3D Printing of a Heart With Amyloidosis

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Abstract

Cardiac Amyloidosis is a restrictive cardiomyopathy caused by the accumulation of amyloid protein in the heart. The advances in non-invasive diagnosis have been increasing its identification among patients with Heart Failure (HF), being previously considered to be a rare condition. Currently, it represents around 13% of the cases of Heart Failure with preserved Ejection Fraction (HFpEF). We report the case of a 72-year-old male patient who presented to the clinic reporting dyspnea and fatigue in low-effort activities. Laboratory exams were conducted, revealing increased cardiac markers, along with evidence of ventricular hypertrophy in electrocardiographic analysis. Cardiac imaging, serum free light chain (AL) assay, and endomyocardial biopsy indicated the diagnosis of AL amyloidosis. A three-dimensional model was constructed using magnetic resonance imaging (MRI) data. This model is intended to increase the awareness around amyloidosis as a possible differential diagnosis of HF, while also promoting patients' and families' education, demonstrating the typical structural abnormalities of the disease.

Introduction

Cardiac amyloidosis results from disorders in the folding of amyloidogenic proteins, leading to the formation of insoluble amyloid fibrils that accumulate in the extracellular matrix of the heart.[1] The most common variants are primary or light chain (AL) and transthyretin-related (ATTR) amyloidosis. AL amyloidosis is caused by the deposition of ALs of immunoglobulin, produced in excess by normal or malignant plasma cells.[2] Cardiac manifestations of amyloidosis include Heart Failure with preserved Ejection Fraction (HFpEF), arrhythmias, angina with non-obstructive coronary lesions, and thromboembolic events. Some cases of cardiac amyloidosis are associated with aortic stenosis, particularly in cases with low flow and low gradient.[3] The three-dimensional printing has been widely explored in the healthcare field for various applications, ranging from the production of surgical parts to educational models. This tool has stood out for allowing the creation of patient-specific materials, which aid in the study and understanding of complex pathological anatomies. We report a case of AL cardiac amyloidosis in which 3D printing was used to model the affected organ. This modeling was intended to increase the awareness of amyloidosis as a possible differential diagnosis of heart failure (HF) with preserved ejection fraction, while also promoting patients' and families' education.

Keywords

Amyloidosis; Heart Failure; Three-Dimensional Printing; Magnetic Resonance Imaging.

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Description

A 72-year-old male patient with a previous history of myocardial infarction presented to the cardiology department with progressive dyspnea and fatigue on exertion for the past year. He reported worsening over the last two months, affecting his usual activities, along with orthopnea, blurred vision, dizziness, and a sensation of imminent fainting upon standing. Physical examination revealed postural hypotension, lower limb edema (++/4), as well as distal hypoesthesia and hypopallesthesia. Cardiac auscultation revealed a holosystolic murmur at the tricuspid focus, with P2 hyperphonesis. Laboratory tests showed proteinuria (+++/4) in routine urine analysis, along with elevated cardiac markers NT-ProBNP and Troponin I, with no further abnormalities. An electrocardiogram indicated left ventricular hypertrophy and left anterior fascicular block. The evaluation was followed by an echocardiogram, which showed thickening of the right ventricle, interventricular septum, and valves. The Global Longitudinal Strain (GLS) displayed an apical sparing pattern. The ratio between the left ventricular ejection fraction (LVEF) and the GLS was elevated, suggesting cardiac amyloidosis. New suggestive findings were observed in Magnetic Resonance Imaging (MRI), which showed diffuse subendocardial late enhancement and confirmed the thickening of the chambers (Figure 1).

With the suspicion established, the investigation proceeded with the assays of free ALs of immunoglobulins. The results were as follows: free light kappa chain 18.1 mg/dL (6.7–22.4), lambda chain 168.4 mg/dL (8.3–27), with a ratio of Kappa to Lambda chains (K/L) of 0,11 (0.31-1.56). The finding of K/L ratio below the reference value is highly suggestive of AL Amyloidosis, due to the deposition of lambda ALs. Bone marrow and skin/subcutaneous biopsies did not show any infiltrations. An endomyocardial biopsy was performed (Figure 2), stained with Congo Red, which exhibited characteristic birefringence of amyloid infiltration under polarized light (Figure 3). Mass spectrometry confirmed the AL typing. The patient had clinical improvement after AL Amyloidosis-specific treatment.

Discussion

AL Amyloidosis

AL Amyloidosis, also known as primary amyloidosis, is the most common form of the disease among systemic variants. It

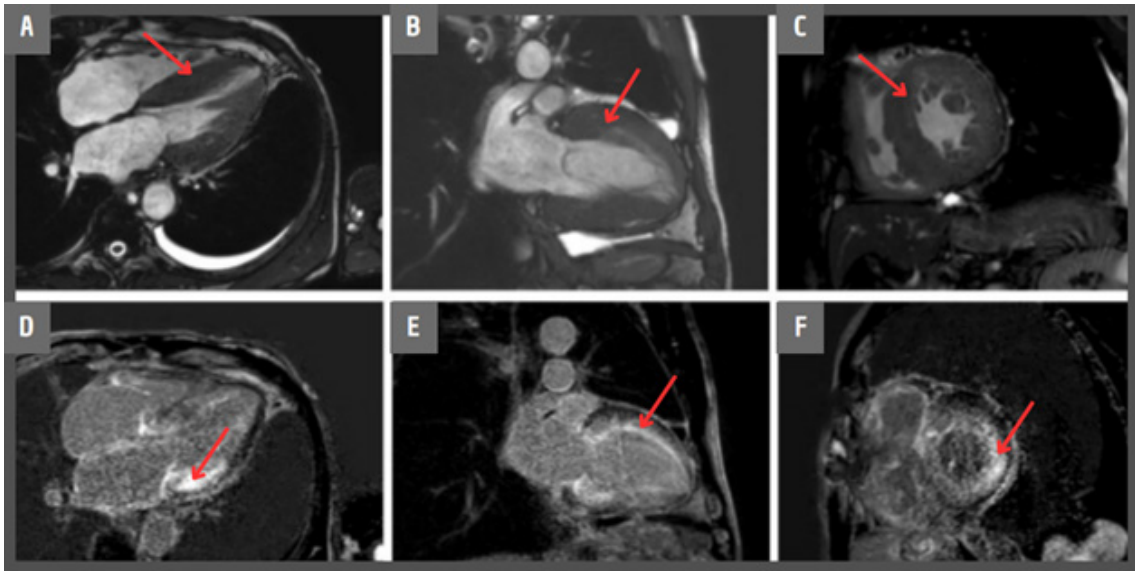

Figure 1 – *MRI showing thickening of the ventricular walls (panels A, B, and C) and diffuse late enhancement patterns in gadolinium contrast (shown in panels D, E, and F). This pattern arises from a difference in contrast uptake throughout cardiac tissue and may be found in various myocardial injuries.*

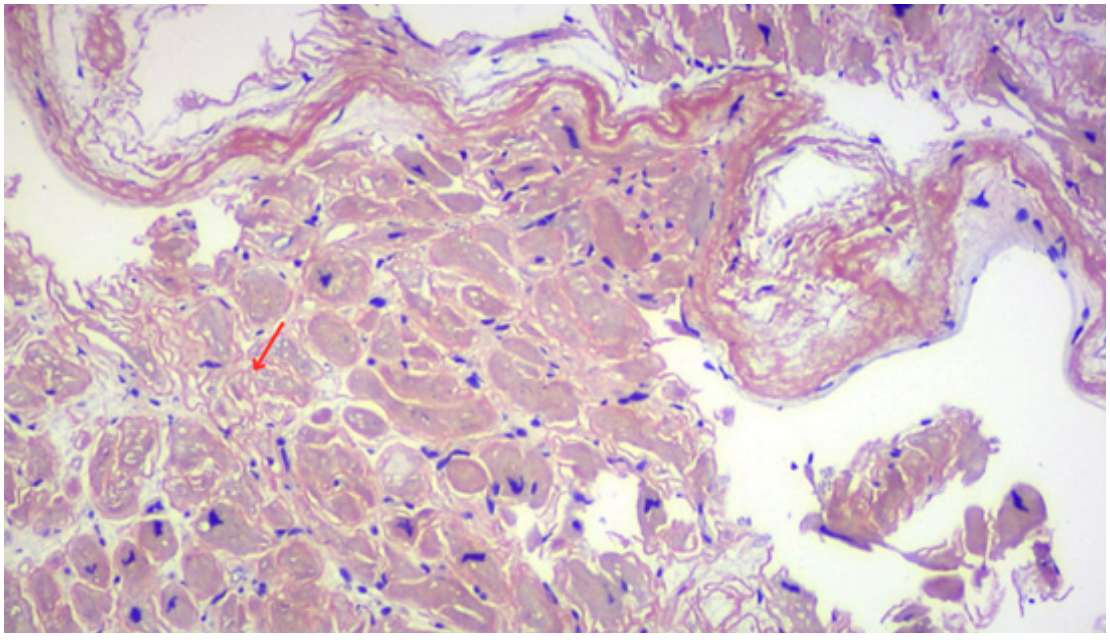

Figure 2 – *Endomyocardial biopsy of the left ventricle, stained with Congo Red, showing subtle red coloring of the amyloid protein deposits. Evaluation under polarized light can be utilized to increase sensitivity.*

arises from the tissue deposition of AL immunoglobulins in cardiac tissue, produced excessively by normal or malignant plasma cells. It is a rare condition, with 5.1 to 12.8 cases per million person-years worldwide. The vast majority of affected patients are over 40 years old, with a median age at diagnosis of 64 years. The progression of the disease is rapid and poses significant risks when not identified early.[2] The deposition of amyloid protein is characterized by significant thickening of the ventricular walls,

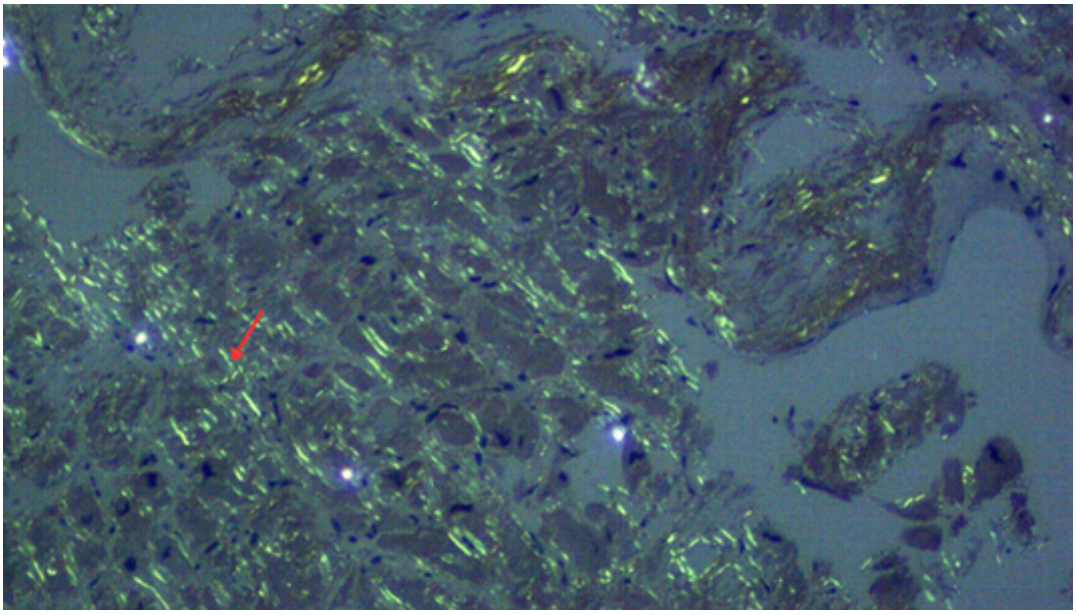

Figure 3 – *Endomyocardial biopsy of the left ventricle, stained with Congo Red, exhibiting a birefringence pattern under polarized light. The apple green birefringence is characteristically found in amyloid protein deposits, as the staining reacts with the misfolded proteins to form complexes that present optical reactivity. The polarized light evaluation enhances the sensitivity of the staining technique.*

septa, and valves, resulting in HF of a restrictive nature. Currently, cardiac amyloidosis accounts for about 13% of cases of HFpEF.[4] Diagnosis begins with the investigation of clinical findings consistent with HFpEF Symptoms may be more associated with left-sided HF (pulmonary congestion, dyspnea) or right-sided HF (edema, ascites). Other important alterations arise from amyloid infiltration in the atria, causing atrial fibrillation and other arrhythmias, and the cardiac conduction system, producing atrioventricular blocks.[5] Elevated serum levels of cardiovascular markers (especially troponin T and NT-ProBNP) should be present. The electrocardiogram of these patients typically shows low QRS voltage, inconsistent with the thickness of the ventricular wall, especially in AL Amyloidosis.

The investigation should continue with echocardiography and MRI, revealing more specific findings of the disease. The reduction in longitudinal strain with an "apical sparing" pattern is an important modification seen on echocardiography, along with thickening of the ventricles and valves. MRI may reveal a pattern of diffuse delayed enhancement using gadolinium-based contrast, with subendocardial or transmural distribution, consistent with the presence of amyloid deposits. Finally, the investigation of immunoglobulin ALs, combined with peripheral biopsy (or, if necessary, cardiac biopsy), will be conclusive for diagnosis. The assessment of ALs is best performed with the combination of three tests: immunofixation in blood and urine, which aids in their detection, and the measurement of the ratio between kappa and lambda chains, which yields a positive result when abnormal.[5]

The most important factor in determining prognosis is the extent of damage to the cardiac tissue. Understanding the physiopathology of amyloidosis and discussing its clinical and morphological manifestations are crucial for the early diagnosis of this increasingly understood yet still underrecognized condition in medical practice.

The 3D model

The three-dimensional model (Figure 4) was produced from the patient's imaging examinations (MRI). The processing of the files includes the steps of segmentation—isolating the desired anatomical structures—and slicing, which involves dividing the structure into printable layers. From these interventions, the final file (in STL format, Standard Tessellation Language) can be read by the machine as a sequence of two-dimensional planes, which are then built on top of each other by the printer (additive manufacturing). The material used in this process was plastic filament, a solid component that is melted by the machine and reshaped into the contours of the desired piece. This type of printer operates using the FDM (Fused Deposition Modeling) technique, which is the most accessible among the options for three-dimensional modeling. Filament modeling was chosen for this project to demonstrate the applicability of the technique even with the simplest forms of this technology.

The model displays the characteristic morphological changes of amyloidosis in cardiac tissue, reinforcing its similarity to the physiology of HF. Notably, there is left ventricular thickening, with a significant reduction in the ventricular lumen, as well as considerable thickening of the interventricular septum. To a lesser extent, the same modification is observed in the right ventricular wall. This type

Figure 4 – *Three-dimensional heart model with AL amyloidosis, produced using imaging data from MRI.*

of material, which has significant anatomical and pathological correspondence with the actual organ, can be applied in various contexts in medical practice. Its use for educational purposes, patient and family instruction, and especially guiding surgical approaches benefits from a more complete and consistent understanding of the studied organ structures. Furthermore, the dissemination and popularization of 3D printers have facilitated the development of more realistic and reproducible models without imposing significant financial costs.[6] Three-dimensional models can improve professional and patient education through the visual and tactile experience they allow.[7] In this regard, we emphasize the great potential for exploring this tool in the healthcare field, complementing imaging studies and possibly revealing new important information that enhances our understanding of diseases.

Author Contributions

Conception and design of the research: Cruz MP, Yahiro DS, Simões MV, Mesquita CT. Acquisition of data: Cruz MP, Yahiro DS, Neves DG, Barbosa RP, Fabro AT, Garibaldi PMM. Analysis and interpretation of the data: Cruz MP, Yahiro DS. Writing of the manuscript: Cruz MP, Yahiro DS. Critical revision of the manuscript for intellectual content: Cruz MP, Yahiro DS, Simões MV, Mesquita CT.

Potential Conflict of Interest

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

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Faculty of Medicine of UFF under protocol number 6.594.419/CAAE:70417223.1.0000.5243. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

All datasets supporting the results of this study are available upon request from the corresponding author: Mariana de Paula Cruz.

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