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Case report

Cardiac progression of systemic light chain amyloidosis

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ABSTRACT

Systemic light chain amyloidosis is a disease characterized by the accumulation of amyloid protein in multiple organs and systems. We present the case of a 52-year-old male patient with a diagnosis of systemic light chain amyloidosis associated with cardiac and renal involvement. A renal biopsy showed the presence of renal amyloidosis associated with proteinuria, and the patient was referred for cardiovascular evaluation. The baseline electrocardiogram (ECG) showed microvoltage in frontal leads that were discordant with the left ventricular hypertrophy evidenced in the transthoracic echocardiogram (TTE). Cardiac magnetic resonance confirmed the presence of cardiac amyloid infiltration with a pattern of extensive ventricular late gadolinium enhancement. Despite being referred and receiving specific systemic chemotherapy treatment, the evolution was not favorable after four months of follow-up with worsening cardiac infiltration, increasing values of biomarkers and progression of dyspnea. The TTE was useful in revealing the unfavorable evolution and worsening of diastolic function parameters and increased wall thickness in the context of infiltration. The ECG and TTE were easily accessible tools that allowed the monitoring of the response to treatment.

Keywords: Inmunoglobulin Light-chain Amyloidosis; Heart Failure; Cardiomyopathies; Electrocardiography; Echocardiography. (Source: MeSH - NLM)

Introduction

Systemic light chain amyloidosis is the clonal formation of altered immunoglobulin light chains that cause misfolding and accumulation at the systemic level. It is associated with plasma cell dyscrasia, which causes myocardial contractility failure; in addition, the light chains cause a direct myocardial toxic effect. It accounts for approximately 80% of all cases of cardiac amyloidosis, there is no gender predilection, and cardiac involvement is thought to be present in 90% of cases [1-3].

Systemic light chain amyloidosis frequently affects the kidney with the presence of proteinuria in nephrotic values with or without renal failure. The main effect on the heart is restrictive cardiomyopathy, with evidence of thickening of the interventricular septum and ventricular wall, and is associated with systolic and diastolic dysfunction, that lead to heart failure symptoms and elevated values of troponins and natriuretic peptides. In addition, there can be gastrointestinal and central nervous system involvement. Frequently, postural hypotension,

erectile dysfunction and alterations in gastrointestinal motility may occur within the autonomic effects [4-6].

Case report

A 53-year-old male patient with no cardiovascular risk factors or known cardiologic history presented with proteinuria and dyspnea on moderate to heavy exertion for several months. Cardiovascular examination showed jugular vein distention, ventilated lung fields without over-aggregation, normal heart sounds without murmurs, and discrete edema of the lower limbs.

An electrocardiogram (ECG) was performed and showed sinus rhythm, heart rate of 75 beats per minute, QRS microvoltage in frontal leads, slow R wave progression in precordial leads, normal repolarization and normal QTc interval **(Figure 1).**

Paraclinical examination showed normal troponin levels of 0.06 ng/mL and increased natriuretic peptide (NT-pro-BNP) values of 1303 pg/dL. The diagnosis of heart failure was established, and a transthoracic echocardiogram (TTE) showed mild left ventricular hypertrophy with septal thickness of 12 mm, left ventricular ejection fraction (LVEF) of 66% with signs of diastolic dysfunction and increased left ventricular (LV) filling pressures **(Figure 2).**

The discordance between left ventricular hypertrophy and microvoltage in ECG suggested the presence of an infiltrative cardiomyopathy due to amyloid as a cause of heart failure, so the determination of light chains and cardiac magnetic resonance (CMR) were performed. This study showed left ventricular hypertrophy with septal thickness of 12.2 mm, preserved LVEF of 66% with normal ventricular volumes, non-dilated right cavities with preserved right ventricle

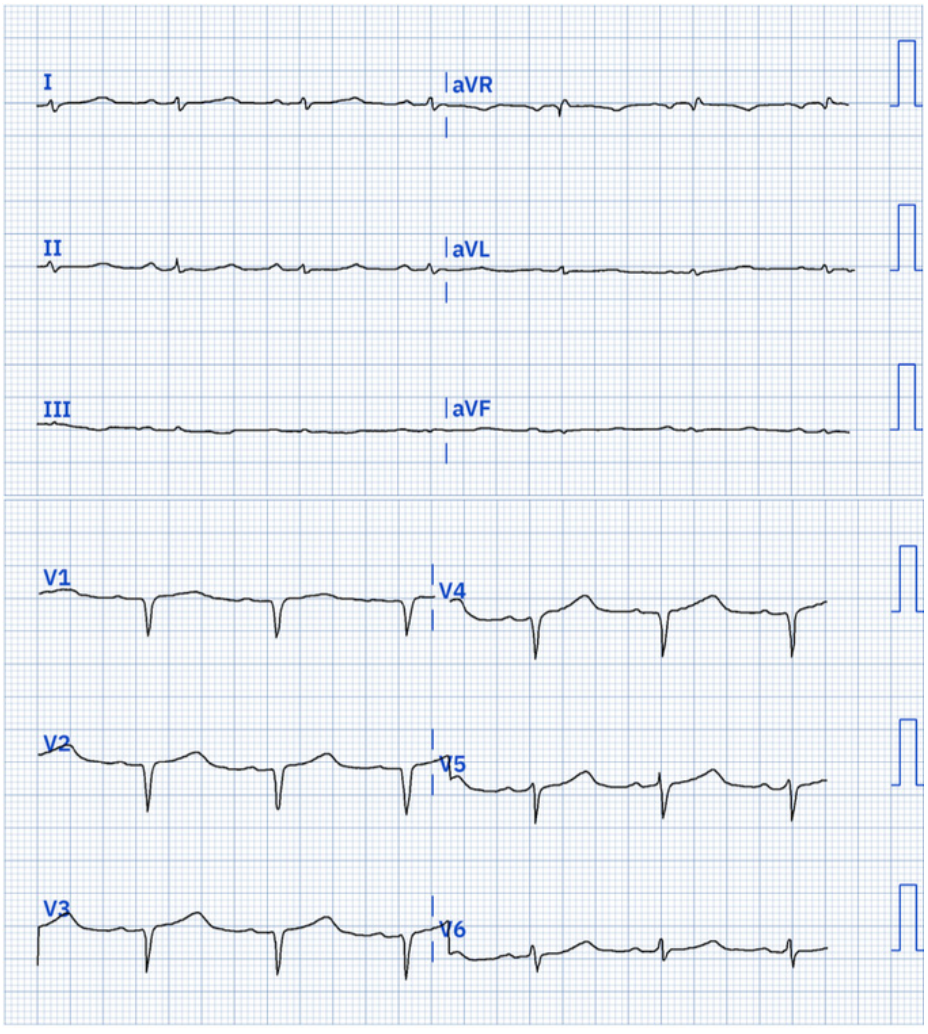

Figure 1. Basal 12-lead electrocardiogram. (Edited with @PMcardioBot)

size and systolic function. Tissue characterization after gadolinium contrast administration showed late gadolinium enhancement with non-ischemic type pattern with global biventricular involvement highly suggestive of amyloid type cardiac infiltration **(Figure 3).**

The renal biopsy was compatible with amyloid infiltration and altered light chains, making the diagnosis of light chain amyloidosis with stage II cardiac involvement, so he was referred to oncohematology for specific treatment. The bone marrow biopsy was not consistent with associated multiple myeloma and it was decided to initiate systemic chemotherapy treatment with CYBORD (cyclophosphamide, dexamethasone and bortezomib) for six cycles prior to the evaluation of bone marrow transplant.

After four cycles of chemotherapy, the patient evolved unfavorably, with progression of dyspnea (NYHA III) and signs of water retention four months after initiating treatment. Physical examination showed increased jugular vein distention and edema of the lower limbs. At the pulmonary level, he presented bilateral basal crepitations, and cardiac auscultation showed the presence of a third heart sound. The ECG was repeated and showed lower voltage QRS complexes in all leads (compared to the previous study), and QS morphology from V1 to V4 in precordial leads **(Figure 4).**

A new control TTE was performed. In relation to the previous one, it showed increased wall thickness, greater atrial dilatation, increased ventricular filling pressures, slight pericardial effusion, and right pleural effusion (Figure 5). Biomarkers also showed progression of cardiac disease with elevated troponin (0.09 ng/mL) and NT-pro-BNP (4069 pg/mL). After reassessment, it was decided to change the chemotherapy regimen. While waiting for the new treatment, the patient developed COVID-19 pneumonia and died due to complications related to the infection.

Discussion

Amyloidosis is an anomaly of plasma cells characterized by clonal production of light chain immunoglobulins, generating deposits of amyloid fibrils in the interstitial space of the myocardium [5,7]. In our case, is clear the progression of the primary systemic light chain amyloidosis. In this pathology, in addition to the symptoms of heart failure, angina may

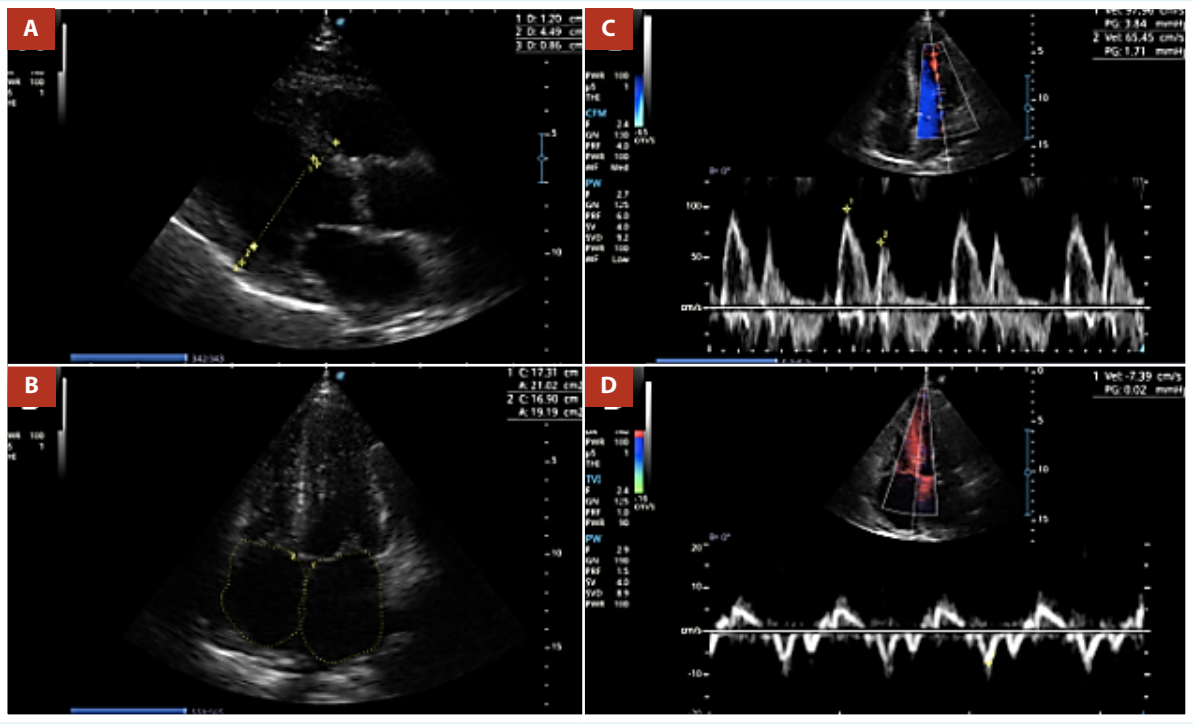

Figure 2. Transthoracic echocardiogram. **A.** left parasternal long-axis view showing a non-dilated left ventricle with mild basal septal hypertrophy of 12 mm**. B.** Apical four-chamber view with mild dilatation of both atria. **C and D.** Pulsed Doppler and tissue Doppler with pseudonormal left ventricular relaxation pattern with decreased tissue velocities, which allows estimation of an E/e' ratio of 13.

appear because of amyloid infiltration in the intramyocardial vessels without alteration of the epicardial arteries, sensory-motor neuropathy, pleural effusion due to infiltration in the parietal pleura, nephrotic syndrome, Waldenstrom's macroglobulinemia or associated multiple myeloma [8].

The diagnostic algorithm includes the ECG, where microvoltage, conduction disturbances of the electrical stimulus and atrial fibrillation can be found, while the manifestations of TTE include LV hypertrophy, diastolic dysfunction and alteration of the global longitudinal deformation [6,9]. To demonstrate cardiac amyloid infiltration, CMR is a versatile technique that specifically evaluates the presence of diffuse or transmural subendocardial late gadolinium enhancement and abnormal gadolinium kinetics [10]. The initial study to evaluate cardiac involvement generated by amyloid deposits is TTE; this study allows the identification of increased wall thickness, decreased systolic and diastolic function and alterations in tissue Doppler [11]. Other frequent findings are atrial dilatation, mottled myocardial appearance, valvular and atrial septal thickening, generated by the accumulation of amyloid; it can also be accompanied by small pericardial effusion; however, these alterations are nonspecific and could also be found in other infiltrative cardiomyopathies [5,8,12].

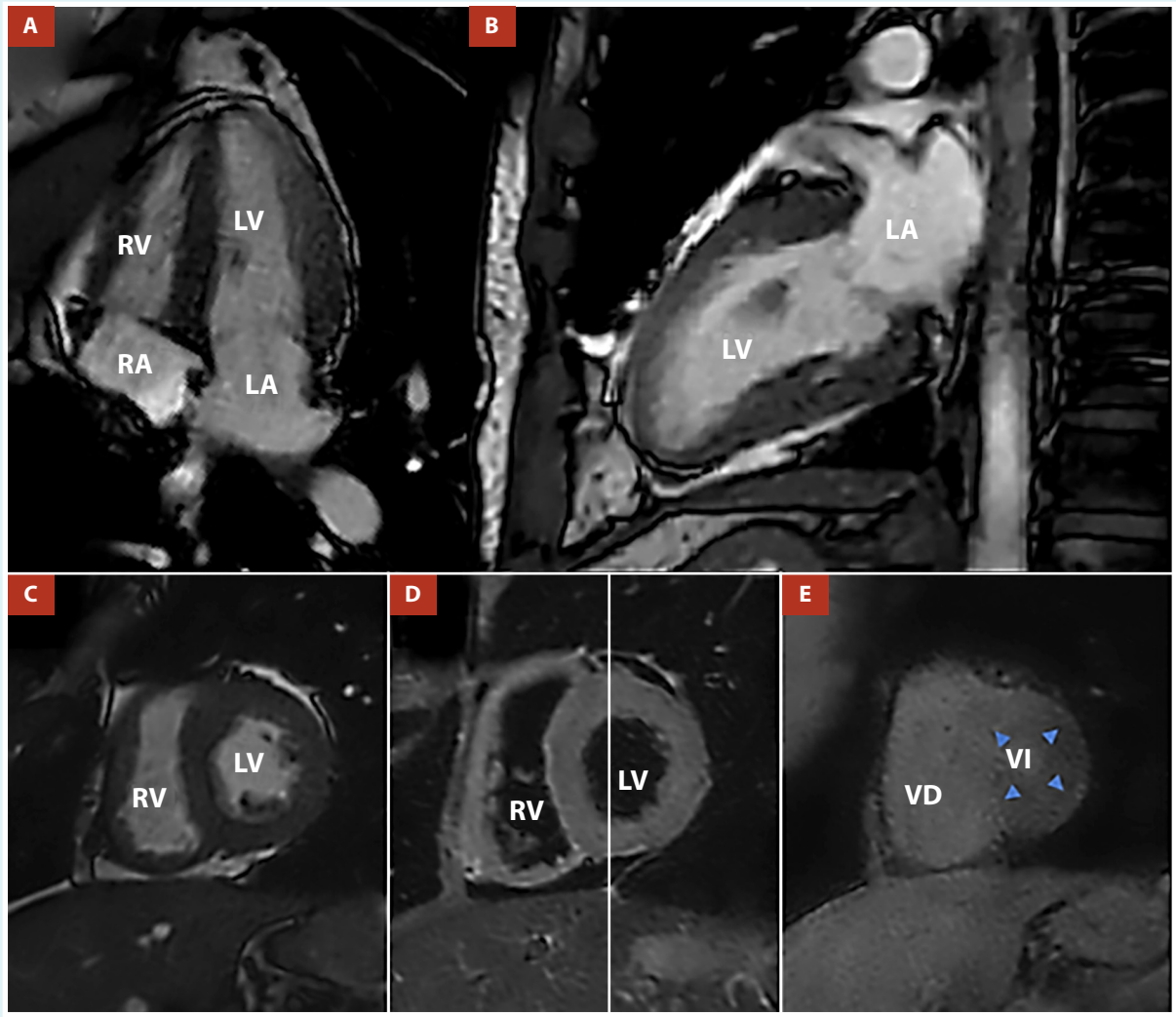

Figure 3. Cardiac magnetic resonance. **A, B, C.** white blood four-chamber, two-chamber, short-axis images showing left ventricular hypertrophy and mild dilatation of both atria. **D.** T1-weighted black blood T1-weighted tissue characterization images to assess anatomy (lower middle) and extensive and global late gadolinium enhancement at the bi-ventricular level (blue arrows) (lower right). LA: left atrium, RA: right atrium, LV: left ventricle, RV: right ventricle.

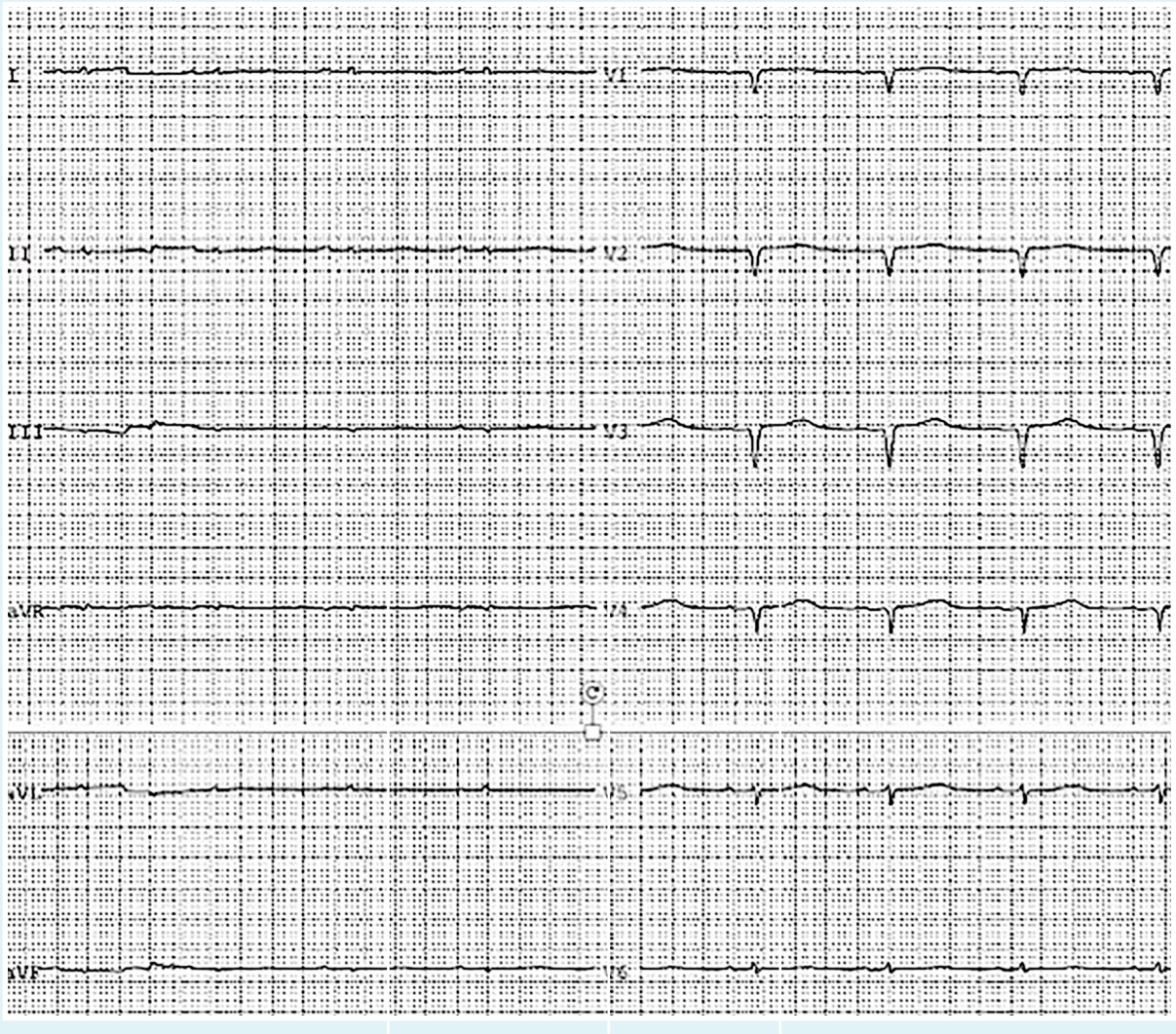

Figure 4. Follow-up 12-lead electrocardiogram.

The ECG can be a useful tool in the diagnosis and progression of amyloidosis by defining microvoltage as a decreased QRS amplitude of 0.5 mV in all limb leads or less than 1 mV in precordial leads. Low voltage is usually present in 84% of patients. The identification of a microvoltage pattern is related to low survival rate [6,13]. As demonstrated in this case, both TTE and ECG are easily accessible tools that allow evaluation of the progression of this disease.

In conclusion, primary systemic light chain amyloidosis is a pathology that produces accumulation of amyloid protein in different organs and systems. Cardiac involvement changes the prognosis and clinical evolution of patients. Disease progression is rapid and response to treatment can be assessed by complementary studies. ECG and TTE are easily accessible tools that allow the evaluation of the structural progression of this disease, such as the decrease in QRS complex voltage, increase in wall thickness, atrial dilatation, diastolic dysfunction and the decreased of LVEF.

Author´s Contributions: DXCHA and JFPV participated in data extraction and analysis, review, drafting and approval of the final version of the manuscript. RLFT, VVLP and JDTO performed data extraction and analysis, review and drafting of the manuscript.

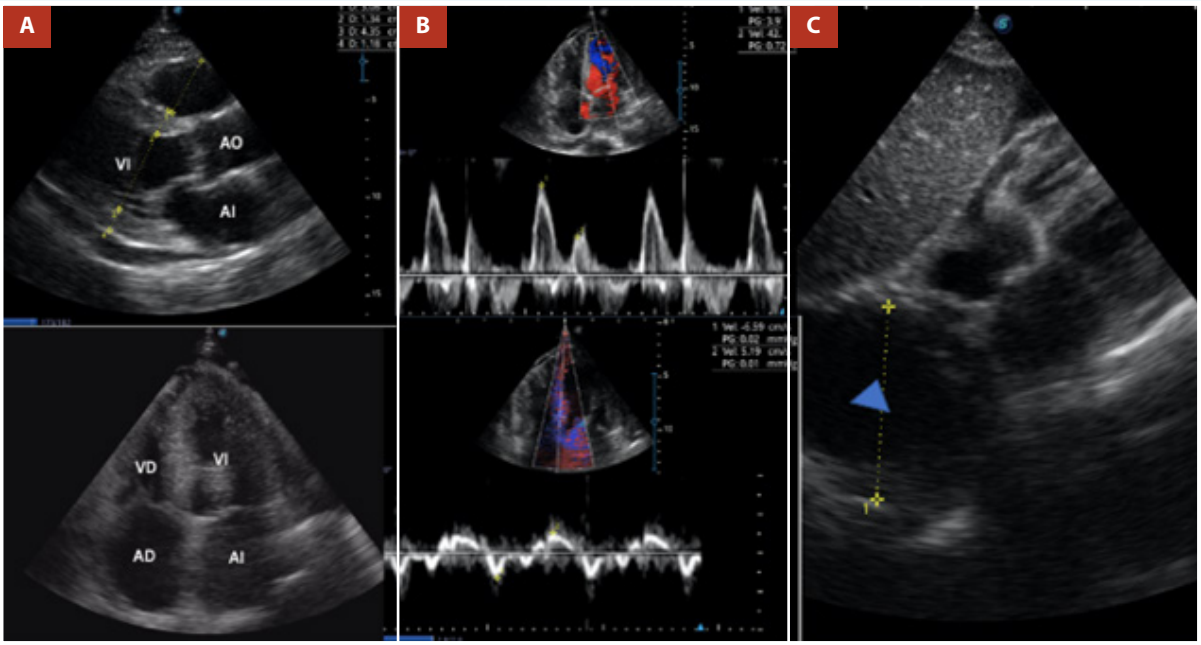

Figure 5. Follow-up echocardiogram. **A.** right parasternal long axis view (top) and apical four-chambered view (bottom). **B.** Tissue Doppler findings with increased E/e' ratio estimated at 17. **C.** subcostal view with presence of pleural effusion (blue triangle). LA: left atrium, RA: right atrium, LV: left ventricle, RV: right ventricle, Ao: Aorta

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