CARDIAC AMYLOIDOSIS IN A PATIENT WITH MULTIPLE MYELOMA IN A LOW RESOURCE SETTING: A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

This is a case of a 43-year-old man presenting with features of congestive heart failure and confirmed multiple myeloma that has been on chemotherapy. Electrocardiogram and transthoracic echocardiography (TTE) were oriented towards diagnosing cardiac amyloidosis, showing mild pericardial effusion, restrictive cardiomyopathy and low voltage QRS criteria on electrocardiogram. Lymph node and bone marrow biopsies had confirmed the diagnosis of multiple myeloma. Patient had diuretics and other supportive medications, did well and was discharged home on oral medications.

Key words: secondary amyloidosis, primary amyloidosis, transthoracic echocardiography

INTRODUCTION

Amyloid cardiomyopathy happens as a result of extracellular deposition of insoluble fibrils resistant to proteases and is a rare disease. It may be secondary to chronic inflammatory conditions, hereditary diseases or to the production of a light chain of monoclonal immunoglobulin. It usually leads to infiltrative cardiomyopathy that has a restrictive pathophysiology, conventionally associated with significant poor prognosis and morbidity. It has 30% survival at 2years with a life expectancy of 6 months without treatment.1

Some case reports have earlier described and association between multiple myeloma and cardiac amyloidosis. But the interest of our observation is because of the rarity of this association, the diagnostic difficulty cardiac amyloidosis and a bit more to find its aetiology.2

CASE REPORT

Our patient is a 43-year-old man, diagnosed with multiple myeloma via lymph node and bone marrow biopsies for which he has been placed on chemotherapy and follow up about 5 years prior to presentation. He presented with complaints of recurrent breathlessness associated with orthopnea, paroxysmal nocturnal dyspnea and cough productive of frothy sputum with. There was also a history of leg swelling and roughness of skin.

When we examined him, he was not febrile and lying supine position with a blood pressure of 119/77mmHg. He had a regular heart rate of 110 beats per minute with no features of hypotension postural hypotension. He had a respiratory rate of 22 cycles per minute with oxygen saturation of 90% at room air. The rest of the clinical examination had found Bilateral crackles on lung

auscultation, bilateral lower extremity edema and jugular venous distension. Electrocardiogram revealed a rate of 110 beats per minute, in sinus rhythm and low voltage complexes. (Figure 1)

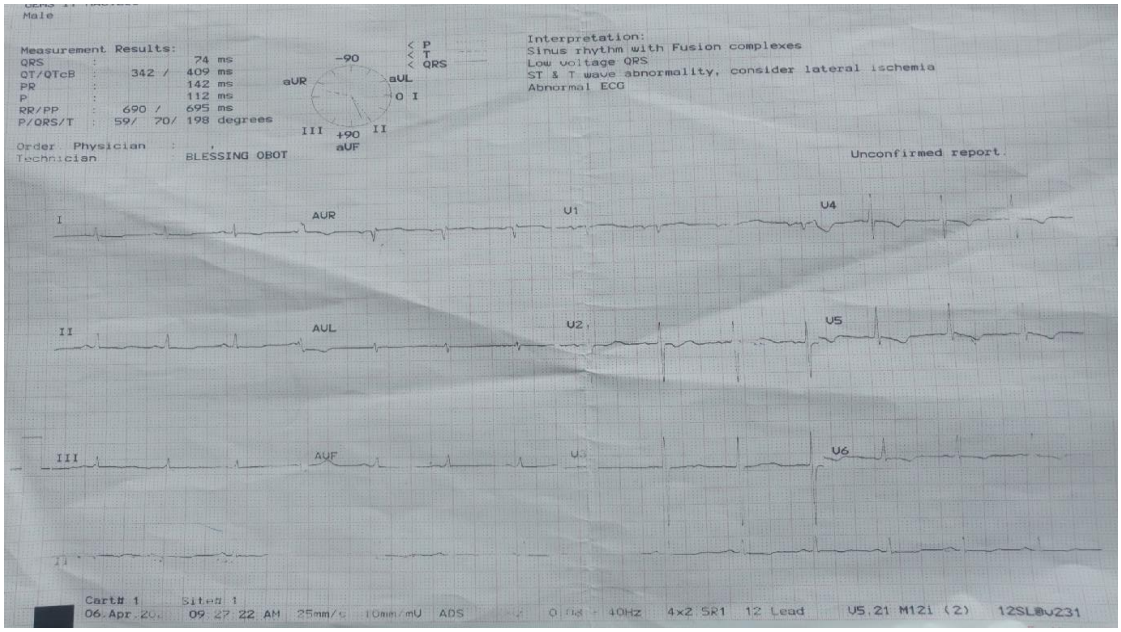


Figure 1: Patients ECG

When the trans-thoracic echocardiography was done early in the assessment of the patient, it showed a restrictive cardiomyopathy with asymmetrical septal hypertrophy and pericardial effusion and no features of cardiac transplant. There was abnormal texture of the myocardial tissue showing a “granular sparkling” appearance, a restrictive mitral profile with a good systolic function (Left Ventricular Ejection fraction of 63%), bi-atrial enlargement, thickened cardiac valves (mitral, tricuspid, aortic and pulmonary). There was pulmonary hypertension of above 2.5m/s and pressure of 25mm Hg (Figure 2).

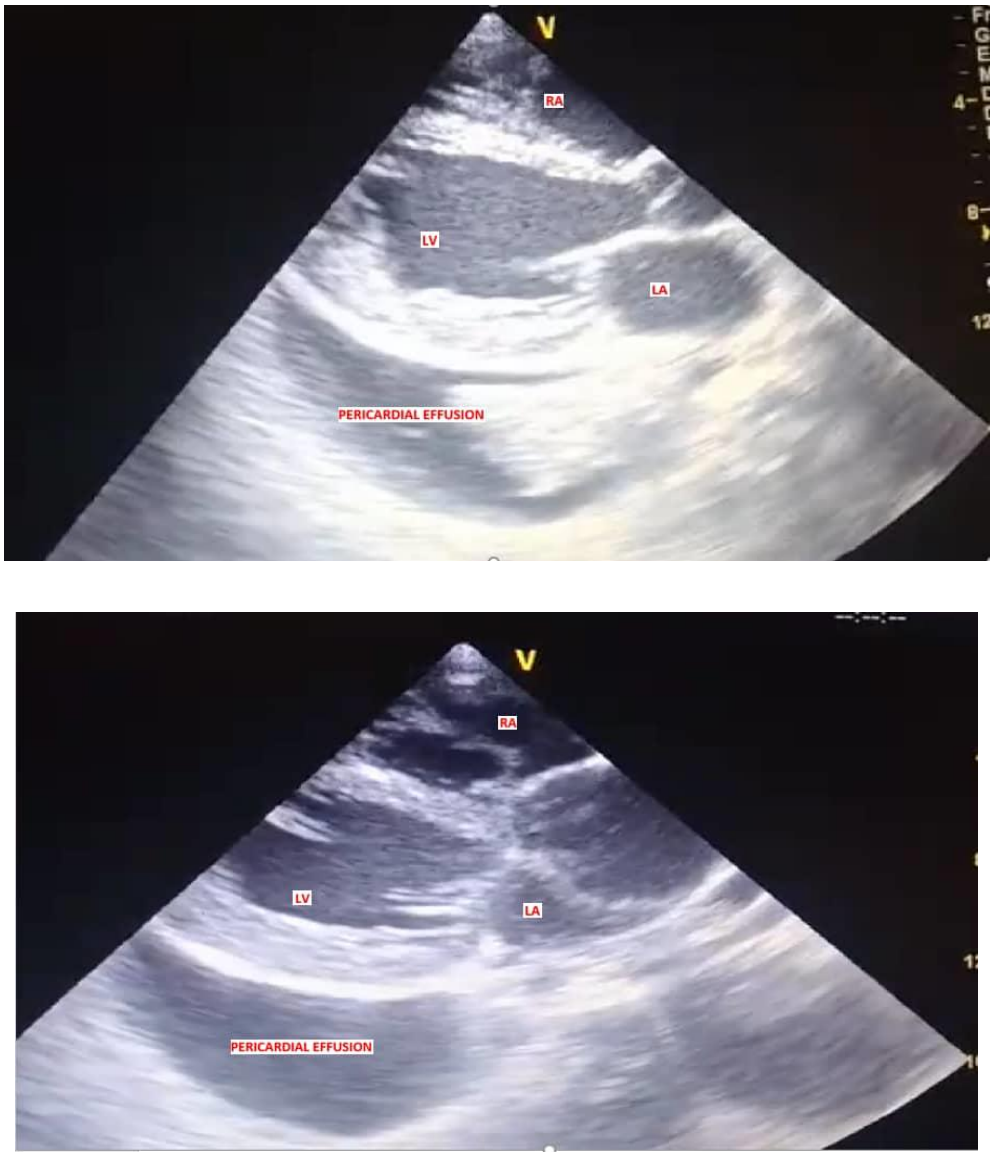
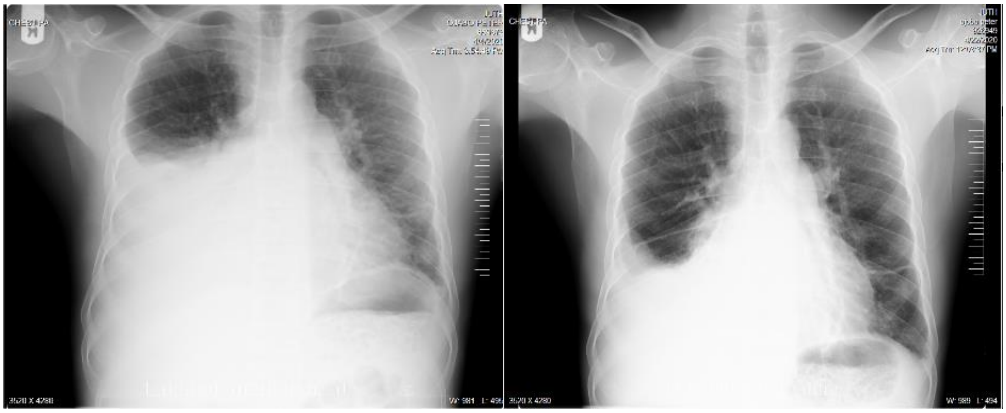


Figure 2: Patient's Echocardiography

Chest X-ray showed cardiomegaly, right sided pleural effusion and pulmonary edema (Figure 3).



Before thoracentesis **after thoracentesis**

Figure 3: chest X-ray- pre and post thoracocentesis

Before thoracentesis after thoracentesis Figure 3: chest X-ray- pre and post thoracocentesis A complete blood cell count revealed mild normocytic anemia at 8.7g/dl, an Erythrocyte Sedimentation Rate at 70 mm/hr with albumin level of 29 g/l (low). The patient received standard therapy for heart failure- iv torsemide 40mg BD, tab metolazone 5mg daily, tab spironolactone 25mg daily, tab clopidogrel 75mg daily, subcutaneous enoxaparin 40mg daily including ACE inhibitors, he also had thoracocentesis done. Patient's condition improved and was discharged home on oral anti-failure/supportive medications to see at medical outpatient clinic for follow up.

DISCUSSION

Amyloidosis is a systemic organ-limited disease in which insoluble homomeric amyloid fibrils that are composed of a variety of serum proteins gradually replace normal tissue in various body organs.3 Major forms of amyloidosis are grouped into 6 subtypes: (1) AL or primary amyloidosis, (2) AA or secondary amyloidosis, (3) familial (Hereditary) amyloidosis, (4) senile systemic amyloidosis, (5) isolated atrial amyloidosis and (6) hemodialysis related amyloidosis resulting from accumulation of beta-2 microglobulin.4 cardiac involvement becomes clinically evident in up to 50% of those that have AL amyloidosis but only 10% of individuals with AA amyloidosis with less than 5% having familial syndrome.5

Importantly, only 10% of patients with multiple myeloma develop systemic light chain amyloid disease with a poor prognosis especially in the presence of cardiac amyloidosis. 6,7 The mean age of diagnosis in patients withal amyloidosis is 64 years.1 Amyloid depositions occur mainly in the interstitium of contractile myocardium but may also involve the pericardium, the endocardium and the conduction system.8 the epicardial arteries in cardiac amyloidosis are usually spared but amyloid fibrils are deposited in the small intramural vessels and coronary angiography when done is normal. 9,10 Few similar cases have been described, the first discovered in postmortem after rapidly progressive heart failure6, the second revealed by a congestive heart failure associated with ventricular tachycardia,

efficiently treated with Bortezomib11, and the third discovered following an asymmetric hypertrophic cardiomyopathy and unexplained heart failure.12 Possibly because of elevated ventricular filling pressures and direct myocyte damage caused by amyloid deposition, B-natriuretic peptides are elevated in the plasma.13 Increase in ventricular thickness is brought about by accumulation of electrically inert amyloid protein in the extracellular matrix of the myocardium giving a false impression of ventricular hypertrophy on sonography.

Electrocardiography shows low voltages with no features of ventricular hypertrophy. Sonographic images shows “snow storm” or “sparkling’’ appearance.14 A thickened interatrial septum, which is rarely present even in the later disease stages have 100% specificity.15 Cardiac amyloidosis diagnosis can be ascertained by either (1) a positive biopsy from a non-cardiac tissue in addition to sonographic evidence of amyloidosis, which includes a mean LV wall thickness of greater than 12mm in the absence of other causes of LV hypertrophy, or (2) an endomyocardial biopsy illustrating amyloid deposition in addition to laboratory and clinical evidence of organ involvement.

Biopsy specimen from the involved organ, such as the heart or from the abdominal fat pad, exhibits a red or pink color under light microscopy after chemical staining with Congo red and a dramatic apple-green birefringence under polarized light.16 The primary manifestation of amyloid cardiomyopathy is congestive heart failure with preserved systolic and abnormal diastolic function. Because of the so called restrictive mitral inflow pattern of Doppler imaging, cardiac amyloidosis was classically described as a restrictive cardiomyopathy.

But this severe form of left ventricular diastolic dysfunction is only present in the late stage of the disease. In the earlier stage of the disease process, diastolic dysfunction is only mild and is characterized by the Doppler pattern of abnormal relaxation. Cardiac magnetic resonance imaging will show diffuse myocardial amyloid deposits lead to decreased tissue signal intensity along with a specific pattern of global late subendocardial tissue enhancement.6 Cardiac MRI in amyloidosis patients usually demonstrates global and late subendothelial gadolinium enhancement in the myocardium.

However, gadolinium-based MRI should be used with extreme caution and preferably avoidance in those individuals with moderate to severe renal disease, due to the risk of nephrogenic systemic fibrosis.17. Aside from the management of the underlying cause of amyloid deposition, the treatment of symptomatic cardiac amyloidosis is primarily supportive. Preload and afterload reduction using diuretics alone or in combination with vasodilators, or long-acting nitroglycerin preparations, may be helpful.

The symptoms of heart failure may be reduced by digitalis glycosides but the dysrhythmia and sudden death have been reported following their use.6 patients with heart failure and AL amyloidosis who are not treated have a median survival of 6 to 9 months.1 Patients who are not candidates for hematopoietic stem cell transplantation, the preferred regimen is melphalan plus dexamethasone18 or cyclophosphamide plus thalidomide and dexamethasone19, which prevents further amyloid deposition, gradual amyloid regression and marked improvement in New York Heart Association (NYHA) class.20 Sustained improvement in cardiac

function with persistent amyloid deposition is provided in a patient with multiple myeloma-associated cardiac amyloidosis treated with Bortezomib.11 Cardiac transplantation may be a lifesaving measure for those patients with preserved extra cardiac organ function who are also fit to undergo subsequent chemotherapy.

Post-transplant successful for 2 months has been shown to increase survival of patients possibly for up to 10 years. 21

CONCLUSION

In conclusion, cardiac screening in patients with multiple myeloma should include at least an electrocardiogram and complete echocardiography. Conversely, all patients with cardiac amyloidosis, multiple myeloma should be sought for its poor prognosis. Even though there is no single noninvasive test that can accurately diagnose cardiac amyloidosis, the consolation of heart failure symptoms, sonographic findings, and low-voltage complexes at the electrocardiogram are highly suggestive of disease.

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