrhythmias; however, sustained ventricular arrhythmias are quite uncommon.

Case Report: A 71-year-old man with a history of hypertension developed a sudden onset of shortness of breath, profuse diaphoresis, lightheadedness, and presyncope. Upon emergency medical services' arrival, an initial electrocardiogram revealed wide complex tachycardia with a heart rate of 220 to 230 beats per min. He was subsequently given, in succession, magnesium, adenosine, and amiodarone with no change in heart rate or rhythm. Due to ongoing symptoms of diaphoresis and the development of dyspnea, he underwent direct current cardioversion and was converted from ventricular tachycardia to atrial fibrillation at controlled rates. A transthoracic echocardiogram and cardiac magnetic resonance imaging showed features suspicious for cardiac amyloidosis. A subsequent 99m technetium pyrophosphate single-photon emission computerized tomography scan revealed a grade 3 visual uptake and a heart-to-contralateral lung ratio of 1.92, consistent with transthyretin amyloidosis. The patient was treated with tafamidis and an implantable cardioverter-defibrillator for secondary prevention of ventricular arrhythmia.

Conclusions: This case highlights the need to consider cardiac amyloidosis in the differential diagnoses of patients with persistent ventricular arrhythmia and no prior history of heart disease.

MeSH Keywords: Amyloidosis • Cardiomyopathies • Electric Countershock • Tachycardia, Ventricular

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/927041>



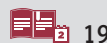
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Background

Cardiac amyloidosis is an infiltrative cardiomyopathy caused by the extracellular deposition of insoluble precursor protein amyloid fibrils [1]. The most common etiologies of cardiac amyloidosis include amyloid light chain amyloidosis and amyloid transthyretin (ATTR). ATTR can be either wild-type (or senile) amyloidosis or mutant/hereditary ATTR [2]. These depositions of protein amyloid fibrils are found on the atria and ventricles and cause restrictive cardiomyopathy and ventricular function deterioration in the late stages [3].

Clinical manifestations of cardiac amyloidosis are protean and include asymptomatic presentation, diastolic heart failure secondary to restrictive cardiomyopathy, and a wide array of arrhythmias. Atrial arrhythmias and nonsustained ventricular arrhythmias are the most common arrhythmias in cardiac amyloidosis, while sustained ventricular arrhythmias are quite uncommon [4]. We report a case of ATTR cardiac amyloidosis in a patient whose only initial presentation was sustained ventricular tachycardia.

Case Report

A 71-year-old man with a medical history of hypertension, bilateral carpal tunnel surgeries, and hypercholesterolemia was shopping in the mall when he developed a sudden onset of

shortness of breath, profuse diaphoresis, and presyncope. He could barely palpate his carotid pulse, which prompted him to call for an ambulance. Upon the arrival of the emergency medical service (EMS), his initial blood pressure was found to be stable at 100/73 mmHg, and the cardiac monitor revealed wide complex tachycardia with a heart rate of 220 to 230 beats per min (bpm). The patient was given 100 mg of lidocaine en route to the hospital. On arrival to the emergency department (ED), a repeat electrocardiogram (ECG) showed the patient had ventricular tachycardia at rates exceeding 200 bpm (Figure 1); however, his blood pressure was normal, at 113/89 mmHg. He was subsequently treated with 2 g of IV magnesium, 12 mg of IV adenosine, and 150 mg of IV amiodarone, with no change in heart rate or rhythm. Owing to the persistence of his symptoms, consent was obtained for direct current cardioversion. Conscious sedation was administered, and 200 J of biphasic synchronized shock was delivered, resulting in the conversion from ventricular tachycardia to atrial fibrillation at controlled rates (Figure 2).

Investigations

The ECG performed in the ED showed monomorphic ventricular tachycardia at rates exceeding 200 bpm (Figure 1). The results of a complete blood count and metabolic panel were unremarkable. The patient subsequently had a transthoracic echocardiogram which revealed severe concentric left ventricular hypertrophy with a posterior wall thickness of 15 mm, interventricular

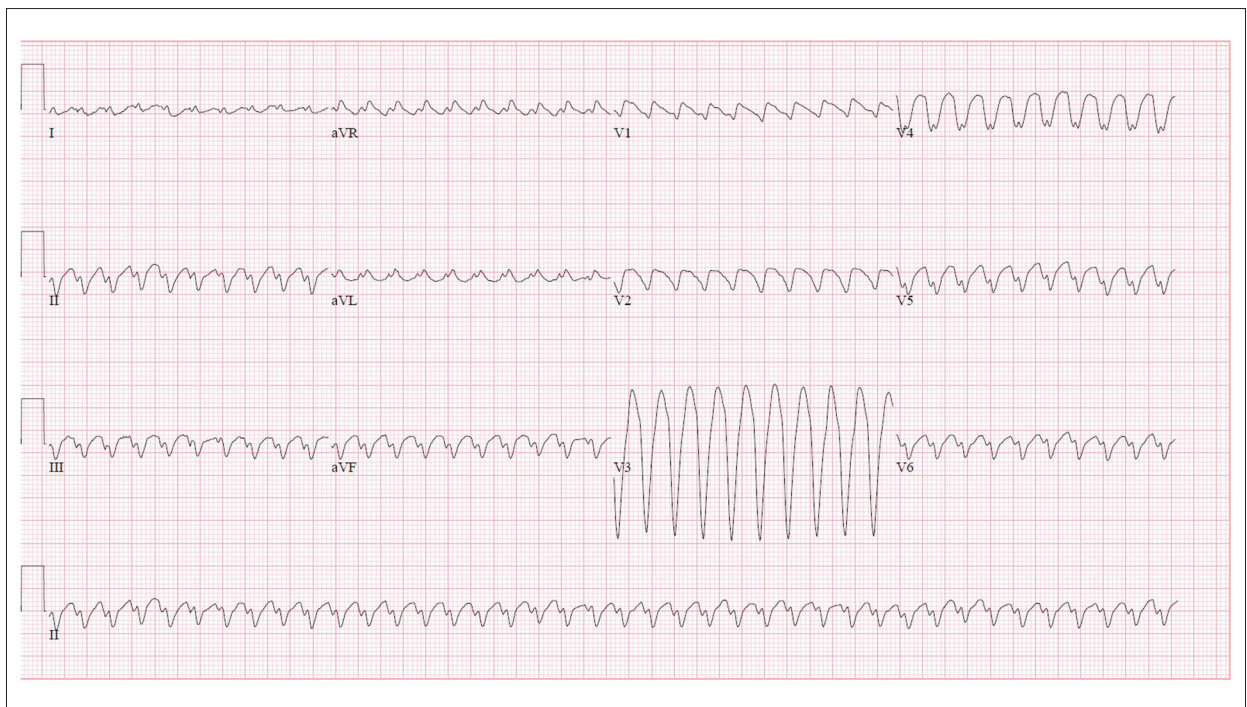


Figure 1. Electrocardiogram showing a monomorphic ventricular tachycardia in a 71-year-old man admitted with sudden onset of shortness of breath, profuse diaphoresis, lightheadedness, and presyncope symptoms.

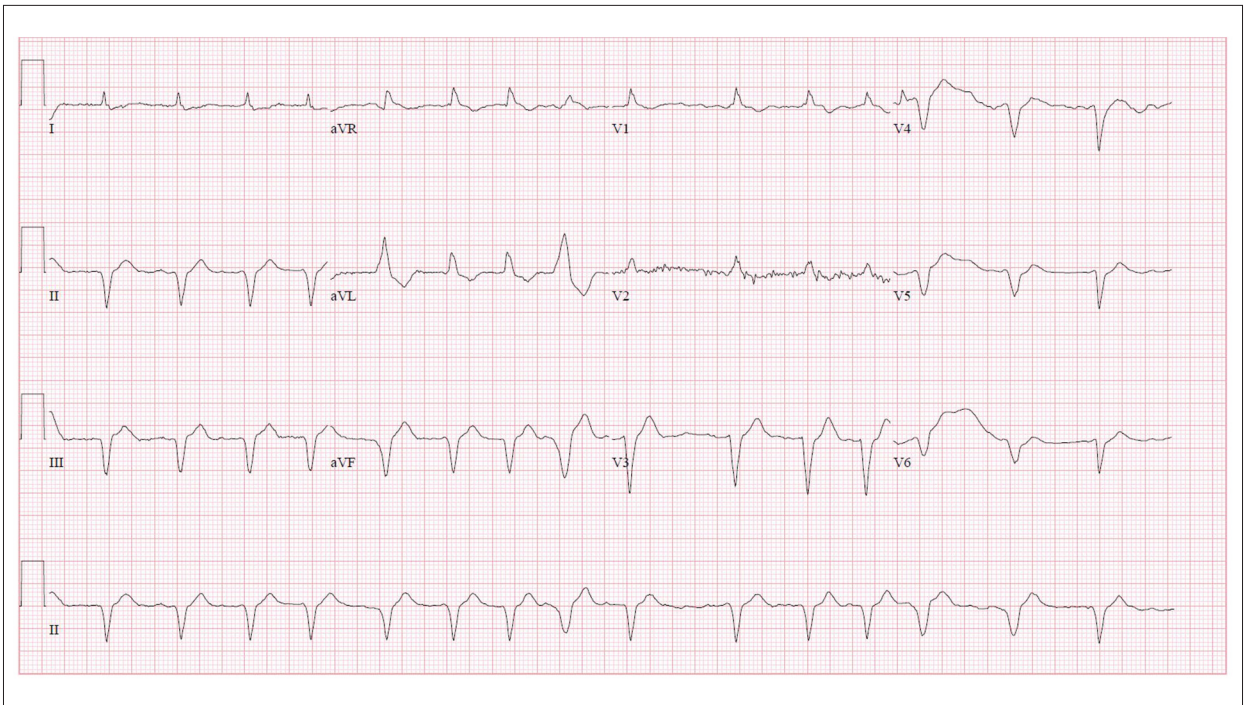


Figure 2. Electrocardiogram showing atrial fibrillation after electrical cardioversion due to unresponsive medical treatment for ventricular tachycardia and voltage discrepancy and pseudo-infarct pattern in a 71-year-old man.

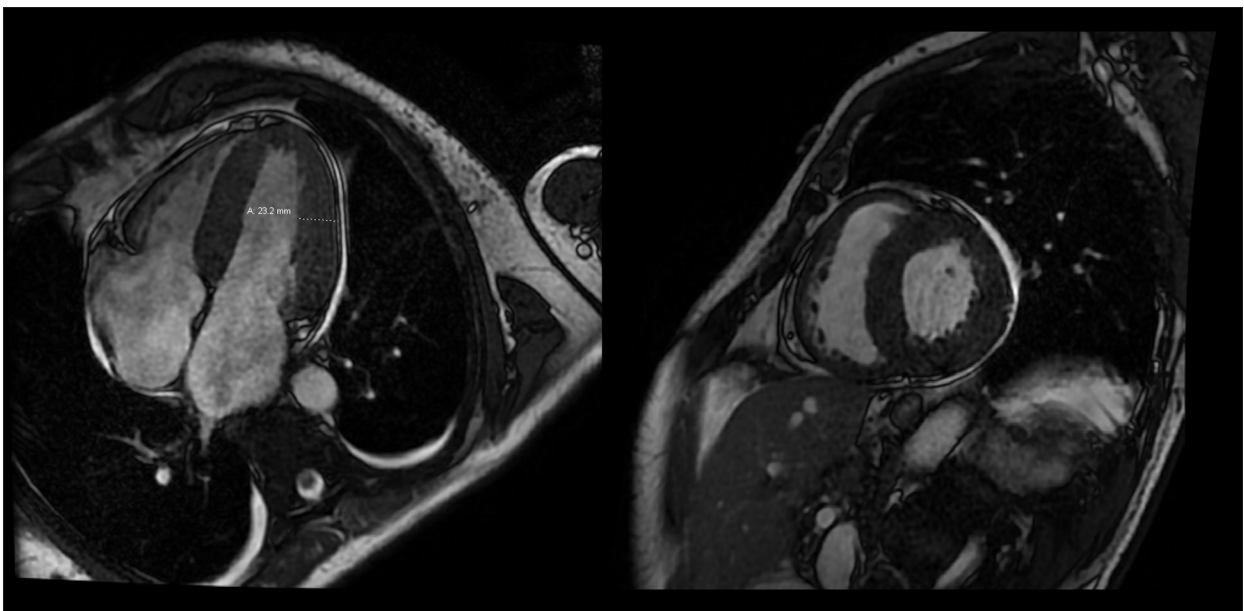


Figure 3. Cardiac magnetic resonance imaging showing a global left ventricular hypertrophic cardiomyopathy with notable diffuse patchy enhancement of the entire left ventricle with thickening of the interatrial septum.

septal thickness of 14 mm, and estimated ejection fraction of 43% with moderate bi-atrial enlargement, and no pericardial effusion. The patient's diastolic function could not be assessed because of the atrial fibrillation. Further ischemic evaluation including coronary angiography revealed widely patent coronary arteries, with minimal atherosclerotic disease. Due to

concern for a primary myopathic or infiltrative process, cardiac magnetic resonance imaging (MRI) was performed, revealing global left ventricular hypertrophic cardiomyopathy with notable diffuse patchy enhancement of the entire left ventricle with questionable thickening of the interatrial septum, findings likely secondary to cardiac amyloidosis (Figure 3). Further

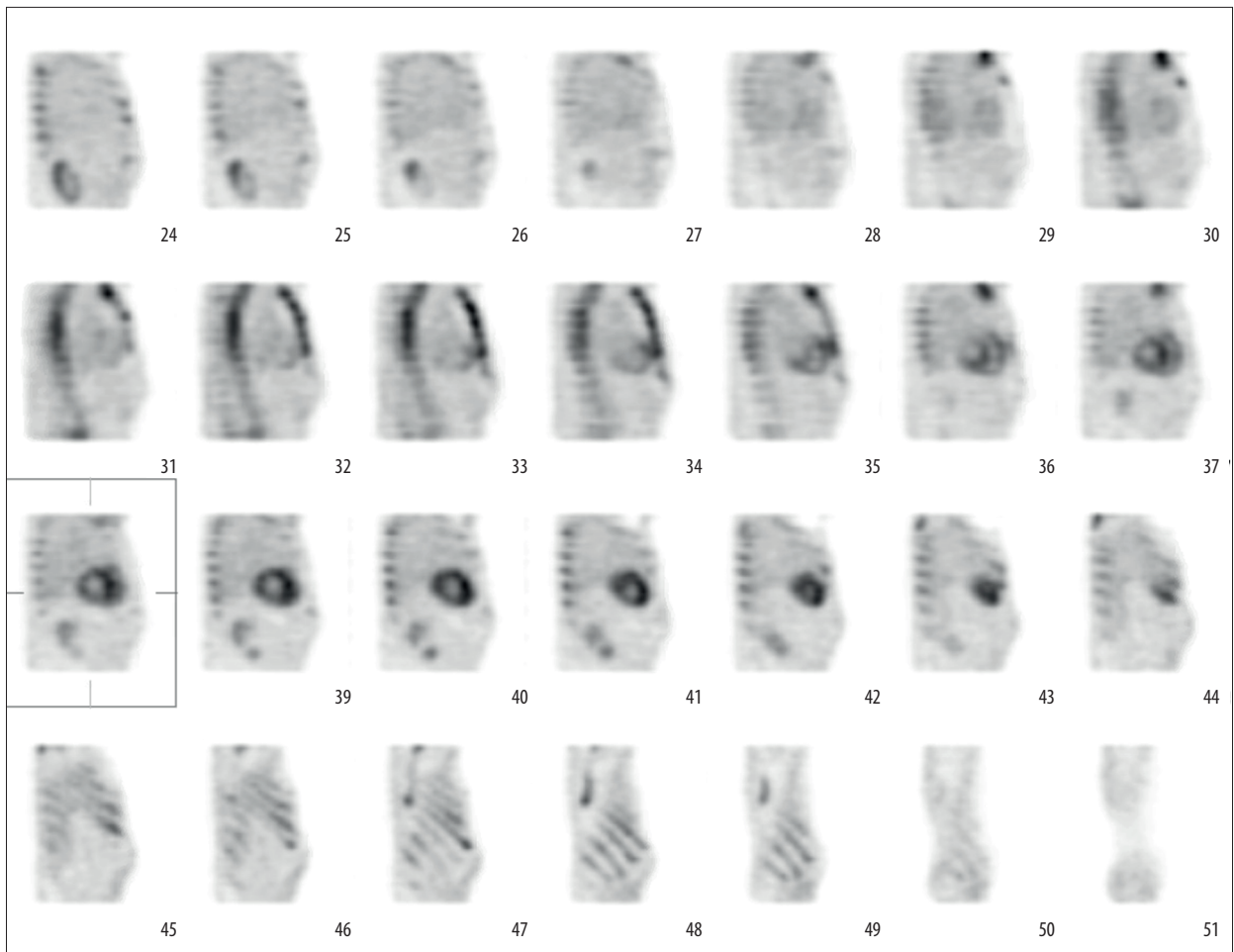


Figure 4. A 99m technetium pyrophosphate single-photon emission computerized tomography scan showing a grade 3 visual uptake and a heart-to-contralateral lung ratio of 1.92.

diagnostic examinations involved serum protein electrophoresis, urine protein electrophoresis, serum free light chains with light chain ratio and immunofixation studies, all of which were largely unremarkable. Finally, a 99m technetium pyrophosphate single-photon emission computerized tomography (SPECT) scan revealed grade 3 visual uptake and a heart-to-contralateral lung (H/CL) ratio of 1.92, consistent with ATTR (Figure 4). The results of genetic testing failed to demonstrate a mutation in the TTR gene, supporting a diagnosis of wild-type ATTR.

Differential diagnosis

The patient had no history of coronary artery disease or cardiomyopathy. An initial differential diagnosis of wide complex tachycardia included ventricular tachycardia or supraventricular tachycardia with aberrant conduction. The presence of concordance in the precordial leads, an RS interval >100 ms in multiple precordial leads, and the presence of a dominant R wave in aVR on the ECG, as well as a lack of any response by the rhythm to adenosine administration, strongly supported

the diagnosis of ventricular tachycardia. A computerized tomography (CT) scan of the chest with contrast was negative for pulmonary embolism. Ischemic evaluation including a coronary angiogram revealed “clean” coronary arteries, excluding the possibility of acute coronary syndrome-induced ventricular tachycardia. Given the patient’s history of weight loss, a malignancy was excluded by a CT scan of chest, abdomen, and pelvis. Other causes of increased left ventricular wall thickness, including aortic stenosis, long standing hypertension, and infiltrative diseases such as cardiac sarcoidosis, were also considered. However, these were systematically excluded based on the patient’s medical history, physical examination, and imaging studies. Ultimately, we made a diagnosis of ATTR cardiac amyloidosis.

Treatment

The patient exhibited no response to IV lidocaine given by the EMS en route to the hospital. The patient also received 2 g of IV magnesium, 150 mg of IV amiodarone, and 12 mg of IV

adenosine without any change in heart rate or rhythm in the ED. Subsequently, because of his ongoing symptoms, a decision was made to proceed with electrical cardioversion under conscious sedation. Following the application of 200 J of biphasic synchronized current, the patient's rhythm converted to atrial fibrillation with a heart rate in the 80s (Figure 2). Regardless of the CHA₂DS₂-VASc score, anticoagulation therapy is recommended for patients with concomitant atrial fibrillation and ATTR cardiac amyloidosis; hence, our patient was started on oral anticoagulation. During his hospitalization, he was evaluated for the placement of an implantable cardioverter-defibrillator for secondary prevention of sudden cardiac death. He was also started on low-dose beta-blocker therapy.

Outcome and follow-up

The patient was discharged home on anticoagulation therapy with apixaban for atrial fibrillation. At his follow-up appointment in our practice a few weeks later, he was started on 81 mg of oral tafamidis once daily for the treatment of ATTR. Genetic testing results were negative for TTR mutations, thereby confirming the diagnosis of wild-type/senile ATTR. In the months that followed, heart rhythm control strategies including amiodarone and direct current cardioversion were administered without success. Eventually, the patient underwent a comprehensive electrophysiologic study with ablation of atrial fibrillation.

Discussion

Cardiac amyloidosis, also known as amyloid cardiomyopathy, refers to a disorder caused by the deposition of amyloid fibrils in the heart's extracellular space [1]. Although several subtypes of cardiac amyloidosis exist, most cases are caused by deposition of either immunoglobulin light chains (amyloid light chains) or TTR protein [2]. While amyloid light chain amyloidosis has similar prevalence among males and females, ATTR occurs more commonly in males [5]. Based on echocardiographic, cardiac MRI, and SPECT scan findings, a diagnosis of ATTR cardiac amyloidosis was made in our patient (Figures 3, 4). ATTR can be further subdivided based on the nature of the TTR protein into senile/wild-type TTR and mutant/hereditary TTR. Our patient's genetic testing was negative for TTR mutations; hence, the diagnosis of senile or wild-type ATTR was made. Among patients with mutant TTR, the most encountered mutation is the Val122Ile point mutation which occurs in 3.5% of Black Americans [6,7]. TTR, previously known as prealbumin, is a transport protein that is produced by the liver and responsible for the transport of thyroxine and retinol [4]. The TTR molecule circulates mostly in the homotetrameric form (made up of 4 identical protein subunits that are associated but not covalently bound) [8,9]. However, a small fraction circulate in plasma in the monomeric form, with a

predisposition for misfolding and forming insoluble amyloid fibrils [4,10]. Amyloid fibrils infiltrate the cardiac musculature, impairing the contractile and conductive functions of the heart, which results in restrictive cardiomyopathy and multiple arrhythmias [2,5], as was the case in our patient. Although the mechanism of arrhythmogenesis in cardiac amyloidosis is not well defined, it is thought to be related to patchy fibrosis, with the resultant scar tissue formation and direct toxic effects of amyloid fibrils. The most common atrial arrhythmia is atrial fibrillation, which likely results from severe bi-atrial enlargement due to the infiltrative process. Nonsustained ventricular tachycardia appears to be the most common type of ventricular arrhythmia [4]. Sustained ventricular tachycardia, which our patient had, is less common. One case series reported that 6 out of 31 patients (19%) with cardiac amyloidosis had sustained ventricular tachycardia or ventricular fibrillation [11]. The combination of the cardiac MRI, immunologic studies, and SPECT scan has a specificity of almost 100% for ATTR [12]. Our initial diagnostic approach was by cardiac MRI, which revealed features suggestive of cardiac amyloidosis (Figure 3). However, cardiac MRI cannot distinguish amyloid light from ATTR; although, recent guidelines and expert consensus by the Amyloidosis Research Consortium suggest that systemic signs and symptoms with biomarkers and imaging should be considered when making a diagnosis of ATTR [13]. While a diagnosis can be obtained by biopsy (fat pad or involved tissue) and immunohistochemical typing, it is not required when other tests are positive, particularly as the sensitivity of a biopsy result is often lower than that of the current imaging techniques [14].

To determine the amyloidosis subtype, we performed serum and urine protein electrophoresis and serum free light chains with ratio and immunofixation. The combined sensitivity of these tests for the diagnosis of amyloid light chain amyloidosis is about 98%. In our patient, these tests were unremarkable and essentially ruled out amyloid light chain amyloidosis and prompted the need for nuclear pyrophosphate scanning, which is nearly 100% specific for diagnosing ATTR [12].

A SPECT scan assesses cardiac retention by a semiquantitative visual score in relation to bone uptake and by quantitative analysis by drawing a region of interest over the heart, which is corrected for contralateral counts and calculation of an HCL ratio [12]; a HCL ratio of greater than 1.5 is considered diagnostic of ATTR. Our patient had a grade 3 semiquantitative interpretation in relation to rib uptake (denoting cardiac uptake greater than rib uptake with mild/absent rib uptake) and an HCL ratio of 1.92 for the quantitative finding. Echocardiographic findings in cardiac amyloid can include an abnormal left ventricular longitudinal strain pattern with apical sparing, increased left ventricular wall thickness (usually without history of hypertension and lacking increased voltage, consistent with left

ventricular hypertrophy on ECG), enlarged atria, thickened valvular leaflets, and small pericardial effusions [15].

Until recently, with the advent of novel therapies, including TTR silencers, tetramer stabilizers, and fibril degradation and reabsorption therapies, patients with cardiac amyloidosis had a grim prognosis with a median survival of <1 year, discouraging the consideration of implantable cardioverter-defibrillator placement in these patients. The 2015 European Society of Cardiology guidelines give a class IIa/C recommendation for the use of an implantable cardioverter-defibrillator for secondary prevention in patients with cardiac amyloidosis with >1 year life expectancy [16], while the 2017 American Heart Association/American College of Cardiology/Heart Rhythm Society guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death recommends individualized decision making, owing to limited

data availability [17]. Prospective studies are needed to investigate the role of an implantable cardioverter-defibrillator in the primary prevention of sudden cardiac death in cardiac amyloidosis [11,18,19].

Conclusions

Cardiac amyloidosis should be suspected in patients with malignant ventricular (or atrial) arrhythmias with no prior evidence of heart disease, as was the case in our patient. This presentation could very well be the first manifestation of this life-threatening disease.

Conflict of interest

None.

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