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Advanced systolic heart failure in undiagnosed cardiac amyloidosis

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Introduction

- Transthyretin (TTR) amyloidosis is characterized by extracellular deposition of hepatocyte derived TTR with hereditary and acquired variants.
- Of the >120 genetic mutations in the TTR gene, only a few are responsible for hereditary amyloidosis[1].
- The most common mutation in African-Americans is Val142Ile substitution, occurring with a frequency of 3.5%[2].
- Accumulation of misfolded TTR within the myocardium results in cardiac restriction and dysfunction, most commonly presenting as heart failure with preserved ejection fraction.
- Delay of diagnosis is associated worsening patient in a potentially treatable and reversible disease[3].
- Our case describes a patient who presented with advanced non-ischemic systolic heart failure with subsequent diagnosis of hereditary TTR cardiac amyloidosis.

History

- EP is a 72 year old African-American male with a past medical history of worsening non-ischemic heart failure diagnosed 20 years ago status post AICD placement in 2016 for low EF.
- Symptoms: worsening fatigue, generalized weakness, and exertional dyspnea limiting ambulation without assistance for two weeks prior to presentation.
- Family history: father and uncle died of heart failure.

Physical Exam and Laboratory Findings

- Vital Sings: Afebrile, SBP 70-80s, MAP 60s, HR 80-90, RR 16.
- Physical Exam: Thin, frail appearing male with JVD, bibasilar crackles and 3+ pitting lower extremity edema.
- BNP: 2,443 pg/mL.
- EKG: low-voltage tracings (Figure 1).
- Transthoracic Echocardiogram: left ventricular wall hypertrophy with biatrial enlargement and ejection fraction of 25% (Figures 2, 3).

Hospital Course

- Hypotension did not improve with dobutamine and norepinephrine was started.
- Genetic testing identified a valine to isoleucine substitution at position 142 (Val142Ile) in the TTR protein.
- Goals of care were discussed with family who decided to pursue comfort measures and the patient was discharged home.

Discussion

- TTR cardiac amyloidosis is the hereditary or acquired extracellular deposition of misfolded TTR proteins in the myocardium.
- Results in restriction and dysfunction, commonly presenting as heart failure with preserved ejection fraction[4].
- Val142Ile mutation has a frequency of approximately 3.5% in African-Americans and is likely to be underdiagnosed[2].
- Subtle clinical and imaging signs include a constellation of ventricular hypertrophy with a low amplitude voltage EKG, biatrial enlargement, heart failure with preserved ejection fraction, and arrhythmias.
- 99Te-pyrophosphate scintigraphy is the most sensitive and specific test for cardiac amyloidosis. Genetic testing has become more accessible if there is and index of suspicion.
- Tafamidis was approved by the FDA in 2019 and prevents progression of disease by stabilizing misfolded protein fibrils[4].
- Liver transplantation is the definitive therapy in patients diagnosed early in the disease course.
- Delay in diagnosis is associated with elevated BNP, troponins, development of systolic heart failure, fatal arrhythmias, or progressive heart failure[3].
- Our case is an example of late diagnosis with systolic heart failure.
- Clinical cues include ventricular wall thickness alongside reduced ejection fraction with absence of ventricular dilation inconsistent with non-ischemic cardiomyopathy.
- Low voltage EKG tracings, family history, and genetic testing further confirmed the diagnosis.

Conclusion

- With advancements in genetic testing, early detection of transthyretin amyloidosis could improve patient outcomes due to novel medical therapies and transplantation, preventing worsening heart failure and fatal arrhythmias.
- Cardiac amyloidosis should be considered in patients with worsening heart failure symptoms despite appropriate medical therapy with clinical findings associated with the disease.

References