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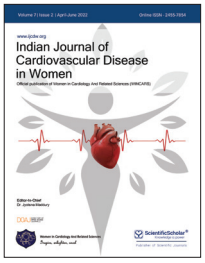

Cardiovascular *Case Report*

Cardiac Amyloidosis Presenting as Isolated Severe Pulmonary Artery Hypertension

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ABSTRACT

A 58-year-old woman presented with dyspnea on exertion and bilateral pedal edema for 3 months. She was found to have severe pulmonary hypertension (PH) with the right ventricular failure. The detailed evaluation did not reveal any secondary cause for PH (cardiac disease, pulmonary embolism, interstitial or other lung disease, collagen vascular disease, portal hypertension, or chronic liver disease). Meanwhile, her workup revealed multiple myeloma. Abdominal fat pad biopsy was performed because PH as an isolated manifestation of cardiac amyloidosis was previously reported. Thus, she was diagnosed to have systemic amyloidosis secondary to myeloma. PH was attributed to cardiac amyloidosis. We present a patient with PH and amyloidosis secondary to multiple myeloma. PH and primary systemic amyloidosis without cardiac or parenchymal lung involvement are extremely rare with only a few cases reported in the past.

Keywords: Cardiac amyloidosis, Pulmonary hypertension, Right ventricular failure

INTRODUCTION

Amyloidosis is characterized by the extracellular deposition of fibrillar proteins in various tissues. The most common presentations are nephrotic range proteinuria, congestive cardiac failure, unexplained hepatomegaly, and peripheral neuropathy. Cardiac amyloidosis causes myocardial involvement secondary to extracellular amyloid infiltration. Cardiac involvement is seen in 25% of patients, usually with unexplained congestive heart failure. Restrictive cardiomyopathy is seen during the later stages of cardiac amyloidosis. Pulmonary hypertension (PH) in patients having amyloidosis with no secondary cause for PH and no evidence of the left ventricle dysfunction is extremely rare.

CASE REPORT

A 58-year-old woman presented with dyspnea on exertion and bilateral pedal edema for 3 months. She had no orthopnea, paroxysmal nocturnal dyspnea, or angina. She had bipolar affective disorder for the past 30 years on regular treatment (lithium, escitalopram, and clonazepam) and autoimmune hypothyroidism for 1 year (thyroxine 100 mcg daily).

She had bilateral pedal edema up to the mid-calf but had no cyanosis, pallor, or clubbing. Cardiovascular system examination showed elevated jugular venous pressure (10 cm above the sternal angle), loud P2, and Grade 2 systolic murmur in the tricuspid area. Respiratory system

examination showed normal vesicular breath sounds bilateral and there were no added sounds. The rest of the examination was unremarkable except for moderate ascites.

Hemoglobin was 10.9g/dl, total leukocyte count 8.200/μL, platelet count 3.2 × 10^9/L, and erythrocyte sedimentation rate 80 mm in 1 h. The peripheral smear showed normocytic normochromic anemia. Urinalysis showed no albuminuria. The urine spot protein-creatinine ratio was normal. Biochemical parameters showed random blood sugar 99 mg%, urea 142 mg/dl, creatinine 2.2 mg/dl, sodium 131 mmol/l, and potassium 3.2 mmol/l. Liver function tests showed hyperglobulinemia with reversal of albumin globulin ratio (total protein 8.2 g/dl, albumin 2.2 g/dl, and globulin 6.0 g/dl). The corrected calcium for albumin was 11.1 mg/dl. Chest x-ray showed cardiomegaly and an electrocardiogram showed sinus bradycardia and occasional ventricular premature complexes. Echocardiogram showed right atrial and ventricular dilatation, moderate tricuspid regurgitation, pulmonary arterial systolic pressure was 64 mmHg, severe PH, and right ventricular dysfunction (tricuspid annular plane systolic excursion was 12 mm and RV fractional area change was 27%) with good left ventricular function. There were no signs of the left to right shunt, restrictive cardiomyopathy, or cardiac amyloidosis on echocardiography. Ultrasonography of the abdomen showed moderate ascites with normal liver. Doppler ultrasonography showed a normal portal vein. Workup for other causes of PH including high-resolution computed tomography angiogram of the chest and anti-nuclear antibody was negative. Spirometry was normal. The thyroid function test was normal but the antithyroid peroxidase antibody titer was high. The blood level of lithium was 0.9 milliequivalents per liter (normal 0.6 and 1.2 milliequivalents per liter). Since the patient had normocytic normochromic anemia, high erythrocyte sedimentation rate, renal failure, and reversal of albumin globulin ratio a possibility of multiple myeloma were considered. Bone marrow showed 40% plasma cells with kappa restriction. Urinary Bence-Jones protein was negative. The serum IgG M-component was 58.0 g/L (5.4–16.1 g/L). The patient was diagnosed to have multiple myeloma but the workup for PH did not reveal any cause. The patient was not willing for myocardial biopsy so an abdominal fat pad biopsy was done which showed deposition of amorphous eosinophilic material stained positively with Congo red stain and apple-green birefringence under polarizing light [Figure 1] suggestive of systemic amyloidosis. She had no clinical or laboratory (normal nerve conduction studies) features of peripheral neuropathy. She was diagnosed to have PH due to cardiac amyloidosis and multiple myeloma. She was started on dexamethasone, thalidomide and bortezomib regimen for multiple myeloma, and sildenafil for PH following which she had improvement in her symptoms.

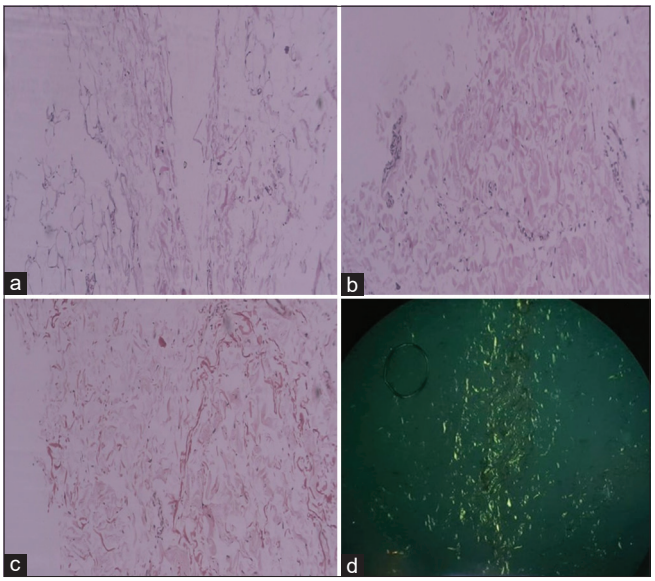

Figure 1: Abdominal fat pad biopsy showing deposition of amorphous eosinophilic material with H&E staining (a and b), positive staining with congo red stain (c), and apple-green birefringence under polarizing light (d).

DISCUSSION

Cardiac amyloidosis is caused by the deposition of insoluble, proteinaceous, and non-branching fibrils amyloid, in the extracellular space of the heart. The common manifestations are restrictive cardiomyopathy, diastolic heart failure, conduction defects, and arrhythmias.[1]

Our patient was diagnosed to have PH and a detailed evaluation did not reveal any secondary cause for PH (cardiac disease, pulmonary embolism, interstitial or other lung diseases, collagen vascular disease, portal hypertension, or chronic liver disease). PH due to lithium and selective serotonin reuptake inhibitors therapy was previously reported.[2,3] Serum lithium level was normal in our patient. The role of lithium and escitalopram in the development of PH in our patient cannot be ruled out. Several studies suggest a high prevalence of transient PH in hypothyroidism which decreases after the achievement of a euthyroid state, but our patient had normal thyroid function.[4] Meanwhile, her workup revealed multiple myeloma. Abdominal fat pad biopsy was performed because PH as an isolated manifestation of cardiac amyloidosis was previously reported. Thus, she was diagnosed to have systemic amyloidosis secondary to myeloma. PH was attributed to cardiac amyloidosis.

PH among patients with primary amyloidosis is commonly due to the left-sided restrictive cardiomyopathy or diffuse lung disease both of which were not seen in our patient.[5] PH and primary systemic amyloidosis without cardiac or parenchymal lung involvement are extremely rare with only a few cases reported in the past[5-9] [Table 1]. Amyloid deposition in the

Table 1: Pulmonary hypertension and systemic amyloidosis without cardiac and lung parenchymal involvement.

Case	Age and sex	Presentation	Multiple Myeloma	Severity of PH	Treatment recieved	Outcome
Present (2022)	58 Female	Dyspnea and pedal edema	Yes	Severe	Sildenafil	Improved
Cirulis *et al*. 2016	53 Female	Dyspnea	Yes	Severe	Sildenafil and macitentan	Improved
Eder *et al*. 2007	73 Female	Dyspnea, leg edema, and abdominal distention.	yes	Severe	nifedipine and diuretics	Died after six months
Chapman *et al*. 1999	91 Female	Dyspnea, Heart failure	no	Severe	-	Not known
Shiue and McNally 1988	65 female	Dyspnea, Heart failure	yes	Severe	-	Died after one and half months
Dingli *et al*. 2001 5 cases	61Female	Dyspnea, Heart failure	Yes	-	-	Died after 29 months
	64 female	Dyspnea, Heart failure	Yes	-	-	Died after 29 months
	82 male	Dyspnea, Heart failure	No	-	-	Died after 34.5 months
	54 female	Dyspnea, Heart failure	No	-	-	Died after 2.5 months
	48 female	Dyspnea, Heart failure, chest pain	No	-	-	Died after 2 months

pulmonary vasculature can cause endothelial dysfunction. Pulmonary vasoconstriction, smooth muscle cell and endothelial cell proliferation, and thrombosis[5] can lead to the development of PH. The treatment of cardiac amyloidosis includes treatment and prevention of complications and prevention of amyloid deposition (treating the underlying hematologic malignancy). In patients with primary amyloidosis, the most common etiologies of PH are left-sided restrictive cardiomyopathy from amyloid deposition or diffuse lung disease.[10] Group I PH in amyloidosis is rare and can be managed with pulmonary vasodilator therapy as in previous reports.[8]

CONCLUSION

We present a patient with PH and amyloidosis secondary to multiple myeloma. PH as an isolated manifestation of cardiac amyloidosis is extremely rare. Amyloidosis should be considered as a possibility in unexplained PH in patients with myeloma.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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