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AMYLOID CARDIOMYOPATHY IN THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: Cardiac amyloidosis is an underdiagnosed cause of restrictive cardiomyopathy resulting from the infiltration of the myocardium by amyloid proteins. Case Report: We report the case of an 83-year-old woman who presented with increasing dyspnea and lower-extremity swelling. She reported a medical history of unspecified heart failure. Evaluation in the Emergency Department (ED) revealed evidence of heart failure on physical examination, low-voltage electrocardiogram, chest x-ray study with mild pulmonary edema, and laboratory evaluation with elevated brain natriuretic peptide and troponin. Bedside cardiac ultrasound illustrated severe concentric ventricular hypertrophy and interventricular septal wall thickening with "sparkling" hyperechoic appearance of the myocardium, mildly reduced left ventricular ejection fraction, and small pericardial effusion. Inpatient comprehensive echocardiogram and follow-up nuclear medicine cardiac amyloid pyrophosphate study were suggestive of cardiac amyloidosis. Why Should an Emergency Physician Be Aware of This?: Emergency physicians commonly treat acute on chronic systolic heart failure with diuresis and reductions in preload and afterload with nitrates. Identifying amyloid cardiomyopathy in the ED is of clinical significance because treatment should include loop diuretics but should avoid β-blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers, and digoxin. Atrioventricular nodal blocking agents may have detrimental effects in cardiac amyloidosis because the cardiac output in this patient population is dependent on heart rate due to a significantly reduced stroke volume from the concentric hypertrophy minimizing diastolic filling. Also, caution should be taken when initiating nitrates in amyloid cardiomyopathy because further reducing preload in an already preload-depleted state can result in hypotension.**

☐ **Keywords—cardiac amyloidosis; amyloid cardiomyopathy; stiff heart syndrome**

INTRODUCTION

Amyloid cardiomyopathy (also known as cardiac amyloidosis and stiff heart syndrome) is an underdiagnosed cause of restrictive cardiomyopathy resulting from the infiltration of the myocardium by amyloid proteins. The hallmark of amyloid cardiomyopathy is severely hypertrophied biventricular and interventricular septal walls. The thickened myocardium causes diastolic dysfunction with reduced stroke volume and a cardiac output that is dependent on heart rate. Although the definitive diagnosis is clinched by endomyocardial biopsy, the patient history, physical examination, electrocardiogram (ECG), and bedside cardiac ultrasound findings can strongly suggest the diagnosis of amyloid cardiomyopathy.

CASE REPORT

An 83-year-old African American woman presented to the Emergency Department (ED) for a 1-week history of increasing shortness of breath and bilateral lower-

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extremity swelling. The patient reported a past medical history of unspecified heart failure and being on home oxygen and "water pills," but had not been able to take her medications recently. The patient also reported a history of hyperlipidemia and asthma, but no history of hypertension or coronary artery disease. She reported a family history of diabetes mellitus and hypertension. She denied a history of cigarette smoking and drank alcohol infrequently in small quantities. It was the patient's first encounter at our medical facility and there were no medical records from prior encounters or other facilities available.

Physical examination demonstrated vital signs of: blood pressure 127/58 mm Hg, heart rate 55 beats/min, respiratory rate 26 breaths/min, temperature 36.8°C, and oxygen saturation 89% on room air. She initially appeared to be in mild respiratory distress, with tachypnea and crackles to auscultation of bilateral lung bases. The patient had 2+ bilateral lower-extremity pitting edema. Jugular venous distention was present. Heart sounds were normal S1 and S2, no murmurs. Her oxygen saturation improved to 96% on 3 L of nasal cannula. An ECG demonstrated sinus rhythm with a heart rate of 55 beats/min, left axis deviation, T-wave inversions in V5–6, I and aVL, biphasic T waves in V3–4, left anterior fascicular block, low-voltage QRS complexes, normal intervals, no hypertrophy, and reduced R wave progression (Figure 1).

A bedside cardiac ultrasound was performed using a SonoSite X-Porte ultrasound machine (FUJIFILM Sonosite Inc., Bothell, WA) with a 5-1 MHz phased array transducer and obtained the following views: parasternal long axis (Figures 2 and 3), parasternal short axis (Figure 4), and apical four chamber (Figure 5). Figures 2–5 illustrate severe concentric ventricular hypertrophy and interventricular septal wall thickening with "sparkling" hyperechoic appearance of the myocardium, mildly reduced left ventricular ejection fraction, left atrial dilatation, and small pericardial effusion. The left ventricular posterior wall diameter measured 22 mm and the interventricular septum diameter measured 27 mm. A one-view portable anterior-posterior chest x-ray study showed interstitial pulmonary edema and cardiomegaly (Figure 6). The pertinent laboratory findings included elevated troponin T 0.340, elevated pro-brain natriuretic peptide 12,721, hyponatremia Na 131, and renal impairment creatinine 1.60 mg/dL, glomerular filtration rate 31 mL/min/1.73m^2.

The patient was managed in the ED for suspected acute on chronic heart failure with furosemide, aspirin, enoxaparin, and oxygen administered via nasal cannula. She was admitted to the inpatient service with Cardiology consultation. Comprehensive cardiac echocardiogram was suggestive of cardiac amyloidosis given the echogenicity of the myocardium (speckled pattern) and severe concentric hypertrophy. Follow-up nuclear medicine cardiac amyloid pyrophosphate (PYP) study demonstrated findings suggestive of transthyretin (TTR)-type amyloid infiltration of the myocardium. Cardiology treated the patient with torsemide and discontinued her previously prescribed spironolactone and metoprolol. She was discharged several days later in stable condition and was instructed to follow up with her cardiologist on an outpatient basis.

DISCUSSION

Cardiac amyloidosis is a form of restrictive cardiomyopathy caused by infiltration of the myocardium by amyloid proteins such as monoclonal light chains and TTR (1,2).

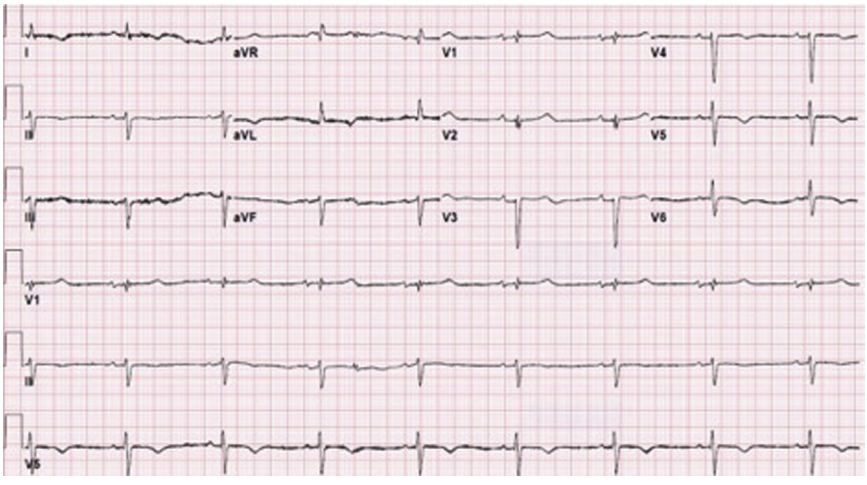

Figure 1. Electrocardiogram: sinus rhythm with a heart rate of 55 beats/min, left axis deviation, T-wave inversions in V5–6, I and aVL, biphasic T waves in V3–4, left anterior fascicular block, low-voltage QRS complexes, normal intervals, no hypertrophy, and reduced R-wave progression.

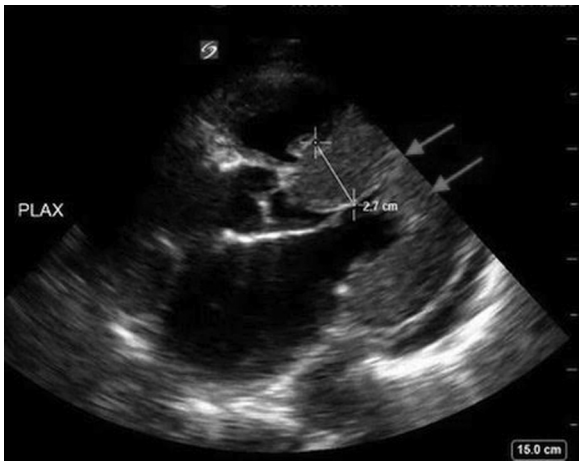

Figure 2. Parasternal long-axis view (PLAX) in diastole. Severe concentric ventricular hypertrophy with "sparkling" hyperechoic appearance of the myocardium (arrows). Interventricular septum thickened at 2.7 cm = 27 mm. Left atrial dilatation. Small pericardial effusion. Mildly reduced left ventricular ejection fraction.

The three main subtypes of cardiac amyloidosis are light chain amyloidosis, TTR, and senile systemic amyloidosis. The patient in this case was found to have TTR-type cardiac amyloidosis, an inherited autosomal dominant disease in which mutant TTR protein infiltrates the myocardium. The TTR-type amyloid pattern was diagnosed with a cardiac amyloid PYP study, which is a nuclear imaging modality that utilizes a PYP bone tracer to localize amyloid deposits (3). PYP cardiac imaging has the ability to identify TTR-type cardiac amyloidosis with a sensitivity of 97% and specificity of 100% (4). The patient presented in this case report demonstrated many of the clinical features of amyloid cardiomyopathy, including

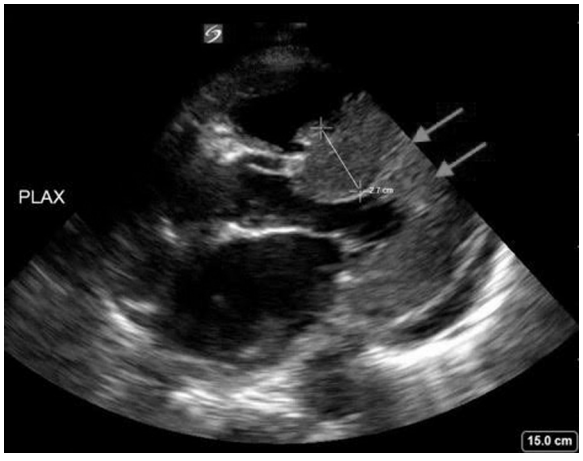

Figure 3. Parasternal long-axis view (PLAX) in systole. Severe concentric ventricular hypertrophy with "sparkling" hyperechoic appearance of the myocardium (arrows). Interventricular septum thickened at 2.7 cm = 27 mm. Left atrial dilatation. Small pericardial effusion. Mildly reduced left ventricular ejection fraction.

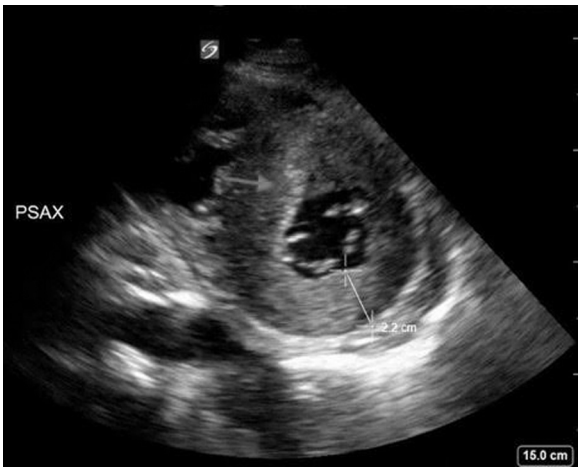

Figure 4. Parasternal short-axis view (PSAX). Severe concentric ventricular hypertrophy with "sparkling" hyperechoic appearance of the myocardium (arrow). Left ventricular posterior wall measures 2.2 cm = 22 mm. Small pericardial effusion. Mildly reduced left ventricular ejection fraction.

classic symptoms of heart failure, ultrasound evidence of concentric ventricular and interventricular septum hypertrophy with diastolic dysfunction, and ECG meeting low-voltage criteria.

The symptoms of cardiac amyloidosis mirror those of classic heart failure with dyspnea, bilateral lower-extremity swelling, orthopnea, paroxysmal nocturnal dyspnea, pericardial disease, and conduction system disease (1,2). Due to infiltration of the interventricular septum, cardiac amyloidosis can mimic hypertrophic cardiomyopathy when the septal wall is > 15 mm and can present with syncope or sudden cardiac death due to left ventricular outflow tract obstruction (5,6). The risk of sudden cardiac death is highest when septal wall thickness is > 30 mm (7).

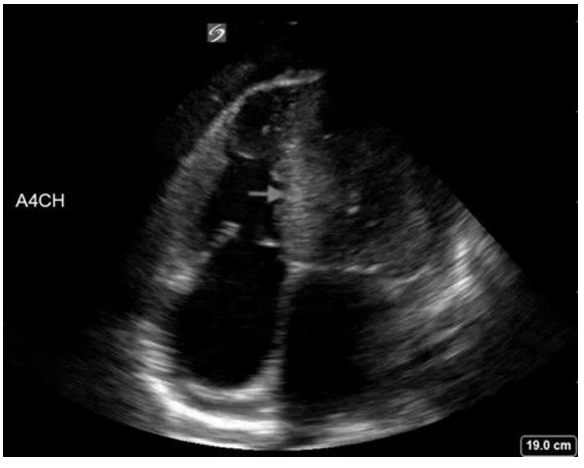

Figure 5. Apical four-chamber view (A4CH). Severe concentric ventricular hypertrophy with "sparkling" hyperechoic appearance of the myocardium (arrow). Interventricular septum thickened. Left atrial dilatation. Small pericardial effusion. Mildly reduced left ventricular ejection fraction.

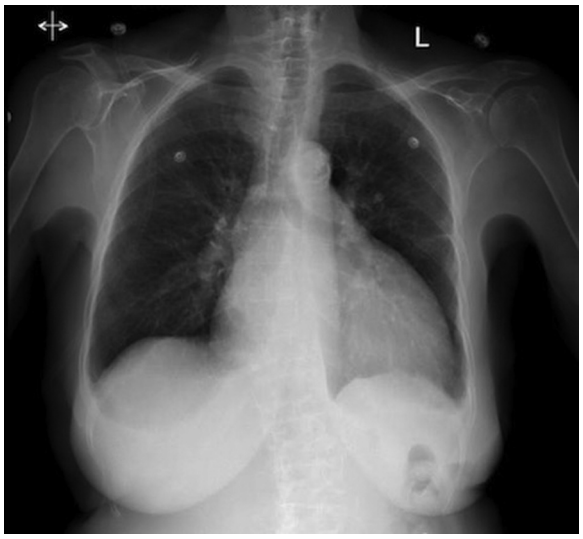

Figure 6. Chest radiograph: interstitial pulmonary edema, cardiomegaly.

Low-voltage ECG, as noted in Figure 1, is another key finding in cardiac amyloidosis, present in 46%–50% of cases. The prevalence of low-voltage ECG ranges from 45%–70% due to the heterogeneous definitions of a low-voltage ECG, with up to 66% of cases of cardiac amyloidosis identified commonly using the definition of QRS complex voltages ≤ 5 mm in each peripheral lead (8). Amyloid cardiomyopathy may also result in poor R wave progression with a pseudoinfarction pattern as well as extreme left- or right-axis deviation. The ECG in this case demonstrated clockwise rotation with reduced R-wave progression and a transition at V4–5. The delay in R-wave transition can be explained by the infiltrative process and is less likely to be due to the left anterior fascicular block. Bundle branch blocks are uncommon, but if present, are more likely to affect the right bundle branch. An isolated left bundle branch block pattern is exceedingly rare (9,10). Other ECG findings seen in cardiac amyloidosis are related to conduction system disease resulting in first-, second-, or third-degree atrioventricular (AV) block, atrial fibrillation, atrial flutter, and ventricular tachycardia (11,12).

The echocardiography findings attributed to cardiac amyloidosis are well described and include severe concentric hypertrophy of both ventricles and thickened interventricular septum with "sparkling" or "granular" hyperechoic appearance of the myocardium, biatrial dilatation, small pericardial effusions, and evidence of diastolic dysfunction (13–15). In advanced cases there may also be evidence of systolic dysfunction.

The diagnosis of amyloid cardiomyopathy in the ED is suggested by heart failure symptoms, bedside cardiac ultrasound findings, and low-voltage ECG. Rahman et al. suggested that the combination of a low-voltage ECG and an interventricular septal wall thickness >19.8 mm can predict the diagnosis of amyloid cardiomyopathy with a specificity of 91% and sensitivity of 72% (16). The diagnosis is even more likely in the presence of severe concentric ventricular hypertrophy in the absence of hypertension, which was the case in our patient. Other imaging modalities such as cardiac magnetic resonance imaging can be utilized to further suggest the diagnosis. Ultimately, the definitive diagnosis of amyloid cardiomyopathy is confirmed by endomyocardial biopsy.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

Identifying amyloid cardiomyopathy in the ED is of clinical significance because treatment should include loop diuretics, salt restriction, and aldosterone antagonists, but should avoid β-blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers, and digoxin (17). Although AV nodal blocking agents have been proven to improve survival in systolic heart failure, they may have detrimental effects in cardiac amyloidosis because the cardiac output in this patient population is dependent on heart rate due to a significantly reduced stroke volume from the concentric hypertrophy minimizing diastolic filling. The treatment of tachydysrhythmias such as atrial fibrillation with rapid ventricular response can be challenging, with conflicting recommendations including cardioversion, amiodarone, and low doses of digoxin and β-blockers. Although typically contraindicated in amyloid cardiomyopathy, some authors suggest that the use of β-blockers and digoxin in low doses can be used for rate control in tachydysrhythmias given that this approach can enhance ventricular filling and cardiac output. The use of amiodarone for rate control in atrial fibrillation with rapid ventricular response is an alternative approach that is well tolerated (18). Also, caution should be taken when initiating nitrates in amyloid cardiomyopathy because further reducing preload in an already preload-depleted state can result in hypotension (19).

Another reason for early detection of cardiac amyloidosis is that the diagnosis is often identified late in the disease process when prognosis is poor (20). If emergency physicians are able to recognize the pattern of heart failure, low-voltage ECG, and characteristic cardiac ultrasound findings, patients may benefit from earlier treatments, including newer modalities that aim to prevent further infiltration of the myocardium by amyloid proteins.

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