CLINICAL VIGNETTE

A Rare and Interesting Case of Cardiac Amyloidosis

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Introduction

The Amyloidoses are a group of disorders caused by deposition of insoluble amyloid fibrils in tissues.[1] The major subcategories include light chain or primary (AL) which is associated with plasma cell dyscrasias, and secondary (AA), which is associated with chronic inflammatory disorders, and transthyretin-mediated (ATTR). ATTR subtype is further subdivided into hereditary ATTR, caused by mutation in the TTR gene, and wild-type (senile) ATTR which is mostly seen in the elderly.

The incidence of amyloidosis is approximately 0.5 - 1 cases per 100, 000 person-year and the peak age is between 60 – 79 years.[2,3] Frequently involved organ systems include the kidneys, heart, gastrointestinal tract, and peripheral nervous system. Involvement of the prostate is exceptionally rare with only a few cases reported in the literature.[4]

Case

A 71-year-old male with recently diagnosed prostate cancer was referred to cardiology for elevated NT-proBNP level of 452 pg/mL. His only cardiac symptom was mild dyspnea on exertion. He was previously noted to have an elevated prostate specific antigen (PSA) level of 17.8 ng/mL. MRI of prostate showed a lesion on the right side, suspicious for extracapsular extension, without gross adenopathy. Subsequent TRUS MRI fusion prostate biopsy revealed adenocarcinoma. Surgical pathology showed multiple biopsies with prostate adenocarcinoma, Gleason scores 4 + 4, and other biopsies with Gleason scores of 4 + 3. A second review of the biopsies also confirmed multiple amyloid deposits, ATTR subtype (transthyretin). His past medical history also includes carpal tunnel syndrome, prostate cancer, hypertension, prediabetes, dyslipidemia, and coronary artery disease.

His 12 lead ECG showed normal sinus rhythm, low voltage QRS in the limb leads, and nonspecific T wave abnormalities in the inferior leads. Echocardiogram showed normal left ventricular ejection fraction with concentric left ventricular hypertrophy. Cardiac magnetic resonance imaging (MRI) demonstrated biventricular hypertrophy with delayed enhancement in a patchy and sub-endocardial distribution (consistent with infiltrative cardiomyopathy). BNP was within normal limits. He had no family history of cardiomyopathy. ATTR gene sequencing was negative. Technetium Pyrophosphate Scintigraphy showed diffusely increased tracer activity throughout the myocardium consistent with cardiac amyloidosis. Ambulatory cardiac monitoring showed short runs of supraventricular tachycardia.

He underwent radical prostatectomy, and was started on Leuprolide, and for his amyloidosis he was started on Tafamidis, and furosemide. Hypertension was managed with metoprolol and Telmisartan.

Additional follow up imaging showed involvement of an iliac lymph node and he underwent salvage radiation therapy. On his most recent follow up at 31 months after presentation, his PSA level was undetectable with stable cardiac condition.

Discussion

Amyloidosis refers to a number of diseases that share in common the extracellular deposition of insoluble fibrillar proteins in different organ systems. The four major types of systemic amyloidosis include: Immunoglobulin (AL) amyloidosis, hereditary (or familial) amyloidosis, secondary (or reactive) amyloidosis (SAA), and senile amyloidosis. A fifth type has been described in patients with end stage kidney disease who are on hemodialysis.[5-8]

AL amyloidosis is the most common type, with an incidence of approximately 8.9 cases per million person years. Amyloid proteins can infiltrate a number of organ systems resulting in a variety of clinical syndromes that differ according to the type of amyloid protein and the organ system involved.[6]

Cardiac involvement is most common and most severe in AL amyloidosis, but it can be seen in all types of systemic amyloidosis.[6] These patients generally suffer from infiltrative (restrictive) cardiomyopathy and commonly present with signs and symptoms of right sided heart failure including peripheral edema, elevated jugular venous pressure, right sided S3 gallop (third heart sound), and hepatomegaly.[5] The conduction system can also be involved with a variety of cardiac arrhythmias.

Characteristic electrocardiographic findings are low voltage in the limb leads, and or loss of anterior forces consistent with anteroseptal infarction pattern.[6] Many patients with infarct pattern on 12 lead ECG do not have flow limiting atherosclerotic disease, and these abnormalities may be due to amyloid – mediated occlusion of smaller intramyocardial

arteries. The most common arrhythmias are atrial fibrillation and heart block.[9]

The most common echocardiographic findings include increased left and right ventricular wall thickness, valvular thickening and insufficiency, bi-atrial enlargement, pericardial effusion, and may also reveal high left sided filling pressure.[5]

The treatment and prognosis of cardiac amyloidosis depends on the underlying etiology of the disease. The prognosis for patients with AL type is poor median survival of 13 months without treatment and 17 months with cyclic oral Melphalan and prednisone.[10,11]

Only 5% of patients survive more than 10 years. Patients with cardiac involvement from familial amyloidosis have undergone combined heart and liver transplantation.[12]

Congestive heart failure from senile systemic amyloid may be more responsive medial therapy and has a better prognosis.

In AL and AA amyloidosis, treatment usually addresses the underlying plasma cell dyscrasia (AL) or the underlying inflammatory disorder (AA). Unfortunately, treatment options for wild-type ATTR amyloidosis are limited. Patients typically experience progressively debilitating symptoms related to cardiomyopathy and peripheral neuropathy.[13]

The median survival from diagnosis is 56.8 months.[14] More recently, Tafamidis, a small-molecule transthyretin stabilizer, has been shown to reduce all-cause mortality, decrease hospitalization rates, and improve functional outcomes in patients with cardiomyopathy caused by either hereditary or wild-type ATTR amyloidosis.[15]

The clinical presentation of syncope, orthostatic hypotension, nephrotic range proteinuria, pseudo-infarct pattern with low voltage on EKG and restrictive pattern on echocardiography strongly suggests the diagnosis of cardiac amyloidosis. As treatment ultimately depends on the cause of amyloid deposition, it is important to determine the various types of systemic amyloidosis before initiating therapy.

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