

Atypical Case of Wild-Type Cardiac Amyloidosis with Septal Predominance and a Nonapical Sparing Strain Pattern



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INTRODUCTION

Transthyretin cardiac amyloidosis (ATTR-CA) is an underdiagnosed cause of heart failure.¹ Noninvasive imaging techniques are commonly used in the diagnosis of ATTR-CA without the need for biopsy.^{2,3} The presence of apical sparing is a classic sign of ATTR-CA on echocardiography and is associated with an adverse prognosis.^{4,5} However, varying patterns of ATTR-CA such as nonapical sparing forms can add to diagnostic challenges. In such cases, the need for a high index of suspicion together with multimodality imaging can be important to potentially allow for identification of discrete morphological variants and diagnosis at an earlier stage of the disease.⁶⁻⁸

We describe an atypical case of wild-type ATTR-CA with imaging evidence of amyloid deposition predominantly in the interventricular septum and a nonapical sparing pattern on echocardiography.

CASE PRESENTATION

A 62-year-old man with a 2-year history of progressive shortness of breath with moderate exertion presented for cardiac evaluation. He reported having undergone bilateral carpal tunnel release surgery 1 month prior to presentation after which he developed worsened exertional dyspnea, decreased stamina, and lower leg swelling. Electrocardiography showed postoperative typical atrial flutter with variable block associated with low-voltage criteria in the limb leads and poor R-wave progression across the precordial leads (Figure 1A). These symptoms significantly improved to New York Heart Association class I after oral diuresis and restoration of sinus rhythm following successful cardioversion (Figure 1B). Clinical findings suggested the possibility of amyloidosis. Guideline-recommended serum and urine testing to assess for light chain amyloidosis were performed, and this diagnosis was excluded.⁹ Additional lab testing included an elevated pro-brain natriuretic peptide of 1,400 ng/mL and a negative troponin T of <0.01 ng/mL.

Transthoracic echocardiography revealed biatrial enlargement, a left ventricular ejection fraction of 50%, increased septal wall thickness (~15 mm, best seen in the apical three-chamber view), and a

VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiography (apical three-chamber view) revealed moderately increased septal wall thickness (~15 mm) with a prominently echo-bright appearance of the anterior interventricular septum.

Video 2: Follow-up transthoracic echocardiography (apical four-chamber view) revealed stable strain values, again with relatively reduced regional values in the interventricular septum compared with the apex and left ventricular free wall.

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prominently echo-bright appearance of the interventricular septum (Figure 2, Video 1).

Right ventricular function appeared overall preserved, and tricuspid annular planar systolic excursion measurement was normal (visualization of the right ventricular free wall was inadequate for right ventricular strain measurement). Longitudinal strain imaging of the left ventricle revealed reduced septal strains and a nonapical sparing pattern (Figure 3A and B), and findings were replicated across two vendors (Philips Healthcare [Andover, MA]; GE Healthcare [Chicago, IL]).

Cardiac magnetic resonance imaging revealed moderately increased interventricular septal wall thickness (17 mm) with positive delayed gadolinium enhancement involving the right ventricular aspect of the interventricular septum and the right atrium (Figure 4A and B). Native T1 times (1,289 msec) and extracellular volume (52%) were significantly elevated, suggestive of cardiac amyloidosis.

Imaging with 99mTc-pyrophosphate revealed a semiquantitative visual score of grade 3 (heart greater than rib uptake on visual comparison) and a heart-to-contralateral ratio of 2.1 after 3-hour delay (above the threshold of 1.25 for diagnosis of ATTR-CA) with a septal predominance uptake pattern on single-photon emission computed tomography (Figure 5A-C).

Genetic testing for transthyretin mutations was negative. The patient was started on tafamidis, a transthyretin stabilizing agent, and remains stable after 8-month follow-up without deterioration in left ventricular function on follow-up echocardiography (Video 2).

DISCUSSION

This case details an atypical and unusual presentation of wild-type ATTR-CA with imaging evidence of amyloid deposition predominantly in the right ventricular aspect of the interventricular septum

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Conflicts of Interest: None.

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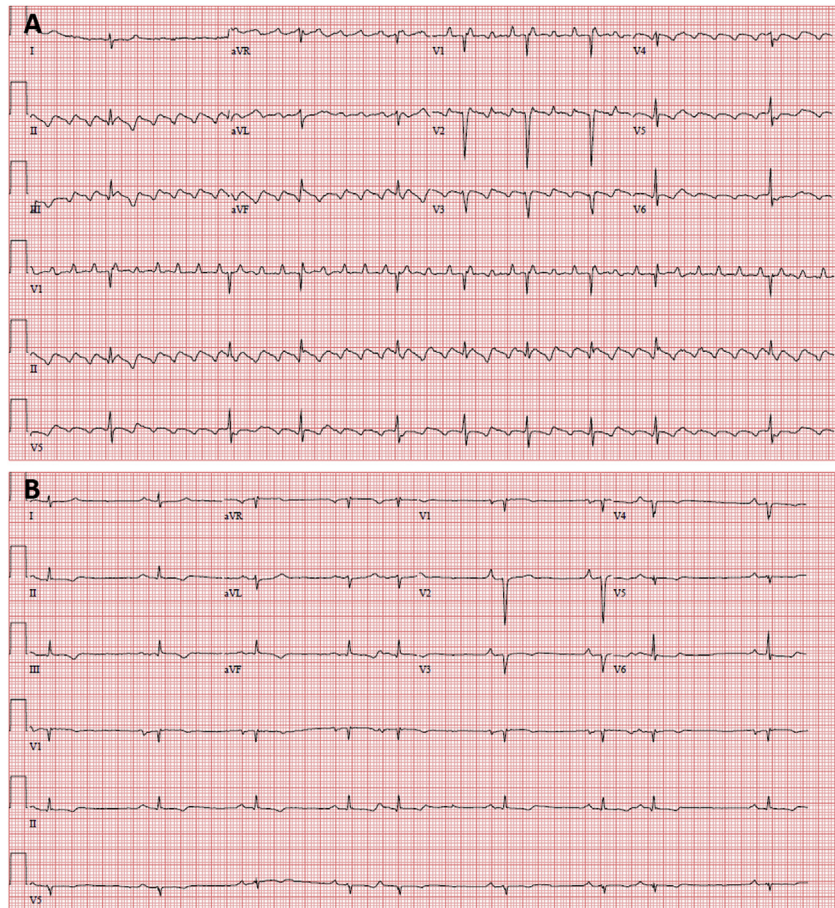


Figure 1 (A) Electrocardiogram-performed postcarpal tunnel surgery revealed typical atrial flutter with variable block, low-voltage criteria in the limb leads, and poor R-wave progression across the precordial leads. (B) Electrocardiogram-performed postcardioversion revealed restoration of sinus rhythm, again with low-voltage criteria in the limb leads and poor R-wave progression across the precordial leads.

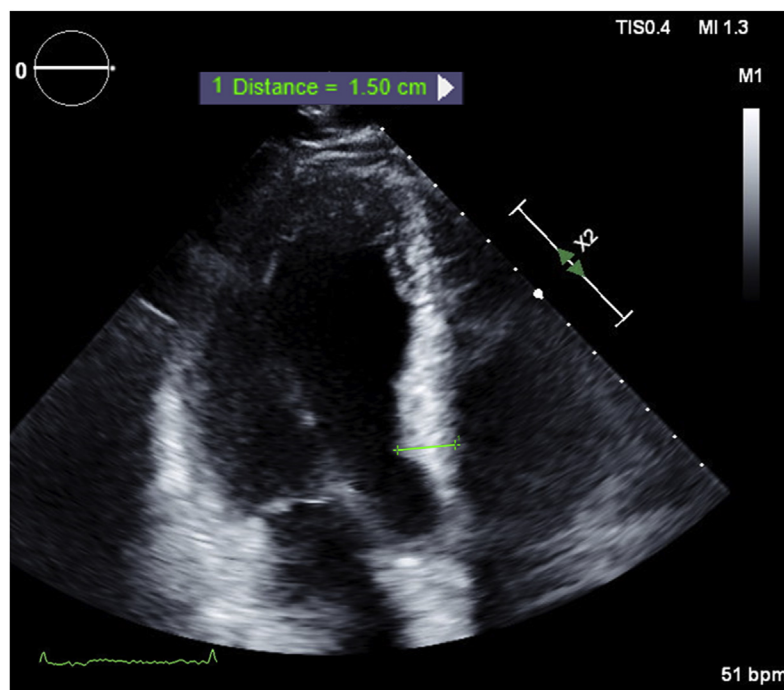


Figure 2 Transthoracic echocardiography (apical three-chamber view) revealed moderately increased septal wall thickness (~15 mm) with a prominently echo-bright appearance of the anterior interventricular septum.

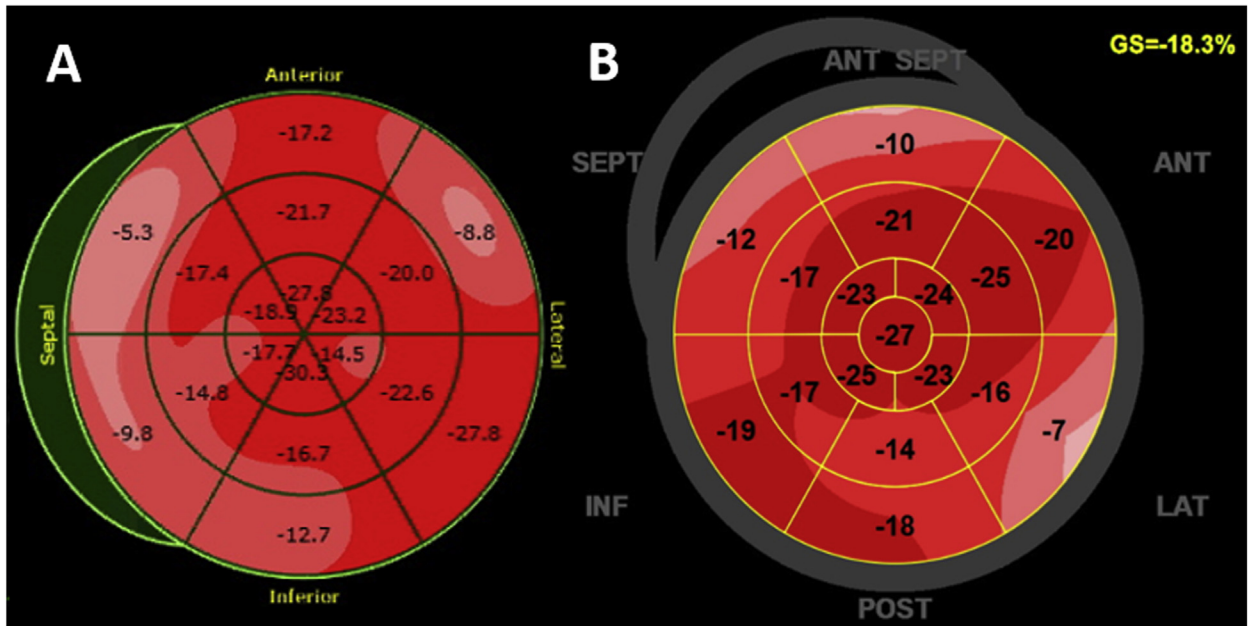


Figure 3 (A) Global longitudinal strain pattern (using GE technology) calculated by speckle-tracking on echocardiography revealed decreased septal strain values but not apical sparing. Note that an apical sparing pattern would imply that the sum of all the apical strains would be more than the sum of the basal and mid strains and is considered to be a highly (but not 100%) sensitive and specific sign of cardiac amyloidosis.⁴ While an overall global longitudinal strain score of -18.3% would be considered in the normal range for this patient, there was relative reduction in regional septal strains as above. (B) Global longitudinal strain pattern calculated by speckle-tracking on echocardiography (this time using Philips technology) replicated the above findings of decreased septal strain values but not apical sparing. Note that segments in panels A and B are rotated relative to each other, according to the specific conventions for each vendor “bull’s-eye” strain pattern output.

and a nonapical sparing pattern on echocardiography. Relative apical sparing on echocardiography and ^{99m}Tc -pyrophosphate imaging is a characteristic pattern in ATTR-CA.^{4,10} Although the lack of apical sparing pattern has been postulated for some patients to be related to early-stage disease,¹¹ this case shows that lack of apical strain in

ATTR-CA may also relate to variant forms such as here, with predominant interventricular septal uptake. The right atrial delayed gadolinium enhancement noted on cardiac magnetic resonance imaging is likely relevant with regard to the patient’s presentation with typical atrial flutter.

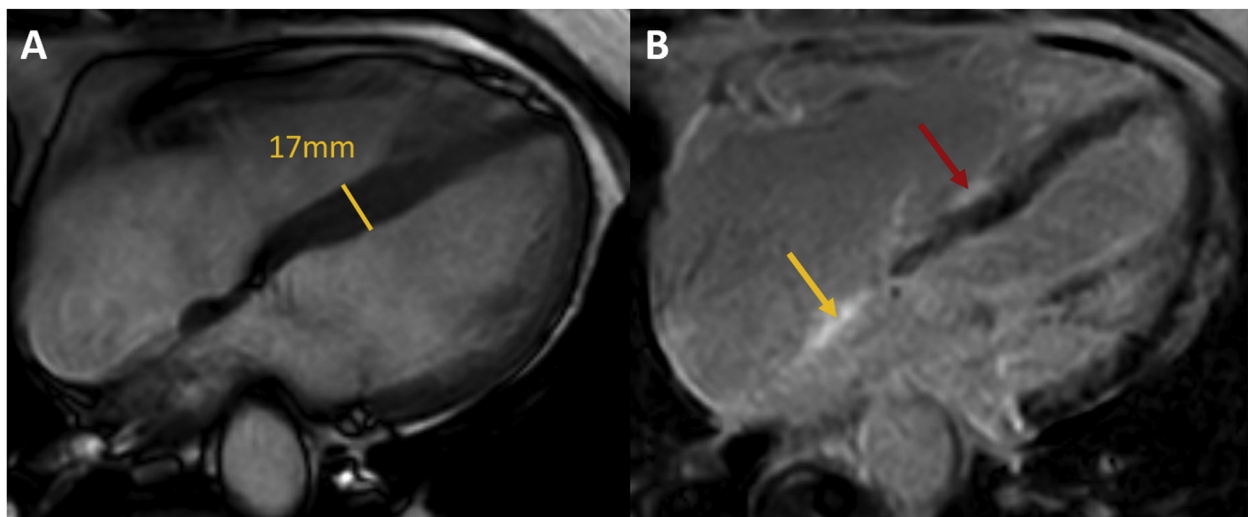


Figure 4 (A) Cardiac magnetic resonance imaging SSFP sequence demonstrating increased wall thickness of the interventricular septum up to 17 mm. (B) Cardiac magnetic resonance imaging demonstrating delayed gadolinium enhancement involving the right ventricular aspect of the interventricular septum (red arrow) and the right atrial aspect of the interatrial septum (gold arrow).

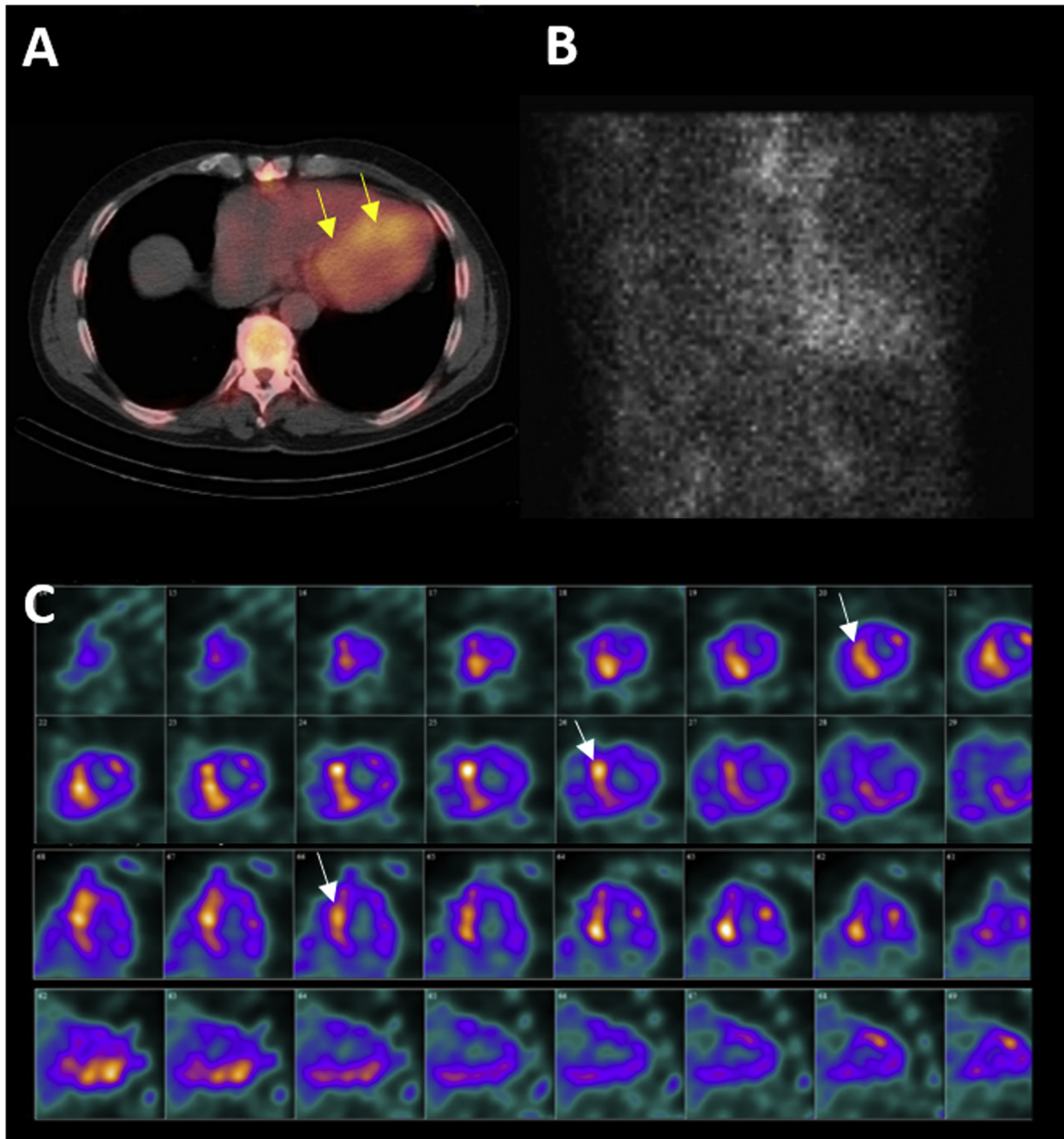


Figure 5 (A) Single-photon emission computed tomography imaging revealing increased uptake in interventricular septum (yellow arrows). (B) ^{99m}Tc -pyrophosphate scan demonstrating increased 3-hour heart-to-contralateral ratio (2.1) consistent with ATTR-CA. (C) Single-photon emission computed tomography imaging revealing increased uptake in interventricular septum (white arrows).

Other discrete morphological variants of ATTR-CA have been described. The description of atrial involvement (limited vs diffuse variant types) and the effect on atrial conduction leading to increased risk of atrial fibrillation have been reported.¹² Another report described a case of left ventricular hypertrophy that was ultimately diagnosed as ATTR-CA.¹³ Other researchers have described a diffuse septal/basal lateral variant and a vascular amyloid phenotype.¹²⁻¹⁴ The precedent of ATTR-CA causing increased echogenicity in the case of an epicardial mass was recently described.¹⁵

Further studies are necessary to better define the clinical relevance of newly identified discrete morphological variants to better risk stratify such patients.

CONCLUSION

We describe an atypical case of wild-type ATTR-CA with imaging evidence of amyloid deposition predominantly in the interventricular septum and a nonapical sparing pattern on echocardiography.

We hope that a major teaching point from this case study is that a high index of suspicion for atypical cardiac manifestations should be sought when the classic apical sparing pattern is absent in patients with other clinical findings of amyloidosis, which should prompt consideration of multimodality imaging.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.case.2021.07.010>.

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