AUCTORES
Globalize your Research

Cardiology Research and Reports
John Davis Cantwell *

Open Access

Case Report

Carpal Tunnel Syndrome, Ruptured Biceps Tendon, History of Spinal Stenosis, And Shoulder Arthroplasty Surgery: Risk Factors for Cardiac Amyloidosis Especially in Older Patients

Thomas H. Murray, John Davis Cantwell *

Piedmont Heart Institute, 275 Collier Road, NW, Suite 500, Atlanta, Georgia 30309.

***Corresponding Author:** John Davis Cantwell, Piedmont Heart Institute, 275 Collier Road, NW, Suite 500, Atlanta, Georgia 30309.

Received date: March 31, 2023; Accepted date: April 10, 2023; Published date: April 18, 2023

Citation: Thomas H. Murray, John D. Cantwell, (2023), Carpal Tunnel Syndrome, Ruptured Biceps Tendon, History of Spinal Stenosis, and Shoulder Arthroplasty Surgery: Risk Factors for Cardiac Amyloidosis Especially in Older Patients, *Cardiology Research and Reports*. 5(1); **DOI:**10.31579/2692-9759/093

Abstract

Cardiac amyloidosis, especially the wild type, is not uncommon if one looks for it in patients with certain prior orthopedic issues, as evidenced by this report of six recent cases.

Keywords: diagnostic test; cardiac amyloidosis; carpal tunnel surgery; heart muscle; blood test

Introduction

With a new diagnostic test to detect cardiac amyloidosis (CA), [1,2] namely the technetium pyrophosphate (PYP) nuclear scan (Tech pyp) and also a new drug to treat the condition, tafamidis (Vyndamax), it behooves us to do a better job identifying the disorder.

A recent study showed that a man over 70 who has had bilateral carpal tunnel surgery in the past 5-15 years has a 20% chance of having CA. [3]

Other risk factors for the disease include prior rupture of a bicep's tendon, spinal stenosis, and shoulder arthroplasty. [4]

Cardiac amyloidosis results from changes in the normal ATTR protein, originally shaped like a 4-leaf clover, produced in the liver, and transports thyroid hormone and vitamin A throughout the body. For various reasons, including heredity and aging, the 4-leaf clover can break down into the individual 4 leaves, becoming amyloid, and invading especially heart muscle and peripheral nerves.

Case Reports

The following six cases illustrate how the disorder can present.

Case #1

A 79 y/o former college football player had a history of a prior carpal tunnel problem. A Tech pyp scan identified cardiac amyloidosis, considered "wild type" in the absence of a positive genetic screening test and blood and urine test to exclude light chain amyloid AL (which can be found in multiple myeloma.)

Case #2

An 80 y/o former professional athlete had a history of a right carpal tunnel syndrome and several prior shoulder replacement surgeries. A Tech pyp scan was ordered and positive again for wild type cardiac amyloidosis.

The patient is on tafamidis and doing well, combining strength and endurance training.

Case #3

An 84 y/o man had a combined history of several back surgeries for spinal stenosis and the presence of peripheral neuropathy.

His evaluation determined wild type cardiac amyloidosis. A recent echocardiogram indicated an ejection fraction of 55-60% and moderate concentric left ventricular hypertrophy, along with evidence of his prior aortic valve TAVR procedure.

Despite successful cardioversion for atrial fibrillation, he remains moderately dyspneic with exercise activity.

Case #4

A 72 y/o former college athlete had a prior history of a ruptured biceps tendon.

A Tech pyp scan was positive for cardiac amyloidosis shown to be the wild type, and he has been clinically stable on tafamidis.

Case #5

A 75 y/o male college professor had a history of a right biceps' tendon rupture and the carpal tunnel syndrome.

A Tech pyp scan was positive for cardiac amyloidosis. He is currently being worked up for likely wild type and awaiting tafamidis therapy.

He continues a distance cycling program without symptoms.

Case #6

An 82-year-old male physician had a history of prior bilateral carpal tunnel surgery. A recent article indicating a 20% chance of having cardiac amyloidosis led to a Tech pyp scan which was positive for what was eventually shown to be wild type.

Transient atrial flutter resulted in some dyspnea on his daily hour walk. When corrected he remains asymptomatic on tafamidis.

Discussion

Transthyretin amyloid cardiomyopathy (ATTR-CM) is a disease, previously considered to be rare, which is often missed as the cause of heart failure. Wild-type ATTR-CM (ATTRwt-CM) was formerly referred to as 'senile' ATTR-CM, as it normally occurs in later stages of life. Amyloid cardiomyopathy is caused by the deposition of amyloid fibrils in the heart. In the case of ATTR-CM, these fibrils come from the dissociation of the transthyretin (TTR) protein. TTR is mainly produced in the liver and is a transporter of retinol binding protein and Vitamin A, as well as thyroxine. TTR is a tetramer (made up of four subunits), and fibrils result from the dissociation of these subunits. The deposition of these fibrils in cardiac tissue causes thickening of the ventricular wall, ventricular stiffening, and left ventricular diastolic dysfunction.

While ATTRwt-CM makes up the majority of ATTR-CM cases, variant ATTR-CM (ATTRv-CM) is another form. ATTRv-CM is an inheritable version of ATTR-CM that is caused by a mutation in the genome, most often of Valine to Isoleucine at position 122 (V122I) of the TTR gene. This genetic mutation is most common in Black populations, with the prevalence being about 3-4% in this population.

ATTRwt-CM has been previously underdiagnosed because biopsy, often performed post-mortem, was the standard for diagnosis. However, more noninvasive screening methods have helped bring awareness and increase diagnosis of the disease. Furthermore, there is now an approved therapy specifically for cardiac amyloidosis, and other therapies are showing promising preliminary results.

When it is suspected that cardiac amyloidosis may be present in a patient, blood tests and scanning are the recommended methods of screening. First, it is important to have a serum free light chain assay, serum protein electrophoresis with immunofixation (SPIE), and preferably urine protein electrophoresis with immunofixation. These tests are important for ruling out amyloid light (AL) chain amyloidosis. AL amyloidosis is a disease caused by the deposition of immunoglobin light chain in tissues. AL cardiomyopathy (AL-CM) progresses rapidly, so it is important to ensure that this can be ruled out prior to proceeding with further ATTR-CM testing.

With AL-CM ruled out, the next step is pyrophosphate (PYP) bone scintigraphy with technetium (Tc) labeled bisphosphonates. These Tc labeled PYPs localize to amyloid and can show if there is amyloid deposition in the heart. Furthermore, a single photon emission computerized tomography (SPECT) scan is also needed to confirm that the amyloid deposition is in the myocardium and not one of the ventricles. With these labs and scans, the specificity of ATTR-CM diagnosis approaches 98%.

Along with increased ease in diagnosing ATTR-CM, newly available treatments have improved care options for patients. Currently, tafamidis is the only US-FDA approved medication for ATTR-CM. Tafamidis is a TTR stabilizer, meaning that it prevents further progression of ATTR-CM by not allowing TTR to dissociate into fibrils. In clinical trials, the patient group receiving tafamidis had a 30% reduction in all cause mortality after 30 months. Cardiovascular hospitalization was also reduced at a similar level (32%) in patients receiving tafamidis treatment. These trials also suggested that tafamidis is more effective the earlier treatment is started in regards to the disease.

While tafamidis is an exciting new therapy for ATTR-CM, its price is a significant barrier to widespread use. Currently, the price of tafamidis annually is $225,000. This high price makes it increasingly important to determine what patients will respond positively and gain the most benefit from this medication.

Other ATTR-CM therapies are currently in clinical trials. One type of therapy that is not yet approved is TTR silencing agents, such as patisiran and vutrisiran. Patisiran and vutrisiran work via small interfering RNA (siRNA) mechanisms. Inotersen is another TTR silencing agent that is effective as an antisense oligonucleotide for TTR. Excitingly, as TTR stabilizers and TTR silencers work via different mechanisms and at different points in the etiology of ATTR-CM, they potentially could be used together for treatment. Therapies that work to reverse amyloid disposition in the heart, rather than prevent further progression, are a goal. This type of therapy is approved of amyloid neuropathy, but thus far trials with cardiac amyloidosis have not been successful.

With these noninvasive screening methods and available treatments for ATTR-CM, it is increasingly important to know who and when to screen patients for the disease. The American College of Cardiology defined the population to screen for ATTR as men over 65 and women over 70 years old who have heart failure and a thickened ventricle, defined as anything 14mm or thicker. Furthermore, they have determined certain 'red flags' that point to a higher possibility of ATTR-CM. These red flags include reductions in global longitudinal strain, diastolic dysfunction on echocardiogram, increased left ventricular thickness, symptoms of polyneuropathy, history of bilateral carpal tunnel syndrome, and mild increases in troponin levels on multiple occasions. As bilateral carpal tunnel and polyneuropathy, along with biceps tendon rupture, shoulder replacement surgery, and spinal stenosis are red flags for ATTR-CM, it is important to spread awareness to other medical specialties so that they can look out for these and refer the patient to a cardiologist.

Tafamidis is an effective drug to treat the condition as it helps to reduce the breakdown of the ATTR protein. So-called silencing drugs are coming soon and will help subsequently reduce hepatic production of ATTR. Immunotherapy and genetic editing via CRISPR are on the horizon.

A support group (amyloidosissupport.com) helps both patients and physicians to keep up with rapid advances in the therapy of this disease.

Acknowledgments

The authors have no conflicts of interest to disclose.

References

1. Bloom MW, Gorevic PD. (2023). Cardiac amyloidosis. *Ann Int Med*; 176: ITC 33-48.
2. (2023). ACC expert consensus decision pathway on comprehensive multi-discipline care for the patient with cardiac amyloidosis. *J Am Coll Cardiol*; 81: 1076-1126.
3. Westin O, Fosbol EL, Mauer MS, et al. (2022). Screening for cardiac amyloidosis 5-15 years after surgery for bilateral carpal tunnel syndrome. *J Am Coll Cardiol*; 80: 967-977.
4. Basdavanos A, Maurer MS, Ives L, et al. (2023). Prevalence of orthopedic manifestations in patients with cardiac amyloidosis with a focus on shoulder pathology. *Am J Cardiol*; 190: 67-74.

DOI:10.31579/2692-9759/093