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Light Chain Cardiac Amyloidosis Presenting with Reversible Mitral and Tricuspid Regurgitation: A Case Report

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Case Report

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Abstract

Background: Light chain cardiac amyloidosis (AL-CA) is a progressive heart disease caused by the deposition of misfolded monoclonal immunoglobulin light chains. It presents as restrictive cardiomyopathy, heart failure with preserved ejection fraction, arrhythmia, atrioventricular block, proteinuria, etc. Cases with cardiac valve insufficiency as the initial main manifestation are relatively rare, and reports of reversible severe mitral and tricuspid regurgitation as the initial presentation are even scarcer. This case is worthy of reporting to enrich the clinical understanding of atypical manifestations of the disease and provide reference for early diagnosis and treatment.

Case presentation: A 61-year-old male was admitted to our hospital in April 2022 with acute heart failure, atrial fibrillation, severe dyspnea and chest discomfort. Physical examination detected a grade 3/6 systolic murmur at the mitral area. Transthoracic echocardiography showed moderate-to-severe mitral regurgitation and moderate tricuspid regurgitation, which improved to moderate mitral and mild tricuspid regurgitation 5 days after admission, and further to mild regurgitation of both valves one month later.

Conclusions: Light chain cardiac amyloidosis can present with reversible severe mitral and tricuspid regurgitation as the initial clinical manifestation, which is easy to be misdiagnosed as primary valvular heart disease. Clinicians should improve their awareness of such atypical cases. Early diagnosis and standardized treatment may help reverse valvular dysfunction and improve the prognosis of patients.

Background

Light chain cardiac amyloidosis (AL-CA) is a rare disorder driven by the abnormal proliferation of monoclonal plasma cells. This proliferation leads to the production of misfolded immunoglobulin light chains, which deposit as amyloid fibrils in the myocardial interstitium, ultimately resulting in reduced myocardial compliance and progressive cardiac dysfunction [1].

In the early stages, the clinical manifestations of AL-CA are nonspecific, often presenting as restrictive cardiomyopathy, arrhythmia, or heart failure. Notably, valvular regurgitation is the initial presenting symptom in fewer than 5% of AL-CA cases [1, 2]. Because of its clinical resemblance to common valvular diseases (e.g., rheumatic heart disease) and dilated cardiomyopathy, AL-CA is frequently misdiagnosed or overlooked in clinical practice.

Previous studies indicate that cardiac amyloidosis is incidentally diagnosed in only 0.2% of patients undergoing mitral valve surgery [3]. Moreover, valvular regurgitation associated with AL-CA is typically persistent and ranges from mild to moderate severity, with its dynamic changes rarely reported in clinical studies. The dynamic evolution of valvular regurgitation in AL-CA patients remains poorly understood, and there is a lack of clear consensus on whether and how such regurgitation can be reversed with clinical intervention. Furthermore, cases of reversible severe valvular regurgitation in AL-CA are extremely rare [2]. Given the rarity of such atypical presentations, the unclear dynamic changes of valvular regurgitation, and the high rate of misdiagnosis, enhancing clinical awareness of the diverse

manifestations of AL-CA is crucial for improving early detection, optimizing treatment strategies, and ultimately improving patient prognosis.

Case Presentation

A 61-year-old male was admitted to our hospital in April 2022 with acute heart failure and atrial fibrillation. His main symptoms included severe dyspnea and chest discomfort. Physical examination revealed a grade 3/6 systolic murmur at the mitral area. Transthoracic echocardiography demonstrated moderate-to-severe mitral regurgitation and moderate tricuspid regurgitation. Five days after admission, a follow-up echocardiogram showed improvement in valvular regurgitation, with moderate mitral regurgitation and mild tricuspid regurgitation. One month later, a third echocardiogram revealed only mild mitral and tricuspid regurgitation (Table 1. Dynamic Changes of Mitral and Tricuspid Regurgitation).

Table 1
Dynamic Changes of Mitral and Tricuspid Regurgitation

Date	Clinical Notes	Mitral Regurgitation (MR)	Tricuspid Regurgitation (TR)
April 18, 2022	Onset of symptoms	Severe (MR++++)	Moderate (TR+++)
April 23, 2022	Follow-up examination	Moderate (MR+++)	Mild (TR++)
May 20, 2022	Follow-up examination	Mild (MR++)	Mild (TR++)
Note: MR = mitral regurgitation; TR = tricuspid regurgitation. The severity of regurgitation is graded as follows: ++ = mild, +++ = moderate, ++++ = severe.			
The patient presented with severe mitral regurgitation and moderate tricuspid regurgitation at disease onset on April 18, 2022. Five days later, mitral regurgitation improved to moderate and tricuspid regurgitation to mild. One month after onset, both mitral and tricuspid regurgitation were mild.			

Comparison of the patient's electrocardiograms (ECGs) from two years prior to admission with those obtained during the current hospitalization revealed low voltage in the limb leads (Fig. 1). Echocardiographic findings showed significant thickening of the interventricular septum. Given the suspicion of cardiac amyloidosis, a technetium-99m pyrophosphate (^{99m}Tc-PYP) single-photon emission computed tomography (SPECT) scan was performed, which suggested cardiac amyloidosis. At this stage, the condition was tentatively classified as transthyretin amyloid cardiomyopathy (ATTR-CA). Subsequent laboratory tests, including serum and urine free light chain assays, and myocardial biopsy confirmed the diagnosis of light chain cardiac amyloidosis (AL-CA) and multiple myeloma.

Chemotherapy was initiated but later discontinued due to treatment-related adverse effects and patient refusal. The patient then received conservative treatment, including diuretics to reduce cardiac preload and anticoagulants for atrial fibrillation management. In the advanced stage, vericiguat was added to

improve cardiac function. Unfortunately, the patient died of progressive heart failure on September 1, 2024. (see Fig. 2). Figure 2. Clinical process of patient onset and course progression.

Two years before the onset of severe valvular regurgitation, the patient experienced recurrent chest discomfort, and his ECG showed T-wave inversion. Coronary angiography revealed severe right coronary artery stenosis, and a stent was implanted. However, chest discomfort persisted after the procedure, and follow-up ECG and echocardiography showed no significant abnormalities.

Discussion

In the early clinical course, the patient experienced exertional dyspnea and chest discomfort, which were initially attributed to coronary artery disease given the presence of severe coronary stenosis. However, his symptoms persisted despite coronary stent implantation. At that time, no alternative etiology was identified, as ECG and echocardiography revealed no abnormalities. Two years after the onset of exertional chest discomfort, the patient presented with acute left heart failure, atrial fibrillation, moderate-to-severe mitral regurgitation, and moderate tricuspid regurgitation. Notably, the valvular regurgitation improved significantly within a few days and decreased to mild severity one month later. This clinical course differs from the previously reported characteristic of "persistent mild-to-moderate" valvular regurgitation in AL-CA [7], suggesting the potential existence of a "reversible window period" for valvular dysfunction in AL-CA. The possible mechanisms underlying this phenomenon are as follows:

1. Multifocal Cardiac Injury Caused by Myocardial Amyloid Deposition

AL-CA leads to widespread structural alterations in the heart, with amyloid deposits accumulating in both the myocardial interstitium and valvular tissue. This dual deposition induces valvular regurgitation through mechanisms acting at both the "valvular" and "myocardial" levels [1, 2]:

Valvular-level Mechanisms

Amyloid deposits directly infiltrate the mitral and tricuspid valve leaflets and chordae tendineae, disrupting the normal architecture of elastic fibers and collagen. This structural impairment causes leaflet thickening, increased stiffness, reduced mobility, and impaired coaptation. Additionally, annular dilation further impairs leaflet coaptation during valve closure, exacerbating regurgitation [2, 5].

Myocardial-Level Mechanisms

Amyloid deposition in the interstitium of the left and right ventricles increases myocardial stiffness and decreases ventricular compliance. This leads to a reduction in left ventricular end-diastolic volume and an elevation in filling pressure, which in turn passively increases left atrial pressure. In this case, the left atrial diameter increased from 43 mm to 53 mm. Mitral annular dilation (anteroposterior diameter: 3.6 cm) creates a vicious cycle in which elevated left atrial pressure leads to left atrial enlargement, which causes further annular dilation and worsening regurgitation, thereby further elevating. Impaired diastolic function of the right ventricle exerts a similar effect on the right atrium and tricuspid valve. Fangmin et

al. previously reported that functional mitral regurgitation (FMR) caused by cardiac dilation in patients with cardiac amyloidosis can complicate clinical decision-making [4]. This observation aligns with the findings in our case.

2. Synergistic Effect of Atrial Fibrillation

Gertz et al. were the first to identify significant functional mitral regurgitation in patients with isolated atrial fibrillation [6]. A small-scale case study demonstrated that isolated atrial fibrillation can affect both mitral and tricuspid regurgitation but typically does not cause moderate-to-severe regurgitation [7]. However, atrial fibrillation can exert a synergistic effect on preexisting valvular regurgitation. In this case, the patient's paroxysmal atrial fibrillation further exacerbated the dynamic changes in valvular regurgitation. During atrial fibrillation episodes, the loss of atrial contractile function reduced left atrial emptying efficiency and increased left atrial volume load. Additionally, the irregular cardiac rhythm contributed to dynamic mitral annular dilation, leading to fluctuating leaflet coaptation during the cardiac cycle and "transiently worsening" regurgitation [6]. In our patient, the systolic pulmonary artery pressure (SPAP) increased from 44 mmHg to 67 mmHg during atrial fibrillation episodes, supporting the synergistic role of atrial fibrillation in aggravating valvular regurgitation.

3. Reversible Effects of Therapeutic Intervention

Following admission, the patient was treated with high-dose torasemide (a potent loop diuretic) combined with nitroglycerin (a vasodilator). This therapeutic regimen rapidly reduced myocardial volume load, alleviated myocardial edema, lowered atrial pressure, and mitigated annular dilation. These changes improved valve leaflet coaptation and led to a rapid improvement in valvular regurgitation [4]. This clinical response suggests AL-CA-related valvular regurgitation may have a reversible component, and that timely therapeutic intervention can effectively improve valvular dysfunction.

Conclusion

This case demonstrates that reversible severe mitral and tricuspid regurgitation can occur in AL-CA in the absence of primary valvular structural disease. The underlying mechanism is likely related to cardiac structural remodeling induced by myocardial amyloid deposition and the synergistic effect of atrial fibrillation. related to its conclusions are not generalizable and require validation by large cohort studies. However, clinicians should consider the possibility of cardiac amyloidosis in patients presenting with reversible severe valvular regurgitation, particularly when accompanied by suggestive ECG findings (e.g., low voltage in limb leads) and echocardiographic findings (e.g., myocardial thickening). Early diagnosis and timely intervention may improve clinical outcomes in such patients.

Abbreviations

AL-CA, light chain cardiac amyloidosis; ECGs, electrocardiograms; 99mTc-PYP, technetium-99m pyrophosphate; SPECT, single-photon emission computed tomography; ATTR-CA, transthyretin amyloid

cardiomyopathy; SPAP, systolic pulmonary artery pressure; FMR, functional mitral regurgitation.

Declarations

Author contributions

JSW wrote the original manuscript and prepared all figures; YHD reviewed the manuscript and administrated the study. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This case report was approved by the Ethics Committee of Jiande Hospital of Integrated Traditional Chinese and Western Medicine.

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Consent for publication

Written informed consent was obtained from the relatives for the publication of this case report.

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Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

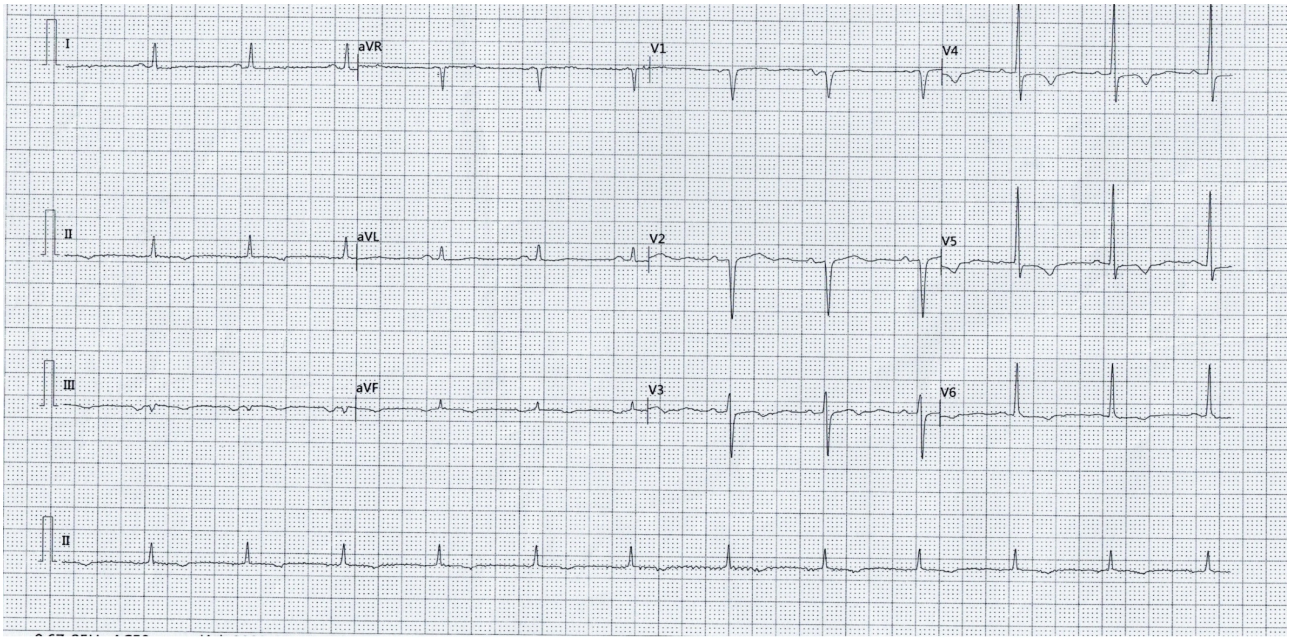
All data generated or analyzed during this study are included in this published case report.

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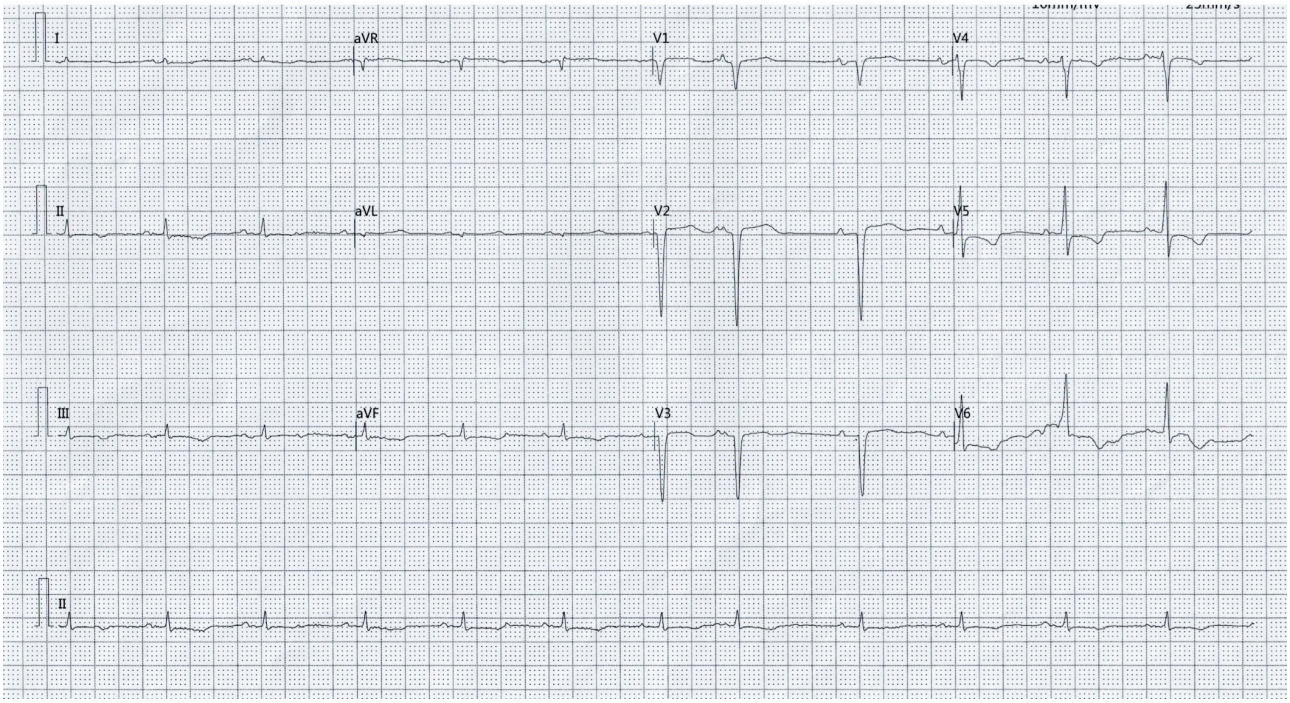
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Figures



Panel A



Panel B

Figure 1

Panel A: Electrocardiogram (ECG) performed in July 2020.

Panel B: Electrocardiogram (ECG) performed in 2022

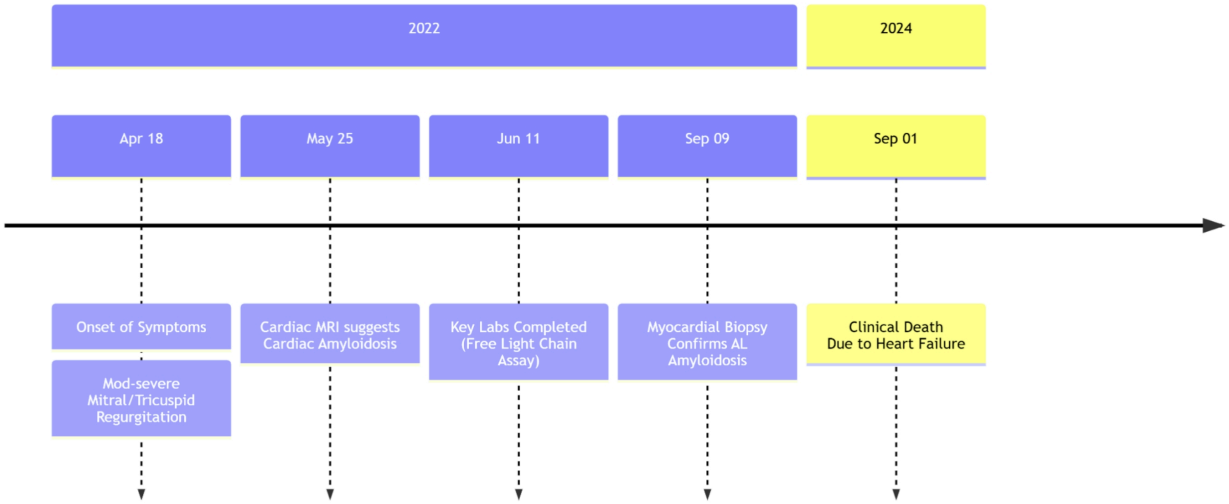


Figure 2

Timeline of disease onset and progression