

## Sustained Ventricular Tachycardia as an Isolated Presentation of Transthyretin Amyloidosis Cardiomyopathy - Val50Met

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### Introduction

Amyloidosis is characterized by extracellular deposition of insoluble proteins (amyloid deposition) in multiple organs and progressive organ dysfunction. It is classified by the type of protein that is deposited, including transthyretin amyloidosis (ATTR), which can occur due to a genetic variant and aging.<sup>1</sup> Approximately 120 genetic variants have been recognized to cause ATTR; one of the most common is Val50Met. The phenotypic presentation of ATTR due to the Val50Met mutation is mostly neurological, known as familial amyloidotic polyneuropathy (FAP), but cardiac involvement is being increasingly recognized.<sup>2</sup> Sporadic cases with strictly cardiac manifestation, causing ventricular wall hypertrophy, dysfunction diastolic, and conduction disturbances have already been described in the literature.<sup>3</sup>

In this article, we report a case of ATTR due to the Val50Met mutation, with the phenotypic expression of cardiac involvement, with sustained ventricular tachycardia as an isolated presentation.

### Case Report

A 61-year-old Brazilian man with hypertension, whose parents were Portuguese, complained of chest pain, followed by palpitations 1 hour before arriving at the emergency room. He presented with intense sweating, elevated heart rate (196 beats per minute) and resting blood pressure of 130/80 mmHg. Electrocardiogram revealed sustained ventricular tachycardia (Figure 1). He was promptly submitted to successful electrical cardioversion, and, 2 days later, an internal cardiac defibrillator (ICD) was implanted. During etiological investigation, several tests were performed, as described subsequently. Myocardial necrosis markers were shown to be elevated, in an ascending curve (peak CK-MB: 31.3 ug/L and ultra-sensitive troponin: 19,400 ng/ml); coronary cineangiography revealed a 30% lesion in the circumflex artery and a luminal area of 8.6 mm<sup>2</sup> (intracoronary ultrasound); echocardiogram showed ejection

fraction of 66%, increased wall thickness (septum 19 mm and posterior wall 15 mm), increased thickness of the right ventricle (RV) and interatrial septum, left ventricle (LV) with 52/33 mm, moderate atrial enlargement (indexed left atrial volume of 45 ml/m<sup>2</sup>), severe diastolic dysfunction (grade III), and pulmonary artery systolic pressure (PASP) of 45 mmHg. In spite of the normal ejection fraction, global longitudinal strain showed impairment of the LV systolic function of -9 (reference value: -18), sparing the apical portion.

Magnetic resonance imaging showed the greatest thickness in the middle inferoseptal wall of the left ventricle (22 mm), diffuse late enhancement with non-ischemic, circumferential gadolinium pattern, and myocardial edema (Figure 2). The investigation of light chains, kappa:lambda ratio, serum and urinary immunofixation were negative, and pyrophosphate scintigraphy showed intense uptake of pyrophosphate labeled with symmetrical technetium in the LV walls and light intensity in the RV, with a left hemithorax to contralateral hemithorax count ratio of 2.3 (positive study > 1.5). Genetic testing revealed a mutation in the p.Val50Met transthyretin gene.

The patient evolved with weight loss, bilateral carpal tunnel syndrome, and a slight decrease in the distal strength of the lower limbs; these symptoms are compatible with impairment of the peripheral and autonomic nervous systems. He started treatment with tafamidis in November 2019. One year later, he showed symptoms of dyspnea upon exertion; upon physical examination, hepatomegaly and jugular swelling were observed. He was given a low dose of a diuretic for 3 days, and his implantable defibrillator heart rate was increased to 80 bpm, which resolved the symptoms. During evolution, he showed appropriate ICD therapy for ventricular tachycardia.

The patient evolved to become asymptomatic, reporting only that his steps slowed when climbing steep slopes. The echocardiogram was repeated 1.5 years after starting the use of tafamidis, revealing ejection fraction of 56%, septal thickness of 18 mm, posterior wall of 16 mm, increased RV and interatrial septum thickness, VE 51/36 mm, moderate atrial volume (indexed left atrial volume 42 ml/m<sup>2</sup>), grade II diastolic dysfunction, PASP of 23 mmHg, and global longitudinal strain of -7.7.

### Keywords

Familial Amyloidosis; Restrictive Cardiomyopathy; Ventricular Tachycardia.

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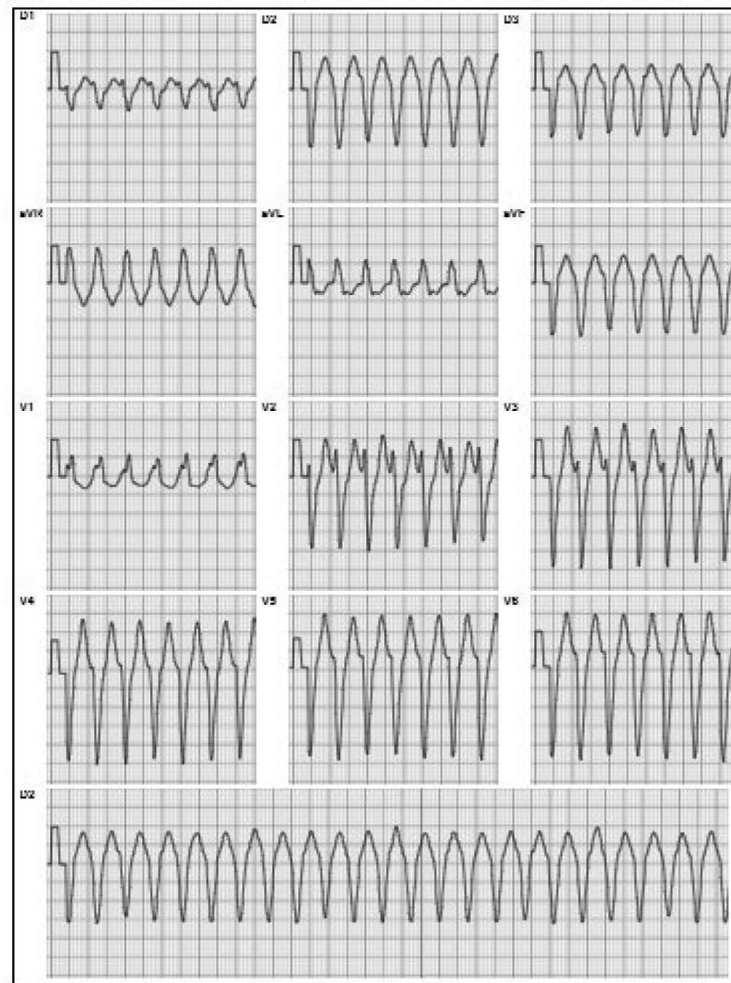
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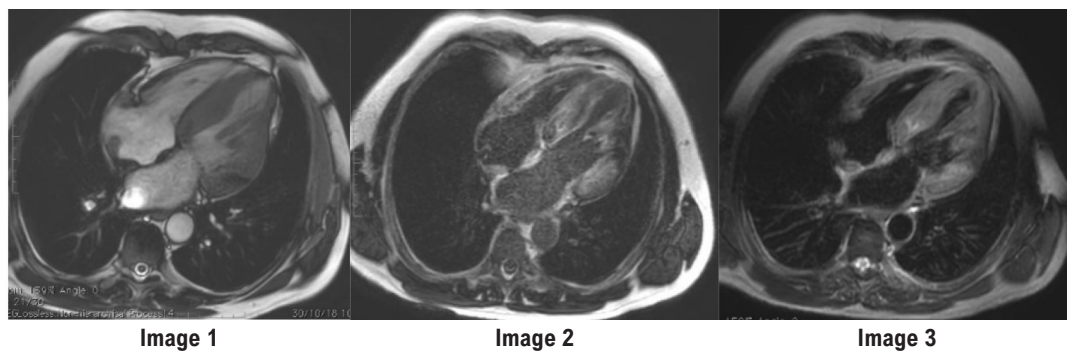
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### Discussion

Ventricular tachyarrhythmia in an elderly patient with curved elevation of troponin levels is highly indicative of acute coronary syndrome.<sup>4</sup> In the present case, this was the first diagnostic hypothesis considered; however, coronary cineangiography ruled out this possibility. The echocardiogram, by demonstrating the presence of a significant increase in thickness in both the septum and the lateral wall, guides us



**Figure 1** – Electrocardiogram showing sustained ventricular tachycardia.



**Figure 2** – Cardiac magnetic resonance showing evidence, in image 1: 4-chamber cine; image 2: 4-chamber late enhancement; image 3: Tripple BB edema.

## Case Report

away from the diagnosis of inflammatory conditions due to the magnitude of hypertrophy and leads us toward diagnosis of a group of diseases that present with increased wall thickness, such as hypertrophic cardiomyopathy, which is the most prevalent after hypertensive cardiomyopathy, Fabry disease, and cardiac amyloidosis.<sup>5</sup> Increased wall thickness, associated with other findings on echocardiography, such as severe diastolic dysfunction, apical sparing, and significantly reduced longitudinal strain, which are typical of amyloidosis, point us toward this diagnosis. Cardiac resonance, in addition to confirming these findings, added more information that is characteristic of this disease, namely, circumferential delayed enhancement and myocardial edema. The finding of myocardial edema has been related to the acute disease; it is more common in light chain amyloidosis, and it is associated with the occurrence of severe complications.<sup>6</sup> In this case, the occurrence of ventricular tachycardia can be related to this structural substrate.

ICD implantation in patients with amyloidosis has conflicting indications in studies conducted before the start of specific therapy, which modifies survival. The progressive character of the disease, with progressive loss of ventricular function, may explain why the benefit of the implantation has not been demonstrated. However, currently, with the introduction of specific treatment, especially if the patient is at an earlier stage of disease evolution, in NYHA functional class I/II, it is likely that this recommendation will be modified in the guidelines, given that it is possible to expect reasonable survival.<sup>1</sup>

## Conclusion

Val50Met is a pathogenic mutation that is characterized, mainly, as being clinically expressed by FAP. Cardiomyopathy, nephropathy, and vitreous humor opacity may be present, but PAF is the main presentation. When cardiomyopathy is present, the main presentation is generally heart failure, but without ventricular arrhythmia. In the patient whose case has been described, ventricular arrhythmia was the only manifestation, and amyloidosis was not even considered in the differential diagnosis, until magnetic resonance was performed. This case highlights the risk of sudden cardiac death in patients with hereditary ATTR. Although the association between hereditary ATTR and sudden death has been well recognized, studies have not shown any survival

benefit from defibrillator implantation, perhaps due to delayed diagnosis. Hereditary ATTR should thus be considered as a cause of sustained ventricular tachycardia.

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## Author contributions

Conception and design of the research and Critical revision of the manuscript for intellectual content: Correia EB, Bruscky LVR; Acquisition of data: Correia EB, Bruscky LVR, Silva LML, Murta ACS; Analysis and interpretation of the data: Correia EB, Bruscky LVR, Chen K, Quagliato PC; Writing of the manuscript: Correia EB, Bruscky LVR, Francisco YA, Silva LML.

## Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

This study is not associated with any thesis or dissertation work.

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