The Medicine Forum

Volume 25 Article 9

2024

Investigating the Etiology of Non-Ischemic Cardiomyopathy; A Case Report of Cardiac Amyloidosis

Zachary Pang, MD
Thomas Jefferson University Hospital, zachary.pang@jefferson.edu

Joshua M. Riley, MD
Thomas Jefferson University Hospital, joshua.riley@jefferson.edu

Yair Lev, MD
Thomas Jefferson University, yair.lev@jefferson.edu

Recommended Citation

Pang, MD, Zachary; Riley, MD, Joshua M.; and Lev, MD, Yair (2024) "Investigating the Etiology of Non-Ischemic Cardiomyopathy; A Case Report of Cardiac Amyloidosis," *The Medicine Forum*: Vol. 25, Article 9.
DOI: https://doi.org/10.29046/TMF.025.1.008
Available at: https://jdc.jefferson.edu/tmf/vol25/iss1/9

CARDIOLOGY

Investigating the Etiology of Non-Ischemic Cardiomyopathy; A Case Report of Cardiac Amyloidosis

Zachary Pang, MD[1], Joshua M Riley, MD[1], Yair Lev, MD[2]

1. Department of Medicine, Thomas Jefferson University Hospital, Philadelphia, PA
2. Division of Cardiology, Jefferson Heart Institute, Department of Medicine, Thomas Jefferson University Hospital, Philadelphia, PA

INTRODUCTION

Amyloidosis is the result of misfolded protein deposition in organs and tissues, including the heart also known as cardiac amyloidosis. We describe a case of a patient presenting with decompensated heart failure, which highlights the importance of identifying the etiology of the patient's cardiomyopathy through a thorough history and physical. This led to a diagnosis of cardiac amyloidosis. The patient was subsequently initiated on tafamidis, a medication that is associated with reductions in all-cause mortality and cardiovascular-related hospitalizations, reduced decline in functional capacity, and improved quality of life of the patient.

CASE PRESENTATION

Subjective

An 87 year old male with a past medical history of heart failure with preserved ejection fraction (HFpEF) with New York Heart Association (NYHA) class IIIC, non-obstructive coronary artery disease, aortic stenosis status post transcatheter aortic valve replacement (TAVR) in 2020, paroxysmal atrial fibrillation on apixaban, hypertension, hyperlipidemia, stage 3b chronic kidney disease, carpal tunnel status post bilateral carpal tunnel release surgery, who presented as a direct admission from his outpatient Cardiologist's office. The patient reported increasing shortness of breath on exertion and lower extremity swelling over the past two weeks with an increase in his weight from 195 pounds to 207 pounds. The patient reported that he felt similar to when he was admitted to the hospital earlier this year for a heart failure exacerbation, where he was seen by cardiology and treated with intravenous diuresis. A few days prior, the patient was told by his outpatient cardiologist to double his home furosemide, but the patient reported poor urinary output response. Due to his progressive symptoms and weight gain, the patient was admitted to for volume overload.

Objective

Upon presentation, the patient's vital signs were stable. The patient was afebrile, with a heart rate of 68, blood pressure of 105/63, and saturating 97% on room air. On physical exam, the patient was well dressed, resting comfortably in bed, and not in acute distress. Jugular venous distention was noted to his jaw with hepatojugular reflex to his ear lobe. Cardiac exam was notable for an irregularly irregular rhythm. Lung exam was notable for decreased breath sounds and crackles at the lower lung bases. Abdominal exam was benign with notable scrotal edema. Lower extremities were notable for +2 pretibial pitting edema bilaterally that was non-tender and non-erythematous.

The patient's laboratory results showed complete blood count, hepatic function panel, and basic metabolic panel grossly within normal limits with the exceptions of a hemoglobin of 9.3 g/dL and a creatinine of 1.6 mg/dL, both near his baseline during his prior admission for volume overload. Brain natriuretic peptide was 4,266 from 4,490 pg/mL during his prior admission. High sensitivity troponin 73 with two-hour repeat of 71 ng/L.

Electrocardiogram (ECG) showed rate controlled atrial fibrillation at 70 beats per minute and low voltage QRS, which was similar to prior ECG (**Figure 1**).

Echocardiogram showed normal left ventricular (LV) chamber size, concentric remodeling with normal LV systolic function without segmental wall motion abnormalities. Estimated LV ejection fraction was 65%. Normal right ventricular (RV) size, mild RV hypertrophy, with low-normal RV function. TAVR valve present in aortic position appeared grossly normal with minimal prosthetic valve stenosis or regurgitation. Compared to prior study, images were grossly similar with gradients through aortic valve slightly higher and pulmonary artery systolic pressure was higher.

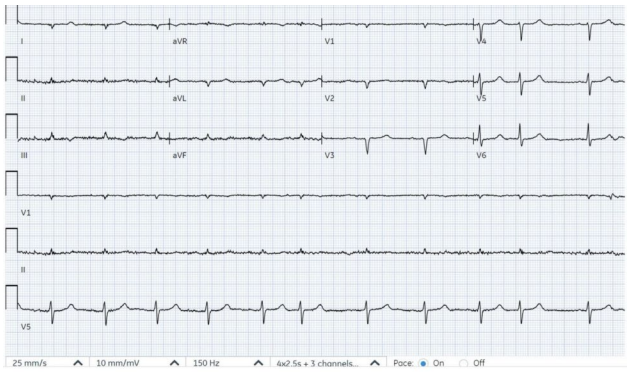

Figure 1: Electrocardiogram on admission

The patient's prior left heart catherization in 2020 showed moderate non-obstructive coronary artery disease with distal left main 10% stenosis, mid left anterior descending 50% stenosis, and minimal luminal irregularities in the ramus intermedius, left circumflex, and right coronary artery.

Diagnosis

The patient's HFpEF was thought to be secondary to non-ischemic cardiomyopathy (NICM). However, the etiology of the NICM was previously unknown. Upon review of the patient's entire history including HFpEF NYHA class IIIC secondary to NICM, aortic stenosis status post TAVR, paroxysmal atrial fibrillation, low voltage ECG, increased RV and LV wall thickness on echocardiogram, stage 3b chronic kidney disease, and bilateral carpal tunnel release surgery, there was a high clinical suspicion for infiltrative cardiomyopathy, specifically cardiac amyloidosis as a cause of the patient's NICM. A technetium-99-m pyrophosphate (T99-PYP) scintigraphy was performed which showed findings strongly suggestive of transthyretin (TTR) amyloidosis (**Figure 2**). Amyloid light chain labs were unremarkable. Thus, the patient was diagnosed with TTR amyloidosis, started on tafamidis, and planned to undergo genetic testing as an outpatient with consideration of starting other cardiac amyloidosis medications such as patisiran and inotersen.

DISCUSSION

Amyloidosis is a serious progressive disease that results from the deposition of misfolded protein fragments into the extracellular space of organs, including the heart. Cardiac amyloidosis has a wide variety of clinical manifestations depending on the organs involved and the type of amyloidosis. There are two main types of amyloidosis which make up approximately 95 percent

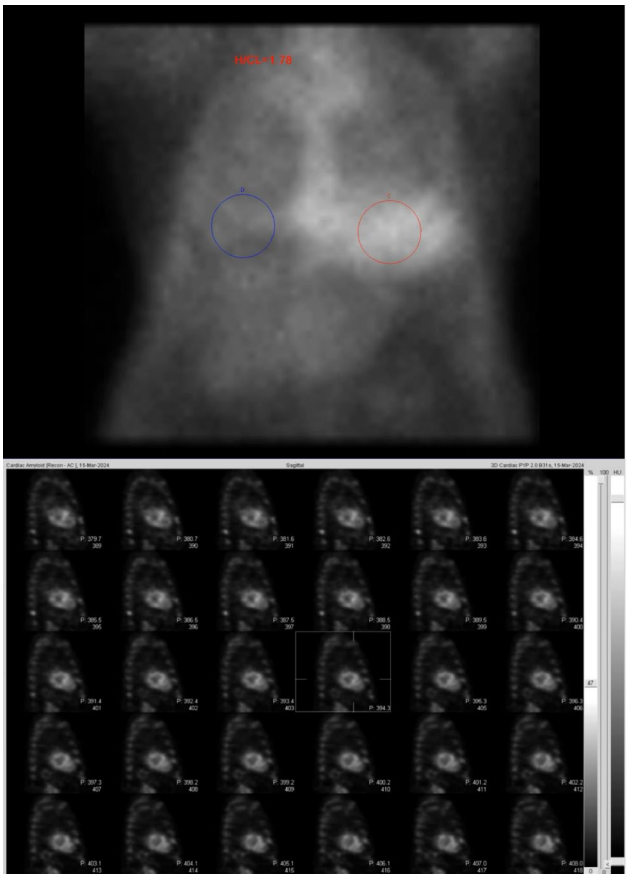

Figure 2: Technetium 99m pyrophosphate scintigraphy of the patient. Top image showing the heart to contralateral lung (H/CL) ratio measuring 1.78, which is strongly suggestive of cardiac amyloidosis. Bottom image confirming radiotracer uptake in the myocardium.

of cardiac amyloidosis, which include light chain amyloidosis and TTR amyloidosis. TTR amyloidosis can be further broken down to wild-type TTR amyloidosis and hereditary TTR amyloidosis. The TTR protein, which is responsible for the transport of thyroid hormone and retinol, is naturally synthesized by the liver. However, when this protein is misfolded, it deposits into systemic organs such as the heart, leading to LV hypertrophy and/or heart failure.

In addition to heart failure, other common cardiac manifestations of TTR amyloidosis include aortic stenosis, atrial fibrillation, syncope, heart block, and a low voltage ECG. Castano *et al.*, studied 151 patients undergoing TAVR for aortic stenosis and of these patients they found that 16% of these patients had TTR amyloidosis by T99-PYP scan. Atrial fibrillation is also associated with cardiac amyloidosis with studies estimating the prevalence of atrial fibrillation to be around 38% in patients with wild-type TTR amyloidosis and these patients are at high risk of thromboembolic events.

https://jdc.jefferson.edu/tmf/vol25/iss1/9
DOI: https://doi.org/10.29046/TMF.025.1.008

Cardiac amyloidosis not only affects the heart, but it can affect various organs as well. Extracardiac manifestations of cardiac amyloidosis include peripheral neuropathy, carpal tunnel, kidney disease, macroglossia, and gastrointestinal manifestations. Sekijima *et al.*, examined 100 patients undergoing carpal tunnel release surgery, and found that one out of every three patients had TTR amyloidosis by tendon tissue biopsy. Kidney disease, including asymptomatic proteinuria and nephrotic syndrome can be prevalent as well and should be screened and monitored for in patients with amyloidosis.

When providing care for patients with NICM, it is important to have a broad differential for their heart failure. When patients present with some or all of the cardiac and extracardiac pathologies as mentioned above, it should raise clinical suspicion for cardiac amyloidosis and further diagnostic testing should be considered. Diagnosing cardiac amyloidosis is not only of academic clinical significance, but it also has important therapeutic implications for the patient. Tafamidis is a medication that stabilizes the TTR tetramers and slows the formation of misfolded amyloid, which is thought to slow the progression of the disease overall. Tafamidis has been associated with reductions in all-cause mortality and cardiovascular-related hospitalizations, reduced decline in functional capacity, and improved quality of life in patients with TTR amyloidosis. Other therapies include RNA-targeted therapies that interfere with hepatic TTR synthesis, such as patisiran and inotersen. In addition, there are many medications currently being studied that have the potential to become therapeutic options in the near future.

CONCLUSION

Cardiac amyloidosis should remain high on one's differential when a patient with non-ischemic cardiomyopathy presents with cardiac manifestations including aortic stenosis, atrial fibrillation, increased LV wall thickness, low voltage ECG, and extracardiac manifestations including carpal tunnel, chronic kidney disease, peripheral neuropathy, macroglossia, and/or gastrointestinal symptoms. Having a high clinical suspicion for cardiac amyloidosis with the aforementioned manifestations is of utmost importance. If a patient is correctly diagnosed with TTR amyloidosis, the patient can be considered for medical therapies that are associated with reductions in all-cause mortality and cardiovascular-related hospitalizations, reduced decline in functional capacity, and improved quality of life of the patient.

REFERENCES

1. Castaño A, Narotsky DL, Hamid N, et al. Unveiling transthyretin cardiac amyloidosis and its predictors among elderly patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. *Eur Heart J.* 2017;38(38):2879-2887. doi:10.1093/eurheartj/ehx350
2. Cavalcante, João L et al. "Cardiac amyloidosis is prevalent in older patients with aortic stenosis and carries worse prognosis." *Journal of cardiovascular magnetic resonance : official journal of the Society for Cardiovascular Magnetic Resonance* vol. 19,1 98. 7 Dec. 2017, doi:10.1186/s12968-017-0415-x
3. Finsterer J, Iglseder S, Wanschitz J, Topakian R, Löscher WN, Grisold W. Hereditary transthyretin-related amyloidosis. *Acta Neurol Scand.* 2019;139(2):92-105. doi:10.1111/ane.13035
4. Gertz MA, Benson MD, Dyck PJ, et al. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. *J Am Coll Cardiol.* 2015;66(21):2451-2466. doi:10.1016/j.jacc.2015.09.075
5. Longhi S, Quarta CC, Milandri A, et al. Atrial fibrillation in amyloidotic cardiomyopathy: prevalence, incidence, risk factors and prognostic role. *Amyloid.* 2015;22(3):147-155. doi:10.3109/13506129.2015.1028616
6. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. *N Engl J Med.* 2018;379(11):1007-1016. doi:10.1056/NEJMoa1805689
7. Sekijima Y, Uchiyama S, Tojo K, et al. High prevalence of wild-type transthyretin deposition in patients with idiopathic carpal tunnel syndrome: a common cause of carpal tunnel syndrome in the elderly. *Hum Pathol.* 2011;42(11):1785-1791. doi:10.1016/j.humpath.2011.03.004
8. Sipe JD, Benson MD, Buxbaum JN, et al. Amyloid fibril proteins and amyloidosis: chemical identification and clinical classification International Society of Amyloidosis 2016 Nomenclature Guidelines. *Amyloid.* 2016;23(4):209-213. doi:10.1080/13506129.2016.1257986