Acute Mitral Regurgitation Due to Chordae Tendineae Rupture: A Rare Presentation of Cardiac Amyloidosis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Regina Aguilar-López**
ABCDEF 2 **Cristopher Cándido Sánchez-Rodríguez**
ABCDEF 2 **Daniel Manzur-Sandoval**
ABCDEF 1 **María Flores Calvo**
ABCDEF 3 **Alberto Aranda-Fraustro**
ABCDEF 4 **Antonio Jordán-Ríos**
ABCDEF 3 **Alejandro Francisco-Cruz**
ABCDEF 2 **Gustavo Rojas-Velasco**

1 Medical Student, La Salle University, Mexico City, Mexico
2 Cardiovascular Critical Care Unit, National Institute of Cardiology Ignacio Chavez, Mexico City, Mexico
3 Department of Pathology, National Institute of Cardiology Ignacio Chavez, Mexico City, Mexico
4 Department of Echocardiography, National Institute of Cardiology Ignacio Chavez, Mexico City, Mexico

Corresponding Author: Gustavo Rojas-Velasco, e-mail: gustavorojas08@gmail.com
Financial support: None declared
Conflict of interest: None declared

Patient: **Male, 22-year-old**
Final Diagnosis: **Cardiac amyloidosis**
Symptoms: **Functional class deterioration (I-IV) • ascending pelvic extremity edema • chest pain**
Medication: **—**
Clinical Procedure: **—**
Specialty: **Cardiology**

Objective: **Unusual clinical course**
Background: In cardiac amyloidosis (CA), misfolded proteins deposit in the extracellular space of cardiac tissue. These deposits classically cause restrictive cardiomyopathy with diastolic dysfunction. Although there are at least 30 proteins known to cause amyloid aggregates, 2 main types make up most diagnosed cases: light chain amyloidosis (AL) and transthyretin amyloidosis (ATTR). Since CA is considered a rare condition, it is often underdiagnosed or recognized in the advanced stages. Once amyloid deposits involve the heart tissue, they are associated with a worse outcome and higher mortality rates, especially in patients presenting symptoms of heart failure.
Case Report: We report a case of a 22-year-old man presenting with acute severe mitral regurgitation, secondary to posterior mitral leaflet chordae tendineae rupture (CTR). Surgical mitral valve replacement with a mechanical prosthesis was performed, and cardiac tissue biopsy samples were obtained. After surgery, the patient improved significantly but suddenly presented with hemodynamic deterioration, until he died due to severe hemodynamic compromise and multiorgan failure. Although the etiology of the CTR was not established before surgical intervention, the histopathological analysis suggested CA.
Conclusions: CA diagnosis can be complex, especially in a 22-year-old-man with atypical clinical and imaging manifestations. In this patient, other differential diagnoses were considered, since CA presenting in a young patient is a rare phenomenon and acute mitral regurgitation secondary to CTR presents more frequently in other heart conditions. Furthermore, rapid postoperative deterioration resulted in the patient's death before biopsy samples were available because suspicion of amyloidosis had not been raised until that point.

Keywords: **Amyloidosis • Heart Failure • Mitral Valve Insufficiency**

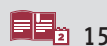Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/936545
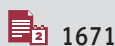
📄 1671   🗂 —   📊 6   📖 15

Background

Cardiac amyloidosis (CA) is a disorder in which misfolded proteins deposit in the extracellular space of cardiac tissue. Classification is based on the amyloid precursor that accumulates in the interstitium of the heart. Although there are at least 30 proteins known to cause the amyloid aggregates, only 9 can affect the heart, and 2 main types make up more than 98% of diagnosed cases: light chain amyloidosis (AL) and transthyretin amyloidosis (ATTR) [1]. Since CA is considered a rare condition, it is often underdiagnosed or recognized at advanced stages of the disease. The presence of amyloid deposits in the heart tissue is associated with a worse outcome and higher mortality rates, especially in those patients presenting with symptoms of heart failure [2,3].

Amyloid deposits in the myocardial interstitium can cause myocyte dysfunction, necrosis, and electrical disturbances, resulting in classic amyloid restrictive cardiomyopathy [2]. This type of cardiomyopathy usually presents with normal or increased ventricular wall thickness, bi-atrial enlargement, preserved systolic function, severe diastolic dysfunction, and restrictive filling patterns with increased filling pressures [3]. When proteins accumulate in the heart valves, they can cause thickening but no significant dysfunction. In addition, involvement of the coronary vessels can lead to cardiac ischemia, and pericardium implication can result in pericardial effusion [2].

CA diagnosis can be complex since suspicion of CA is based on a variety of clinical and imaging warning signs. For all types of CA cardiac or extracardiac-site positive tissue, a biopsy is needed to confirm the diagnosis. In the case of ATTR amyloidosis, additional noninvasive techniques can be used, including negative serum and urine protein electrophoresis with immunofixation and nuclear scintigraphy [1]. Lack of early diagnosis is related to disease intrinsic factors such as heterogeneity of presentation, and extrinsic factors include lack of suspicion, confusion in the type of amyloidosis, and absence of acknowledgment regarding diagnostic strategies [3].

We report a case of a young man who presented to the emergency department (ED) with acute severe mitral regurgitation as an atypical presentation of CA.

Case Report

A 22-year-old man presented to the ED with a history of functional class deterioration (I-IV), ascending pelvic extremity edema, and chest pain. Vital signs revealed normal body temperature, oxygen saturation of 88%, blood pressure of 114/72 mmHg, heart rate of 100 beats per min, and respiratory rate of 24 breaths per min. Physical examination showed preserved mental status, dyspnea, jugular venous distention, peripheral edema, generalized rales, a regurgitant mitral systolic murmur, and S3 heart sound. Acute mitral regurgitation was diagnosed, and during the patient's evolution at the ED, he developed cardiogenic shock (SCAI-B), requiring inotropes, vasopressors, intubation, and management with an intra-aortic balloon pump.

Two years before his admission, the patient received medical attention for paroxysmal palpitations. He underwent an electrocardiogram that was consistent with the diagnosis of atrioventricular reciprocating tachycardia caused by a Wolff-Parkinson-White syndrome; no ablation treatment was carried out. At the same time, a transthoracic echocardiogram was done, suggesting a left ventricular (LV) noncompaction cardiomyopathy with left ventricular ejection fraction (LVEF)
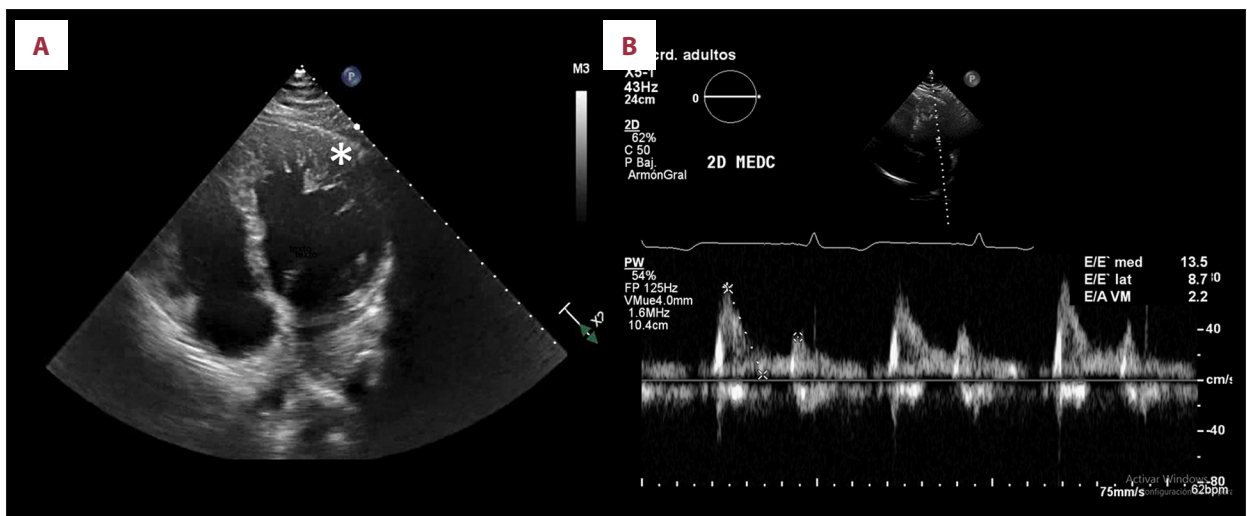
Figure 1. **Transthoracic echocardiogram 2 years prior to admission.** (**A**) Four-chamber view showing left ventricular apical segments with hyper-trabeculation (white asterisk). (**B**) Trans-mitral flow velocity revealed a restrictive pattern (E/A >2).
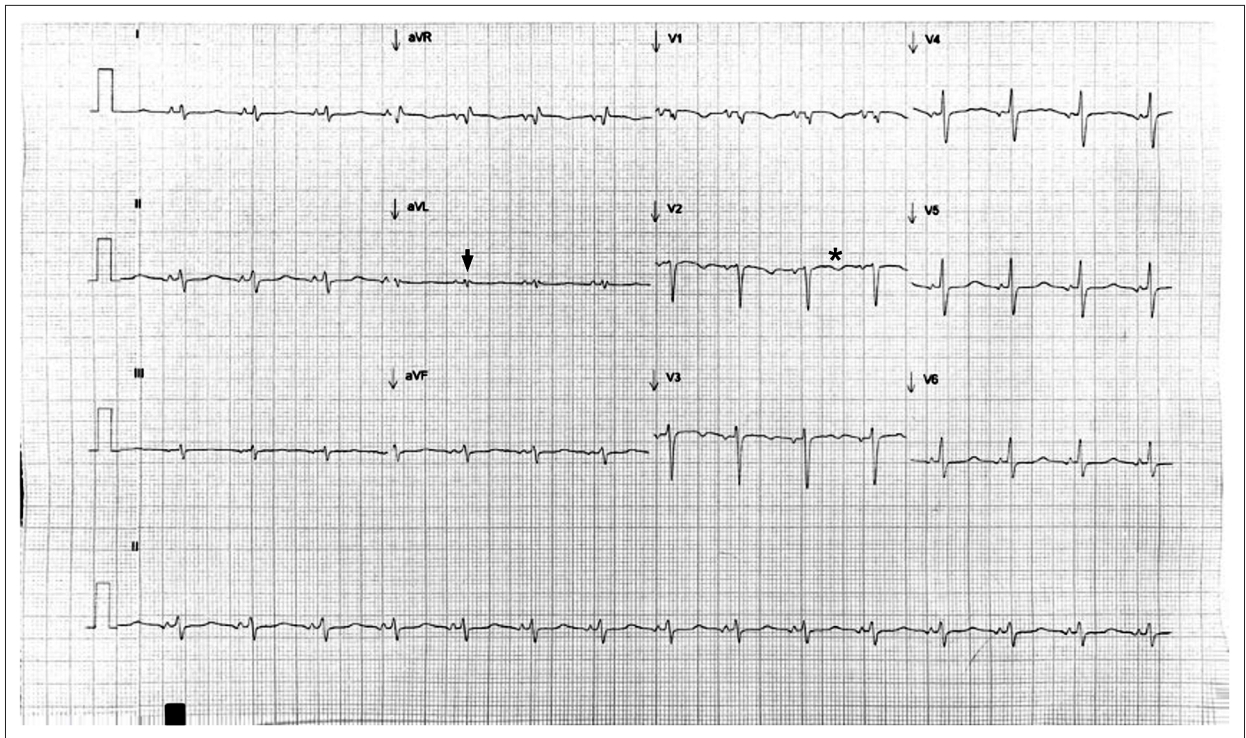
Figure 2. Electrocardiogram upon patient's admission. Electrocardiogram exhibiting sinus rhythm with low voltage QRS complexes in limb leads (black arrowhead), shortened PR interval (80 ms), and negative T waves in precordial leads (black asterisk).

of 44% (**Figure 1**), interventricular septal thickness in diastole of 1.03 cm, LV posterior wall thickness in diastole of 1.01 cm, no valve thickening, and no pericardial effusion.

Cardiac magnetic resonance was not performed, and the patient continued in functional class I for 2 years.

At admission, laboratory findings showed the N-terminal pro-B-type natriuretic peptide level was elevated (12 231 pg/mL) with increased liver enzyme concentrations: alanine aminotransferase 722 U/L, aspartate aminotransferase 310 U/L, and total bilirubin 4.82 mg/dL. Moreover, renal function parameters were also high: creatinine 1.96 mg/dL and blood urea nitrogen 90.3 mg/dL. Hematological results showed mild thrombocytopenia: 125 000 platelets per µL, international normalized ratio of 1.95, prothrombin time of 21 s, and partial thromboplastin time of 41 s. The electrocardiogram exhibited low voltage QRS complexes in limb leads (**Figure 2**). Transthoracic echocardiogram revealed severe hypokinesis, LVEF of 28%, interventricular septal thickness in diastole of 1.2 cm, LV posterior wall thickness in diastole of 1.2 cm, 4-chamber dilation, moderate pericardial effusion, with maximal separation of 24 mm at the posterior wall, and severe mitral valve regurgitation due to chordae tendineae rupture (CTR) of the posterior mitral leaflet (**Figure 3**).

Surgical mitral valve replacement with a mechanical prosthesis was performed and cardiac tissue biopsy samples were obtained. Upon decannulation, the patient presented a sustained monomorphic ventricular tachycardia, which was resolved with medical treatment. Once in the Critical Care Unit, the patient required inotropic and vasopressor support. Transthoracic echocardiogram showed an LVEF of 10%. Since clinical improvement was observed after 48 h, with a decrease in lactate serum levels and an increase in LVEF of 25%, inotropic and vasopressor support was withdrawn. Suddenly, acute hemodynamic deterioration was observed, and vasopressors were restarted. Two events of pulseless electrical activity occurred, requiring advanced cardiopulmonary resuscitation and support with veno-arterial extracorporeal membrane oxygenation. Transthoracic echocardiogram revealed severe myocardial systolic dysfunction. Finally, the patient died due to severe hemodynamic compromise and multiorgan failure caused by a low perfusion status and cardiogenic shock. One week later, the biopsy results were available and the diagnosis of CA was established.

Biopsy samples were obtained from myocardial and mitral valve tissue. Myocardiocyte disarray, coagulative myocytolysis with contraction bands necrosis, and fibrosis were observed, supporting the diagnosis of chronic cardiac ischemia (**Figure 4**). In addition, amorphous aggregates were noted in the subepicardial stroma, resembling amyloid deposits. Congo red staining showed anomalous color in polarized light, suggesting the
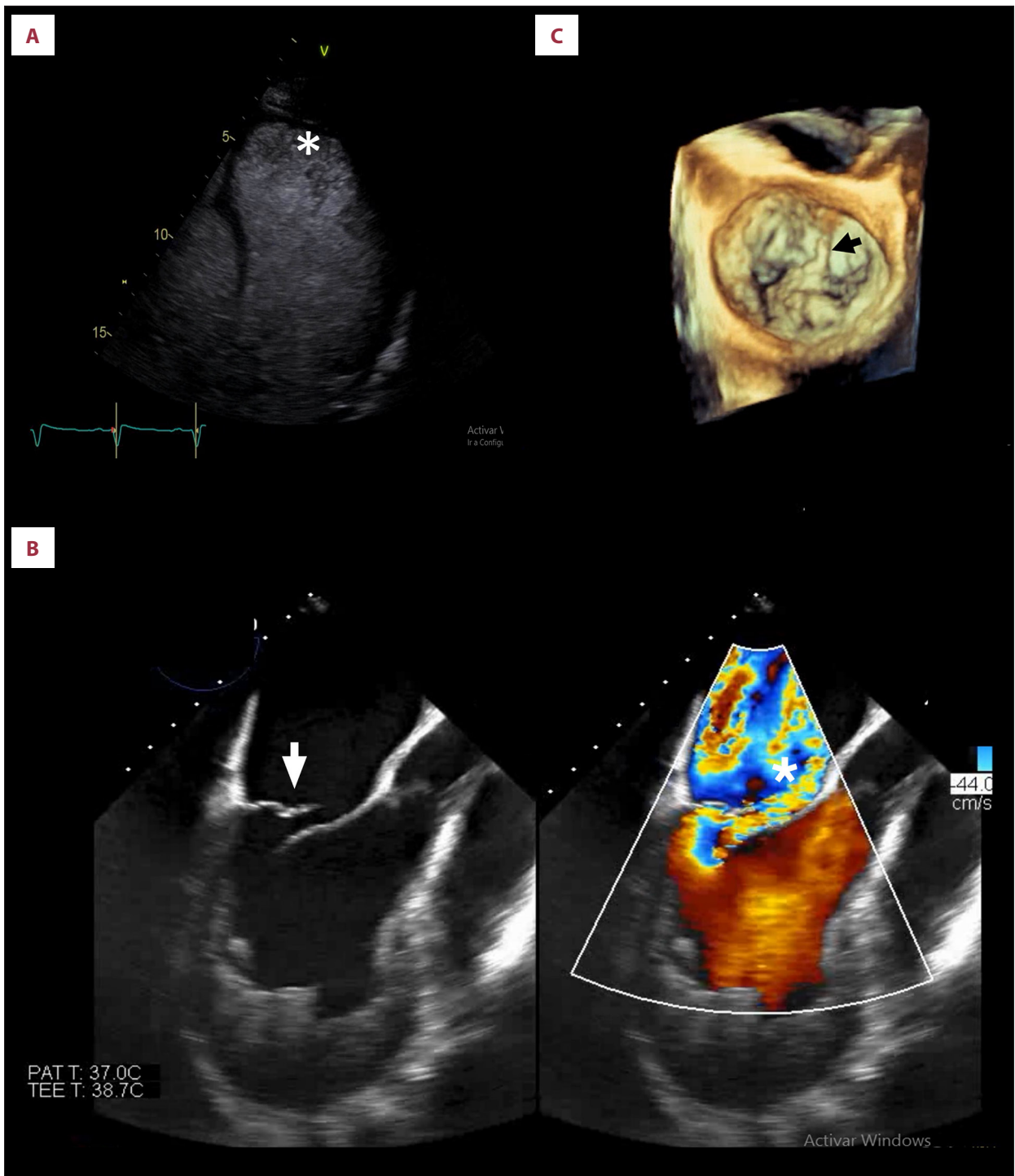
Figure 3. Echocardiographic findings upon patient's admission. (A) Contrast echocardiography in a 4-chamber view showing apical left ventricular hyper-trabeculation (white asterisk). **(B)** Transesophageal echocardiography 3-chamber view demonstrating P2 mitral valve leaflet flail (white arrowhead) causing significant regurgitation (white asterisk). **(C)** 3D mitral valve reconstruction showing P2 segment flail (black arrowhead).
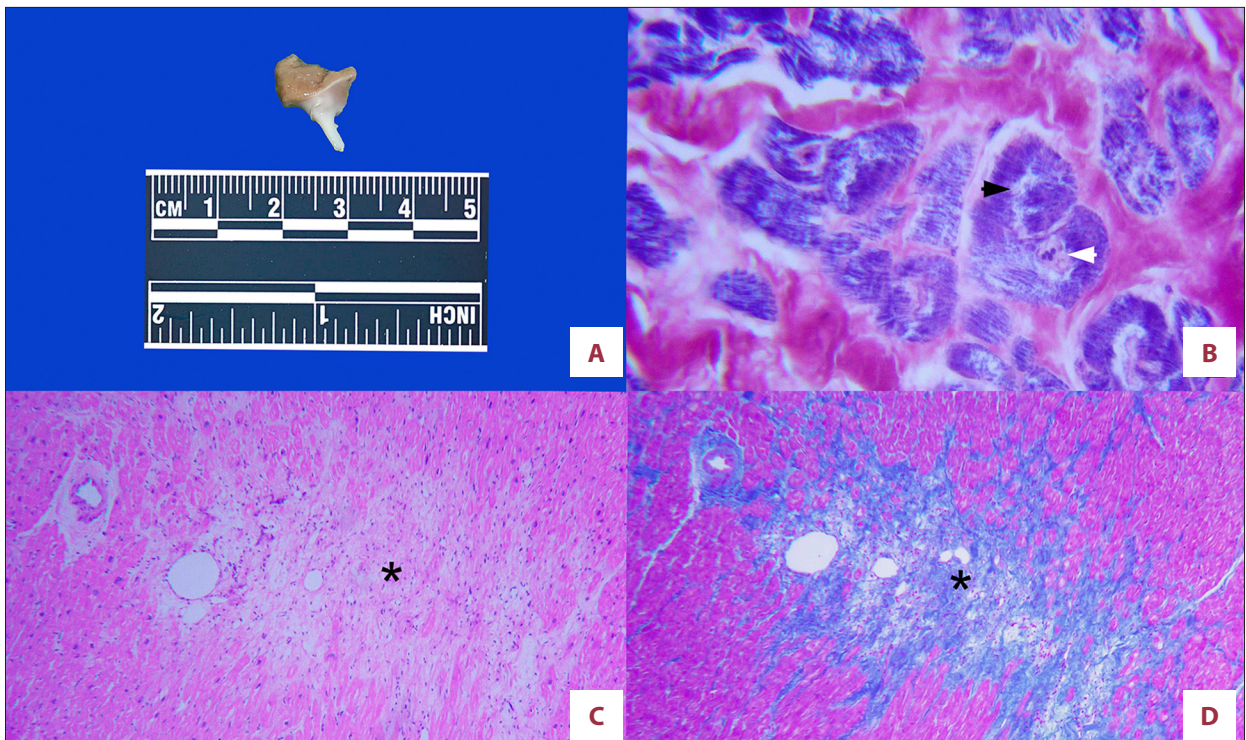
Figure 4. **Cardiac tissue biopsy with chronic ischemic cardiomyopathy changes.** (**A**) Gross pathology of the heart biopsy specimen. (**B**) Coagulative myocytolysis with contraction bands (black arrowhead) and pyknotic nuclei (white arrowhead) (phosphotungstic acid-hematoxylin; ×250). (**C**) Chronic ischemic cardiomyopathy with myocardiocytes disarray, fibrosis (black asterisk) (hematoxylin and eosin ×100) and (**D**) collagen deposits revealed with Masson's trichrome (black asterisk).
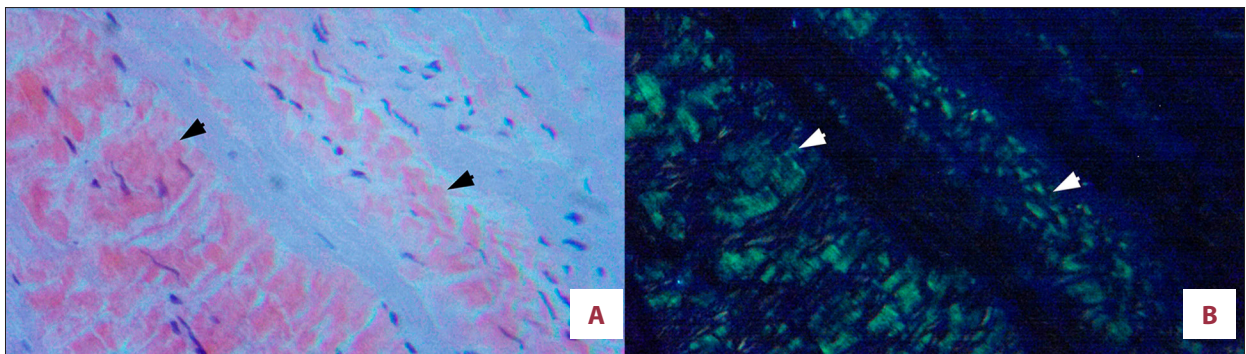

Figure 5. **Congo red staining and polarized light positivity suggested cardiac amyloidosis.** (**A**) Heart biopsy slide stained with Congo red showing amorphous cytoplasmic aggregates (black arrowheads) and (**B**) anomalous green color revealed using polarized light (white arrowhead) (×100).

diagnosis of CA (**Figure 5**). Reparative tissue and a unique staining pattern were revealed in the subendocardial stroma of the chordae tendineae using Congo red and crystal violet staining (**Figure 6A-6C**). Extensive, diffuse, and granular calcium deposits in the cytoplasm of endothelial and stromal cells from the subendocardial and spongiosa stroma of the mitral valve were observed (**Figure 6D**).

Discussion

This case exhibits a rare presentation of CA related to cardiogenic shock and multiorgan failure caused by mitral valve CTR. Although CA classically appears as a restrictive cardiomyopathy with diastolic dysfunction, less frequently it can present with severe systolic dysfunction, as in this case [2].

In this patient, CA was confirmed by heart biopsy, which has a sensitivity of 100% for the detection of any type of CA [3].
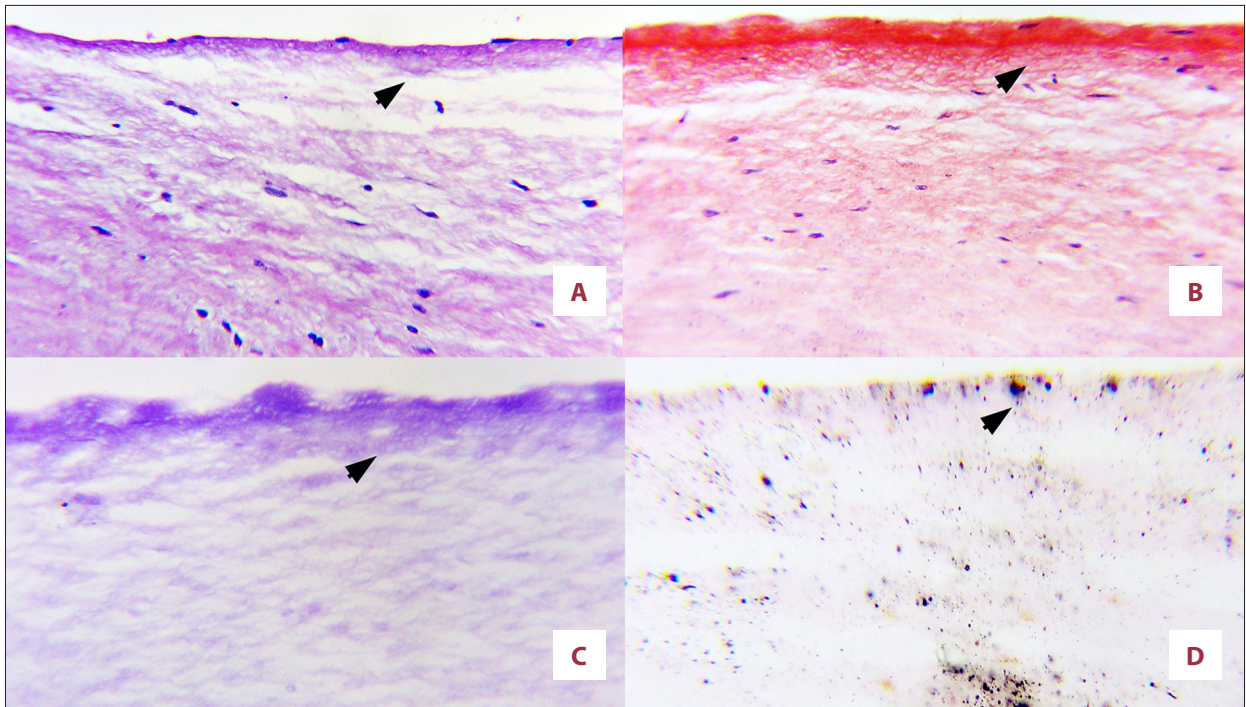
Figure 6. **Native mitral valve showing Congo red positive deposits.** (**A**) Subendocardial and spongiosa stroma with mild thickening (black arrowhead) (hematoxylin and eosin ×250). (**B, C**) Laminar and linear positive staining pattern in the subendothelial stroma (black arrowheads) (Congo red and crystal violet, ×100 and ×250). (**D**) Granular calcium pattern in the cytoplasm of endothelial and stromal cells (black arrowhead) (Von Kossa; ×100 and ×250).

Attention was drawn to the results, suggesting chronic cardiac ischemia. It has been reported that amyloid deposits can infiltrate the heart microvasculature causing alterations in coronary flux reserve, leading to angina syndrome or myocardial infarction [4]. In addition, CA can infiltrate heart valves and reduce their elasticity, causing higher fragility and weakness [5,6]. In our patient, it is possible that the CTR was the result of the loss of elasticity and chronic cardiac ischemia due to CA. However, this mechanical complication has not been properly established, with only a few cases reported in the literature [5,7,8].

Most of the echocardiographic images of this patient showed no typical qualitative findings of CA. However, diastolic dysfunction is a central aspect of CA, and this case was no exception, since grade III diastolic dysfunction was found with increased LV filling pressures and restrictive trans-mitral flow velocity (E/A 2.9, E wave 1.18 m/s, A 0.40 m/s, acceleration 111 ms), and the estimation of spectral Doppler velocities showed E/e' 29.5 relation. In addition, there was bi-atrial enlargement (left atrial volume index: 74 ml/m2 and right volume index: 50 ml/m^2), which aided the diagnosis [9-11]. Unfortunately, the acoustic window for this patient did not allow the determination of the global longitudinal strain where the "apical sparing" phenomenon is characteristic of CA.

From the echocardiographic point of view, the noncompacted layer to the compacted layer ratio, in this case, was <2, which makes it less likely to be an LV noncompaction cardiomyopathy myocardium. According to the criteria of Jenni et al, the presence of 2 layers of myocardium must be observed (a light compact layer and a thick noncompact layer) whose ratio, as previously mentioned, should be more than 2, preferentially located in the inferior and lateral walls; this patient did not meet either of these criteria. Moreover, the color Doppler images were not as expected either since there was no color perfusion of the trabecular recesses [12]. The restrictive physiology, its complications, and positive biopsy results tipped the balance to an infiltrative process such as amyloidosis, over NCCM; however, we acknowledge that it could have been an overlap of these both.

AL is caused by the deposit of misfolded immunoglobulin chains and has the worst prognosis, since it can affect any organ [13]. This type of amyloidosis was considered, as our patient had suggestive images and laboratory findings of multiorgan involvement; however, the cardiogenic shock could also explain these observations. In addition, AL prevalence increases with age, with a mean age of diagnosis of 63 years [14]. Therefore, this disease in a 22-year-old patient is an uncommon phenomenon. Monoclonal gammopathy tests were not performed on this patient.

In contrast, ATTRv affects the nervous and cardiac systems predominantly [13]. Even though amyloid deposits can appear earlier in life compared to AL, our patient had a premature disease presentation and no previous history of neuropathy [13,15]. Furthermore, ATTRv has an autosomal dominant pattern inheritance; however, our patient had no documented family history of amyloidosis or any type of cardiomyopathies. Gene testing was not performed on this patient [15].

In either type of amyloidosis, when misfolded proteins deposit in the heart, patients have a poor prognosis in a short time [3]. This could explain why treatment strategies did not improve our patient's clinical condition, which resulted in rapid deterioration and death, preventing the clinical suspicion of his definitive diagnosis.

Conclusions

This case illustrates the variety of manifestations CA can show. Although the consequences of amyloid deposition in cardiac tissue are well described, the diagnosis, in this case, was challenging, since CA presenting as acute mitral regurgitation due to CTR in a young patient is a rare phenomenon.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Garcia-Pavia P, Rapezzi C, Adler Y, et al. Diagnosis and treatment of cardiac amyloidosis: A position statement of the ESC Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2021;42(16):1554-68

2. Bozkurt B, Colvin M, Cook J, et al. Current diagnostic and treatment strategies for specific dilated cardiomyopathies: A scientific statement from the American Heart Association. Circulation. 2016;134(23):e579-646

3. Pereira NL, Grogan M, Dec GW. Spectrum of restrictive and infiltrative cardiomyopathies: Part 1 of a 2-part series. J Am Coll Cardiol. 2018;71(10):1130-48

4. Siddiqi, Omar K. Ruberg FL. Cardiac amyloidosis: An update on pathophysiology, diagnosis, and treatment. Trends Cardiovasc Med. 2018;28(1):10-21

5. Nishi H, Mitsuno M, Ryomoto M, Miyamoto Y. Severe mitral regurgitation due to cardiac amyloidosis – a rare reason for ruptured chordae. Interact Cardiovasc Thorac Surg. 2008;7(6):1199-200

6. Masugata H, Mizushige K, Senda S, et al. Physical properties of the mitral valve tissue assessed by tissue sound speed in cardiac amyloidosis: Relationship to the severity of mitral regurgitation. Ultrasound Med Biol. 2000;26(7):1191-98

7. Aktas Yilmaz B, Düzgün N, Mete T, et al. AA amyloidosis associated with systemic lupus erythematosus: Impact on clinical course and outcome. Rheumatol Int. 2008;28(4):367-70

8. Taiwo AA, Alapati L, Movahed A. Cardiac amyloidosis: A case report and review of literature. World J Clin Cases. 2019;7(6):742-52

9. Pagourelias ED, Mirea O, Duchenne J, et al. Echo parameters for differential diagnosis in cardiac amyloidosis: A head-to-head comparison of deformation and nondeformation parameters. Circ Cardiovasc Imaging. 2017;10(3):e005588

10. Agha AM, Parwani P, Guha A, et al. Role of cardiovascular imaging for the diagnosis and prognosis of cardiac amyloidosis. Open Hear. 2018;5(2):e000881

11. Kiotsekoglou A, Saha SK, Nanda NC, Lindqvist P. Echocardiographic diagnosis of cardiac amyloidosis: Does the masquerader require only a "cherry on top"? Echocardiography. 2020;37(11):1713-15

12. Jenni R, Oechslin E, Schneider J, et al. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: A step towards classification as a distinct cardiomyopathy. Heart. 2001;86(6):666-71

13. Adam RD, Coriu D, Jercan A, et al. Progress and challenges in the treatment of cardiac amyloidosis: A review of the literature. ESC Hear Fail. 2021;8(4):2380-96

14. Merlini G, Dispenzieri A, Sanchorawala V, et al. Systemic immunoglobulin light chain amyloidosis. Nat Rev Dis Prim. 2018;4(1):38

15. Adams D, Koike H, Slama M, Coelho T. Hereditary transthyretin amyloidosis: A model of medical progress for a fatal disease. Nat Rev Neurol. 2019;15(7):387-404