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(CASE REPORT)

Wild-Type Transthyretin Cardiac Amyloidosis with Multiple Organs Involvement: Case Report and a Brief Review of the Literature

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Abstract

Wild-type transthyretin cardiac amyloidosis (ATTRwt-CA) is a progressive, underdiagnosed, and lethal restrictive cardiomyopathy, which is gaining more recognition as a heart failure with preserved ejection fraction (HFpEF) cause in the elderly. The diagnosis is challenging because this condition occurs without distinctive manifestations. Older methods of diagnostic intervention were mainly based on invasive endomyocardial biopsy. This paper provides the case of a 66-year-old male with progressive dyspnea, a bilateral carpal tunnel syndrome history, with echocardiographic findings of concentric left ventricular hypertrophy with apical sparing strain pattern. Diagnosis was made without the use of invasive methods: a positive Technetium-99m PYP scintigraphy (Grade 3 uptake) and a rule out of monoclonal gammopathy, which were later confirmed by endomyocardial biopsy and mass spectrometry.

This case illustrates the importance of identifying non-cardiac warning signs and utilizing a streamlined diagnostic algorithm to achieve early and accurate subtyping. Following the necessary evaluations by a multidisciplinary team, the patient was diagnosed with Stage II ATTRwt-CA disease and started undergoing disease-modifying therapy, Tafamidis meglumine, in conjunction with optimized heart failure management. The patient clinical course had been stable over the last two years, which determines the significance of timely and accurate diagnosis and the introduction of effective treatment in altering the natural history of ATTRwt-CA. This report can be used to raise the awareness of clinicians about the contemporary diagnostic pathway and therapeutic imperative of this challenging condition.

Keywords: Cardiac amyloidosis; Wild-Type Transthyretin; Light Chain; Hereditary; Heart failure; Genetic sequencing

1. Introduction

An example of a relatively newly recognized and potentially lethal restrictive cardiomyopathy is wild-type transthyretin cardiac amyloidosis (ATTRwt-CA), also known as senile systemic amyloidosis. This condition is due to an aberrant folding and accumulation of wildtype (non-mutated) transthyretin protein in amyloid fibrils within the myocardial interstitium, which results in progressive ventricular wall thickening, stiffening, and development of heart failure with preserved ejection fraction (HFpEF). [1] The clinical presentation is usually indolent with features of heart failure and frequently preceded by noncardiac warning symptoms including bilateral carpal tunnel syndrome, spinal stenosis, and tendon ruptures. [2] ATTRwt-CA and AL (Light Chain) AMY are two distinct forms of amyloidosis with dissimilar pathogenesis, and prognostic implications. AL amyloidosis results from aberrant light chains released by plasma cells,

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whereas ATTRwt (wild-type transthyretin) is the consequence of deposition of anormal protein in myofibrils that becomes unstable with time. [1] **Table 1** summarizes the characteristics of AL (Light Chain) and ATTRwt (Wild-Type Transthyretin) amyloidosis.

ATTRwt-CA has had a difficult history of diagnosis because it can be present in a non-specific manner, which is usually confused with hypertensive heart disease. Nevertheless, the diagnostic picture has changed greatly, and the current standard is based on a non-invasive method including a positive Technetium-99m pyrophosphate (PYP) scintigraphy in combination with the exclusion of monoclonal gammopathy beyond any doubt. [3] The diagnosis should be accurate and timely since the development of disease-modifying therapies has changed the paradigm of managing the disease. The management is focused on TTR stabilizers, including Tafamidis that are designed to prevent the disease progression by blocking the dissociation of the tetramer, and careful supportive management of the symptoms of heart failure. [4] As the underdiagnosis still occurs and early intervention is a key to better results, we present this case to expand the literature, thus increasing clinical awareness and supporting the use of contemporary diagnostic and treatment methods of the problematic condition.

Table 1 Summary of key features of AL (Light Chain) and ATTRwt (Wild-Type Transthyretin) amyloidosis

Feature	AL (Light Chain)	ATTRwt (Wild-Type Transthyretin)
Pathogenesis	Immunoglobulin light chain deposition (plasma cell clone)	Wild-type transthyretin deposition
Typical Patient	~60–70 y/o, slight male predominance	>65–70 y/o, strong male predominance
Systemic Involvement	Multisystem (kidneys, liver, GI, nerves)	Mainly cardiac; carpal tunnel/spinal stenosis
Onset/Progression	Rapid, poor prognosis untreated (<1–2 yrs)	Indolent, median survival 4–5+ yrs
Cardiac Features	Restrictive cardiomyopathy, low ECG voltage	Restrictive cardiomyopathy, preserved voltage, conduction disease
ECG Clues	Low QRS, pseudoinfarct	Normal/mildly reduced voltage, arrhythmias
Biomarkers	Monoclonal protein, ↑NT-proBNP, ↑troponin	No monoclonal protein, ↑NT-proBNP
Diagnostic Confirmation	Tissue biopsy + immunotyping	99mTc-PYP/DPD/HMDP scintigraphy (grade 2–3) + gene testing
Treatment	Chemotherapy (bortezomib), stem cell transplant, supportive	Tafamidis, supportive, TTR silencers (research)
Prognosis	Poor unless treated early	Better, slower progression

2. Case presentation

2.1. Clinical presentation and initial assessment

A 66-year-old male presented to the cardiology clinic with eight months of progressive exertional dyspnea, fatigue, and lower extremity edema. The symptoms were originally perceived to be due to the aging process and deconditioning, though they steadily worsened up, even with mild exercise efforts.

Initially, symptoms occurred with moderate exertion, but later he had trouble breathing at rest. New orthopnea with the use of three pillows and paroxysmal nocturnal dyspnea occurred. He denied chest pain but reported unusual fatigue that restricts his daily activities. The patient had a medical history of hypertension for 15 years, osteoarthritis (involved bilateral carpal tunnel release 3 years ago), and chronic back pain (lumbar spinal stenosis). Five years ago, he had bilateral knee replacement operations. The patient had Type 2 diabetes that was diagnosed two years ago and was managed by lifestyle modifications. The patient was a non-smoker, rare alcohol use, and reported frequent rotator cuff tendinopathy. No significant family history was reported.

2.2. Physical examination and laboratory studies

The patient was a well-developed man in mild distress. Vital signs included; blood pressure 118/68 mmHg, heart rate 78beats /minute, regular, respiratory rate 18/minute, oxygen saturation 94% room air. Jugular venous pressure was increased to 10 cm. Cardiac examination showed that the apical impulse is laterally displaced, there was S4 gallop and soft systolic apical murmur. Bibasilar rales were exhibited by the lungs. Abdomen soft hemidiaphragm hepatomegaly 2 cm below the costal margin. Pitting edema of the knees. Bilateral carpal tunnel surgery scars were evident in the musculoskeletal examination. Laboratory results indicated normal hemoglobin (14.1 g/dL), slightly increased creatinine (1.4mg/dl), normal albumin (4.1 g/dl), high NT-proBNP (3300 pg/mL) low eGFR (eGFR 55 mL/min), and slightly high troponin-T (0.06 ng/mL). ECG showed low voltage in the limb leads with a pseudo-infarct pattern (poor R-wave progression in the precordial leads).

2.3. Imaging studies and differential diagnosis

Echocardiography revealed concentric left ventricular hypertrophy (septum 17 mm, posterior wall 16 mm), small cavity, preserved ejection fraction (58%), restrictive filling, and grade III diastolic dysfunction. Granular texture of the myocardium was present. Longitudinal strain imaging showed an apical sparing pattern with less global strain (-9%), a typical "bulls-eye" pattern. Mitral and tricuspid regurgitation were mild. The cardiac MRI displayed enlargement of the left ventricular wall thickness, biatrial enlargement, and diffuse subendocardial late gadolinium enhancement. High native T1 (1100 ms) and extracellular volume (42%), suggestive of an infiltrative process. Technetium-99m PYP scintigraphy exhibited grade 3 cardiac uptake (greater than ribs) with a heart-to-contralateral lung ratio of 1.8 (>1.5 diagnostic), very specific to ATTR cardiac amyloidosis in the presence of absent monoclonal protein. Chest X-ray showed cardiomegaly without pulmonary edema. Differential diagnosis included ATTR cardiac amyloidosis (wild-type vs hereditary), hypertrophic cardiomyopathy, hypertensive heart disease with heart failure with preserved ejection fraction, AL amyloidosis, restrictive cardiomyopathy (sarcoidosis, hemochromatosis), aortic stenosis with LVH.

History of carpal tunnel syndrome, spinal stenosis and a combination of cardiac hypertrophy, grade 3 PYP uptake and red flags in the clinical setting are strong indicators in support of ATTRwt amyloidosis.

2.4. Diagnostic Studies and Final Diagnosis

Screening of monoclonal protein of serum and urine immunofixation electrophoresis showed provided results. Free light chains in serum were normal and with kappa/ lambda of normal 1.1 ratio. This ruled out high sensitivity AL amyloidosis. Genetic testing for the TTR gene sequence showed that there are no pathogenic variants, which identifies the wild-type ATTR phenotype instead of a hereditary variant (ATTRv). Endomyocardial biopsy (done to confirm despite non-invasive diagnosis) showed massive amorphous hyaline, eosinophilic extracellular deposits. Apple-green birefringent Congo red stain was positive. (**Figure 1 A, B, C**) Transthyretin was strongly positive with immunohistochemical staining, without light chains and amyloid A protein. The presence of wild-type transthyretin proteins was verified by mass spectrometry.

With a grade 3 cardiac PYP uptake, lack of monoclonal gammopathy, a wild-type TTR gene, non-invasive diagnosis was made based on the current guidelines. Biopsy was confirmatory of ATTRwt (wild-type transthyretin, also known as senile) cardiac amyloidosis, non-hereditary age-related systemic amyloidosis.

2.5. Other Organ Involvement

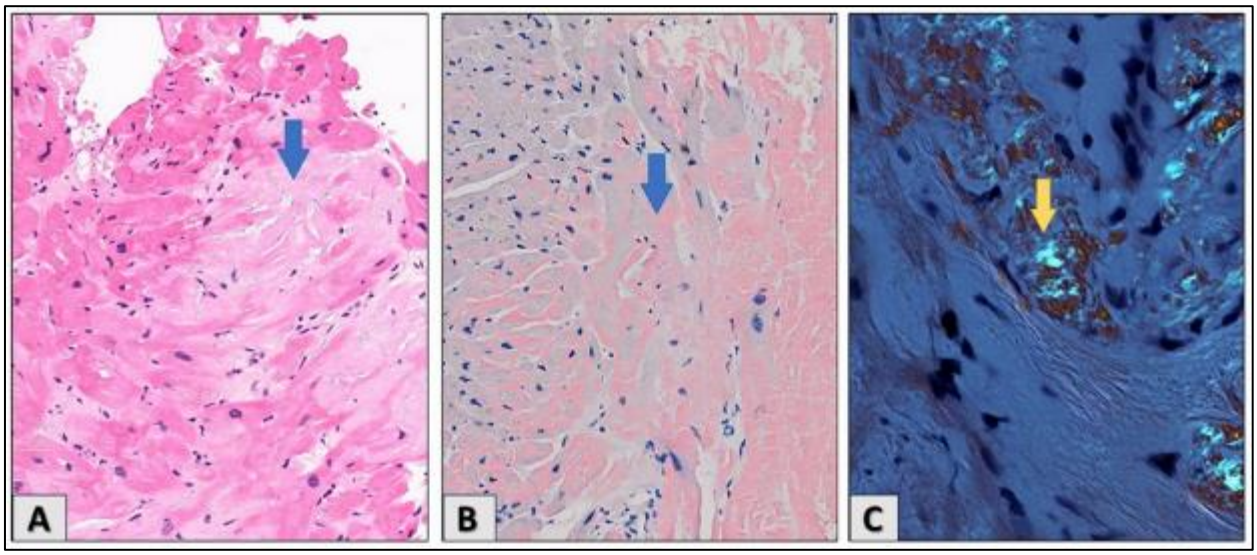
History of bilateral carpal tunnel syndrome undergoing surgical release three years prior to cardiac diagnosis is a typical red flag of ATTRwt. A lumbar spinal stenosis with chronic back pain is probably an indication of deposition of amyloid in the spinal ligamentum flavum. History of biceps tendon rupture and the frequent rotator cuff problems related to ATTRwt. A regular imaging is not undertaken unless there is an urgent need to undergo symptomatic management. In ATTRwt there is minimal involvement of the kidneys as compared to AL. Mild renal dysfunction (eGFR 55 mL/min) is probably an effect of hypertension, diabetes, and decreased cardiac output and not direct amyloid nephropathy. Urinalysis revealed trace protein, no nephrotic-range proteinuria. Amyloid deposition of the kidneys was possible, but with few clinical consequences. Mild distal sensory neuropathy was present on examination, but not as pronounced as expected in AL amyloidosis. Nerve conduction examination revealed mild axonal neuropathy. Mild orthostatic hypotension was present (blood pressure decreases 20/10 mmHg on standing). No other organs involvement was detected.

2.6. Multidisciplinary Tumor Board Discussion, Treatment, and outcome

The case was discussed in a multidisciplinary team of cardiologist, heart failure specialist, amyloidosis specialist, geneticist, radiologist, clinical pharmacist, pathologist, advanced practice providers, and palliative care team. Points of discussion were the confirmed diagnosis cardiac amyloidosis ATTRwt without any hereditary component (no need of genetic counseling), disease stage, II or III, based on eGFR and NT-proBNP, treatment options available with disease-modifying therapy, symptom management and quality of life optimization, education regarding natural history. With the high NT-proBNP (3300 pg/mL) and low eGFR but higher than 45 (eGFR 55 mL/min), the case was classified as Stage II based on the National Amyloidosis Centre (NAC) staging criteria.

Disease modifying therapy was provided including Tafamidis meglumine 61 mg one tablet daily, orally. This drug is an anti-tetrameric TTR stabilizer to inhibit dissociation of tetramers to amyloidogenic monomers. For management of heart failure, loop diuretics were used cautiously (beginning with 40 mg per day), and the patient was kept euvolemic. For management of arrhythmia, minute by minute monitoring of the development of atrial fibrillation (in sinus rhythm) was initiated. Other supportive care measures included physical therapy to decondition, occupational therapy to activities of daily living, nutritional counseling with sodium limitation(2grams/day) to fluids and Midodrine to orthostatic symptoms when required, compression stockings, and musculoskeletal symptom management.

Monitoring protocol included monthly visits to optimize volume initially, NT-proBNP and troponin after every 3 months, echocardiography after every 6 months, annual cardiac MRI, 6-minute walk-test every 3 months, quality of life measures (Kansas City Cardiomyopathy Questionnaire). The patient responded well to the treatment and experienced a stable condition during a two years period, after which he was lost to follow-up.



1A: High power view of cardiac muscle showing amyloid pale-pink deposits, blue arrow (H&E stain X20); **1B:** Positive Congo red stain showing red to red-orange color (without polarized microscopy), blue arrow; **1C:** Positive Congo red under polarized microscopy showing amyloid deposits exhibiting a characteristic apple-green birefringence, yellow arrow

Figure 1 Microscopic features of cardiac amyloidosis biopsy

3. Discussion

3.1. Background (History, Epidemiology, risk factors, classification, treatment, and outcome)

3.1.1. History

ATTRwt-CA has historically been described as senile systemic amyloidosis or senile cardiac amyloidosis due to its association with aging. The earliest descriptions related to "age-related cardiac amyloidosis" were in 1876 by Soyka. [**5**] Early autopsy studies have shown that older individuals regularly had amyloid deposits in their hearts, despite displaying no obvious clinical symptoms. With the advent of more advanced diagnostic tools in histology, immunohistochemistry, advanced imaging, and more recently, non-invasive nuclear scans, the comprehension of ATTRwt-CA has significantly expanded. It is now recognized that ATTRwt involves non-mutant (wild type) transthyretin causing a clinically relevant disease and not just incidental clinical findings noted at autopsy. [6]

3.1.2. Epidemiology and risk factors

ATTRwt-CA has a greater occurrence in older age groups than previously acknowledged. Elderly individuals, especially those in their 70-80s, have the majority of ATTR cases. [6] [7] However, males are most of the diagnosed cases. For instance, in a Mayo Clinic pre-mortem diagnosis cohort, about 91% of the patients were men. [7] Even so, autopsy studies covering TTR deposition showed that women did have some clinically insignificant TTR deposition, but these deposits are generally clinically silent and less extensive compared to men. [5] [7] Due to underdiagnosis, estimating true prevalence of the disease is challenging. Autopsy studies also indicate that about 1 in 4 (25%) elderly individuals above the age of 80 have TTR deposition in the heart. In patients diagnosed with HFpEF and left ventricle hypertrophy, bone scintigraphy studies report 13% prevalence rates among older patients. [6] [9] Also, without disease-modifying therapy, median survival after diagnosis is roughly 3.6 years. Patients typically present with heart failure symptoms, especially diastolic dysfunction, and may present with atrial arrhythmias, as well as a history of carpal tunnel syndrome or lumbar spinal stenosis in earlier years. [6] [7]

Older age and male gender are the primary risk factors of developing ATTRwt-CA. Although the precise pathogenesis has not been determined, it is a disease that occurs more often in men than women and the symptoms commonly begin after the age of 65 years. [8]

3.1.3. Classification

Diagnosis, prognosis, and treatment of cardiac amyloidosis, especially ATTRwt-CA, depend on sheer knowledge of the complexities of the disease. The protein precursor that leads to the formation of amyloids is an important component to the classification. Therefore, classification is based on the identification of the precursor protein, distinguishing between the wild-type and hereditary forms, as well as staging the disease by using the appropriate clinical biomarkers. [8] [9] The timely identification and classification of the condition are a prerequisite to the introduction of specific treatments that rapidly and markedly alter the course of the disease. For this condition, hereditary (variant) ATTRv amyloidosis is caused by certain pathogenic mutations or the misfolding of TTR gene. [6] As such, ATTRwt denotes the cases with wild-type (non-mutated) TTR and represents the non-hereditary TTR amyloidosis type. ATTRwt is also systemic (with predominant cardiac involvement and often soft-tissue deposits) and acquired (not inherited). It typically develops with age rather than being present from birth or due to inherited mutations. [6]

Because of the wide range of severity and prognosis, clinical classification and staging have been proposed. For instance, Grogan et al. from the Mayo Clinic described a staging system using biomarkers: N-terminal pro-B-type natriuretic peptide (NT-proBNP) and troponin T thresholds. [10] Based on these, three stages are defined, with markedly different median survivals: stage I (both biomarkers below threshold) ~ 66 months; stage II (stage I elevated) ~40 months; and stage III (both elevated) ~20 months. In addition, different societies provide diagnostic and disease classification guidelines. [7] [11] For example, the European Society of Cardiology and the Japanese Circulation Society have frameworks for the classification of cardiac amyloidosis, particularly by type (AL, ATTRv, and ATTRwt) and recommend diagnosing distinctions as treatments vary across types. [12]

3.1.4. Pathogenesis and pathophysiology

Senile systemic amyloidosis (renamed Wild-type transthyretin cardiac amyloidosis) is a progressive infiltrative cardiomyopathy that is caused by the misfolding and deposition of the non-mutated or wild-type transthyretin (TTR) protein [1]. TTR is a homotetrameric protein that is primarily synthesized in the liver and utilized to transport thyroxine and retinol. [13]

The disease mechanism involves the dissociation of full-size TTR tetramers into unstable monomers, followed by different folding into amyloidogenic intermediates. [14] These mediators accumulate and precipitate insoluble amyloid fibrils in the myocardial interstitium, leading to restrictive cardiomyopathy. The result of these fibrils is progressive thickening of the ventricular walls, myocardial rigidity, and a reduction in diastolic filling, resulting in HFpEF. [1] The mechanical and direct toxicity of the amyloid deposits contributes to the damage of myocytes, fibrosis, and the release of biomarkers, such as NT-proBNP and troponin, which serve as evidence of ongoing cardiac damage and hemodynamic dysfunction. [8]

3.2. Comparative analysis of our case with the existing literature

3.2.1. Clinical presentation and radiology

ATTRwt-CA is considered a key cause of HFpEF especially in older men. Several series and reviews indicate that extracardiac symptoms including bilateral carpal tunnel syndrome, lumbar spinal stenosis, and rotator cuff disease are

common predicates of cardiac disease. [16] [17] The presence of these symptoms should serve as clinical red flags for early recognition of ATTRwt-CA. [16] Our patient exhibited these precise features, with bilateral carpal tunnel release, spinal stenosis, and tendinopathy predating his cardiology presentation, which is highly consistent with existing patterns that are out there. The progressive dyspnea, orthopnea, and paroxysmal nocturnal dyspnea he developed are characteristic of wild-type transthyretin cardiac amyloidosis cohorts, though his diagnosis was made at a relatively younger age than is often reported. This reflects the trend toward earlier recognition due to greater clinical awareness. [17]

Echocardiographically, ATTRwt-CA typically manifests as concentric left ventricular hypertrophy with preserved ejection fraction, restrictive diastolic filling, and the highly specific "apical sparing" longitudinal strain pattern, which distinguishes it from hypertensive heart disease or hypertrophic cardiomyopathy. [18] The findings in our patient mirrored these canonical features. Cardiac MRI in published studies frequently shows diffuse subendocardial late gadolinium enhancement, elevated native T1, and markedly increased extracellular volume (ECV), correlating with amyloid infiltration and disease severity. [19] Our patient's MRI demonstrated diffuse subendocardial enhancement with increased T1 and ECV of 42%, which lies within the typical range reported in ATTRwt-CA. [20]

Finally, technetium-99m pyrophosphate (99mTc-PYP) scintigraphy has become a cornerstone of non-invasive diagnosis, with grade 2–3 myocardial uptake and a heart-to-contralateral ratio ≥1.5 considered highly specific for ATTRwt-CA when light chain amyloidosis is excluded. [21] [22] Our patient's scan demonstrated grade 3 uptake with a diagnostic H/CL ratio of 1.8 and absence of monoclonal protein, exactly fulfilling these established non-invasive diagnostic criteria.

The clinical profile and multimodality imaging findings in this case strongly align with the prevailing literature on ATTRwt-CA. His history of musculoskeletal red flags, classical echocardiographic and strain abnormalities, confirmatory cardiac MRI parameters, and diagnostic bone scintigraphy summarize the well-described disease phenotype. [**17**] The relatively younger presentation and absence of concomitant aortic stenosis, however, illustrate how ATTRwt-CA is gradually increasing, expanding the recognized spectrum of this underdiagnosed disease.

3.2.2. Diagnosis (Laboratory tests, pathology, IHC, and molecular findings)

The Diagnostic pathway of our patient exemplifies the existing gold standard for ATTRwt-CA, which is consistent with other guidelines. [23] The existence of red flag clinical manifestations, that is, bilateral carpal tunnel syndrome, lumbar spinal stenosis, and heart failure with preserved ejection fraction, was the key to triggering the amyloidosis workup. The utility of the non-invasive diagnostic pathway is confirmed in our case, as demonstrated by a positive Technetium-99m PYP scintigraphy (Grade 3 uptake) and the ultimate elimination of monoclonal gammopathy, as shown by serum and urine immunofixation and free light chain assay. [10]

This method eliminates the need for endomyocardial biopsy in most cases. The confirmatory biopsy in our patient, showing apple-green birefringence in the Congo red stain and high levels of TTR in the immunohistochemistry (IHC) with mass spectrometry confirmation, however, is an invaluable pathological correlate with the imaging data. The fact that no mutation of the TTR gene had been found further confirmed the diagnosis of the wild-type phenotype, which is distinct from the hereditary one (ATTRv). [14] It is a multi-modal method of diagnosis that is essential to proper subtyping, which, in turn, determines the further strategy of therapy.

3.2.3. Management and outcome

The management approach used in our patient can be said to represent a paradigm shift in the treatment of ATTRwt-CA, as it involves replacing the traditional approach of purely supportive care with a disease-modifying one. [4] The introduction of the TTR stabilizer Tafamidis meglumine marks the next step in the history of modern treatment, which aims to prevent the development of the disease by eliminating tetramer dissociation. More recent drugs have been developed since its introduction. [25] The urgency of the disease-specific intervention was justified by the high NT-proBNP level (3,300 pg/mL) and the mildly decreased eGFR level (55 mL/min) of our patient, which placed him in the Stage II disease category.

Additionally, careful monitoring of heart failure symptoms through judicious administration of loop diuretics, along with supportive interventions such as Midodrine for orthostatic hypotension and physical exercise, aligns with best practices in this restrictive cardiomyopathy. [4] The two-year stable course observed in our patient, before he was lost to follow-up, is a positive result that is consistent with the positive effect reported in the clinical trials, highlighting the role of early diagnosis and immediate TTR stabilization therapy. [12] This case highlights the importance of establishing

a systematic monitoring protocol, which should include serial NT-proBNP measurements, echocardiography, and functional testing, to assess disease stability and treatment effectiveness.

3.3. What have we learned from this case?

This case is a significant example of the changing clinical presentation and diagnostic course of ATTRwt-CA, offering practitioners several important lessons. To begin with, the case makes it clear that the non-cardiac "red flags," which include the history of bilateral carpal tunnel release and spinal stenosis, are highly crucial and usually manifest several years before the development of an overt cardiomyopathy [8]. These musculoskeletal signs must raise a high level of suspicion, especially among older male patients with heart failure. Secondly, the effective use of the non-invasive diagnostic algorithm, PYP scintigraphy with monoclonal protein exclusion, is indicative of a streamlined procedure that places patients at minimal risk and shortens the process of diagnosis. Third, the importance of a multidisciplinary team approach, which was key to staging the disease, eliminating hereditary forms, and developing a detailed treatment plan that included disease-modifying therapy (Tafamidis) combined with careful supportive care, is highlighted in the case. Finally, the fact that this patient responded positively to treatment at the beginning serves to remind the reader that the issue of early and proper diagnosis is no longer an academic exercise, but a requirement for successful intervention and life-saving treatment.

Abbreviations

Wild-type transthyretin cardiac amyloidosis (ATTRwt-CA); Immunohistochemistry (IHC); Heart failure with preserved ejection fraction (HFpEF)

4. Conclusion

We present this case of ATTRwt-CA to highlight the importance of increased clinical awareness and the systematic use of modern diagnostic protocols in this rapidly growing cause of heart failure. The combination of typical red flag signs in the patient, along with the ultimate non-invasive and pathological confirmation, provides an excellent case study for educational purposes. This report may assist clinicians in managing the diagnostic and therapeutic dilemmas associated with ATTRwt-CA. As this case illustrates, this can be achieved by outlining the effective adoption of a multidisciplinary approach with disease staging and the introduction of TTR stabilization therapy using Tafamidis. The case highlights that early diagnosis enables the commencement of disease-modifying treatment, which can alter the natural course of the disease that was previously fatal, thereby enhancing patient outcomes and quality of life. This report is added to the growing body of literature that supports the concept of intensive screening and timely intervention in at-risk groups.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors make the following declarations:

- Payment/services information: All authors have declared that they received no financial support from any organization for the submitted work.
- Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of ethical approval

Ethical review and approval were not required for this study involving human participants. The paper has been sufficiently anonymized to maintain the patient's confidentiality.

Statement of informed consent

The patient was lost to follow-up, and all attempts to reach the patient were unsuccessful. Therefore, the paper has been sufficiently anonymized to maintain patient confidentiality.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

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