Atypical Case of Epicardial Amyloid Mass without Classical Features of Myocardial Infiltration

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INTRODUCTION

Cardiac amyloidosis is associated with light-chain (AL) multiple myeloma and is typically diagnosed noninvasively using transthoracic echocardiography (TTE), particularly with speckle-tracking strain, or cardiac magnetic resonance (CMR) imaging. Rarely, amyloid deposition can occur in soft tissue in the mediastinum before the recognition of systemic involvement.[1] Isolated pericardial involvement of amyloid without myocardial infiltration is unusual but has been reported.[2] In this report, we describe a case of an epicardial amyloidoma first detected on TTE without typical features of cardiac amyloidosis other than apical sparing pattern in longitudinal strain and a pericardial effusion.

CASE DESCRIPTION

A 64-year-old man with multiple myeloma presented with recurrent syncope. He was recently diagnosed with immunoglobulin Gκ AL multiple myeloma that was treated with a chemotherapy regimen of bortezomib, lenalidomide, and dexamethasone, with hematologic remission. At the time of diagnosis, bone marrow biopsy showed 60% cellularity with 90% plasma cells, and the free AL (κ/λ) ratio was 570, consistent with a plasma cell myeloma. Initially, the patient displayed mild neurologic symptoms of numbness and tingling. These symptoms progressed to recurrent, profound syncopal episodes with minimal activity or standing. Orthostatic hypotension, which was suspected to be due to autonomic dysfunction or chemotherapeutic toxicity, was initially managed with midodrine, fludrocortisone, and supportive measures, with minimal improvement. He developed a polyneuropathy, confirmed by electromyography, that was treated with intravenous immunoglobulin for a possible autoimmune autonomic neuropathy, and POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma-proliferative disorder, skin changes) syndrome was considered. Workup for a primary central neurologic etiology was negative. Given his multiple myeloma, bilateral carpal tunnel syndrome, and a low-voltage electrocardiogram, AL amyloidosis was suspected. However, abdominal fat pad biopsy was negative for amyloid deposition. Renal function remained normal.

Postural hypotension worsened to the extent that the patient experienced multiple falls and became essentially bedbound. Echocardiography showed a small pericardial effusion without signs of tamponade and a 3.6 × 3.1 cm echogenic epicardial mass in the right atrioventricular groove (Figures 1 and 2, Videos 1-3). There was otherwise normal left ventricular (LV) size, wall thickness, and systolic function. However, global longitudinal strain was reduced at −12.7%, with an apical-sparing pattern and relative apical longitudinal strain of 0.9 (Figure 3). Diastolic parameters were consistent with an impaired relaxation pattern and did not suggest restrictive physiology or elevated LV filling pressures. N-terminal pro–brain natriuretic peptide was elevated at 2,977 pg/mL.

CMR imaging was performed to evaluate for cardiac amyloid and for further characterization of the epicardial mass in the right atrioventricular groove (Figure 4, Video 4). There was no evidence of myocardial fibrosis on the basis of delayed enhancement imaging (Figure 5) or parametric mapping. Native T1 and extracellular volume of the

VIDEO HIGHLIGHTS

Video 1: TTE, parasternal long-axis view, showing epicardial mass adherent to the right atrioventricular groove and a small pericardial effusion.

Video 2: TTE, subcostal view, showing a 3.6 × 3.1 cm epicardial mass adherent to the right atrioventricular groove and a small pericardial effusion.

Video 3: TTE, apical right ventricle–focused view. The echogenic mass in the pericardial mass appears to be contiguous with the right ventricular free wall, concerning for infiltration.

Video 4: CMR four-chamber cine image with balanced steady-state free precession pulse sequence. Moderate, circumferential pericardial effusion and epicardial mass are seen in the right atrioventricular groove. No LV hypertrophy was present, and myocardial mass was normal.

Video 5: CMR first-pass perfusion with injection of gadolinium contrast. There is no significant contrast perfusion of the epicardial mass.

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Dr. Schelbert has accepted contrast material from Bracco Diagnostics for research purposes and has served on advisory boards for Merck and Bayer.

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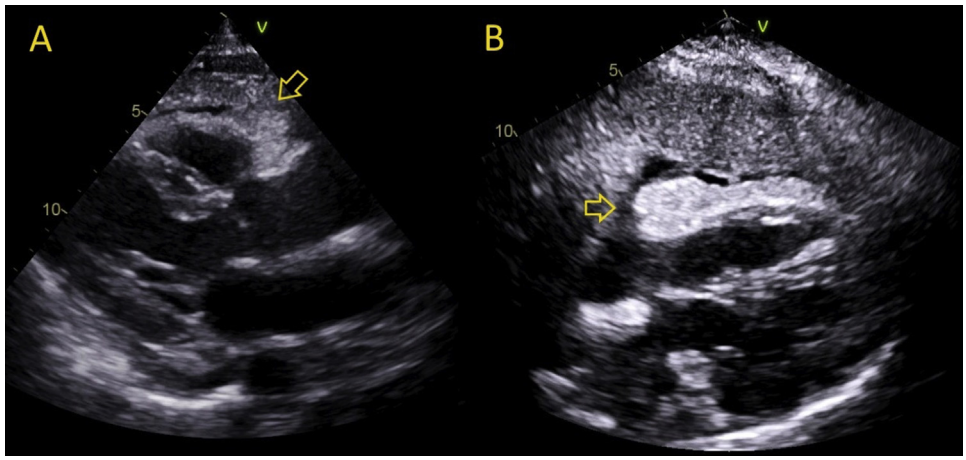

Figure 1 TTE, parasternal long-axis **(A)** and subcostal **(B)** views, showing a 3.6 × 3.1 cm epicardial mass (*yellow arrow*) adherent to the right atrioventricular groove and a small pericardial effusion.

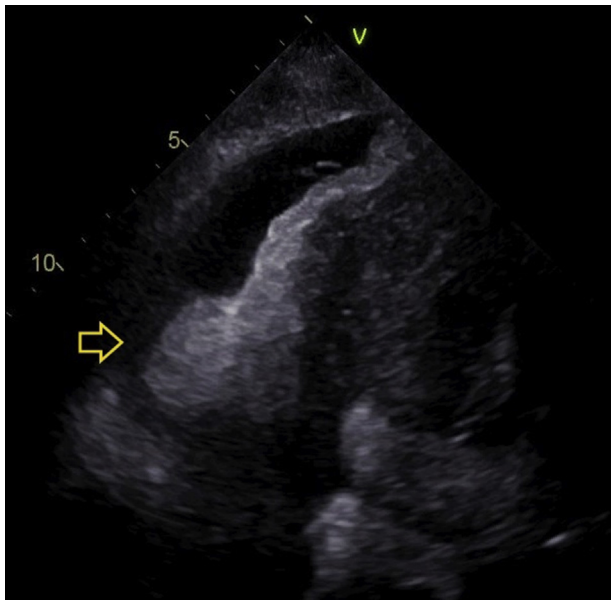

Figure 2 TTE, apical right ventricle–focused view. The echogenic mass in the pericardial mass (*yellow arrow*) appears to be contiguous with the right ventricular free wall, concerning for infiltration.

myocardium were not elevated and thus inconsistent with diffuse fibrosis (Figures 6A and 6C). The epicardial mass had elevated precontrast T1 and extracellular volume consistent with a fibrotic structure (Figures 6A and 6C). T2 was increased compared with myocardium, suggesting higher water content (Figure 6B). On first-pass perfusion with gadolinium contrast, there was no significant uptake in the mass, suggesting minimal vascularity (Figure 7, Video 5). Delayed imaging showed mild, heterogenous uptake in the mass (Figure 5) with corresponding postcontrast T1 shortening, inconsistent with thrombus.

After CMR imaging was completed, the patient experienced another syncopal event upon transfer from the magnetic resonance scanner. With evidence of a pericardial effusion, there was concern for early cardiac tamponade. The patient underwent right heart catheterization, which showed normal filling pressure, normal cardiac output, and no signs of cardiac tamponade. Diagnostic pericardiocentesis yielded a transudative effusate that was negative for malignant cells. Further diagnostic testing included cardiac computed tomographic angiography, which demonstrated no extrinsic compression of the right coronary artery and attenuation of the mass similar to the surrounding pericardial fluid (Figure 8). Whole-body positron emission tomography with ^{18}F-fluorodeoxyglucose was then performed, which did not show ^{18}F-fluorodeoxyglucose avidity in the epicardial mass or any other evidence of extramedullary disease. Given the uncertain etiology of the epicardial tumor and the clinical implications of potential plasmacytoma or other malignancy, surgical biopsy was pursued via the subxiphoid approach. Intraoperatively, the mass was noted to be "boggy" in nature. Congo red staining of the pathologic specimen was positive, and mass spectrometry was consistent with AL κ-type amyloid. There were no malignant cells and no abnormal plasma cell proliferation. Therefore, the mass was diagnosed as an amyloidoma.

Because of the finding of amyloid, the patient's polyneuropathy was attributed to both systemic AL amyloidosis and chemotherapeutic toxicity. Treatment was resumed after the diagnosis with daratumumab and dexamethasone. For his orthostatic hypotension, he was treated with droxidopa, fludrocortisone, midodrine, and pyridostigmine, which greatly improved his symptoms, and he was able to perform household chores. Five months later, repeat echocardiography and CMR imaging showed no change in the epicardial amyloidoma and again no evidence of amyloid infiltration in the myocardium.

DISCUSSION

This case report describes an unusual presentation of systemic AL amyloidosis presenting as an epicardial mass without typical features of myocardial involvement. To our knowledge, this type of presentation of amyloidosis has not been described in the literature. Pericardial involvement of AL amyloid without myocardial

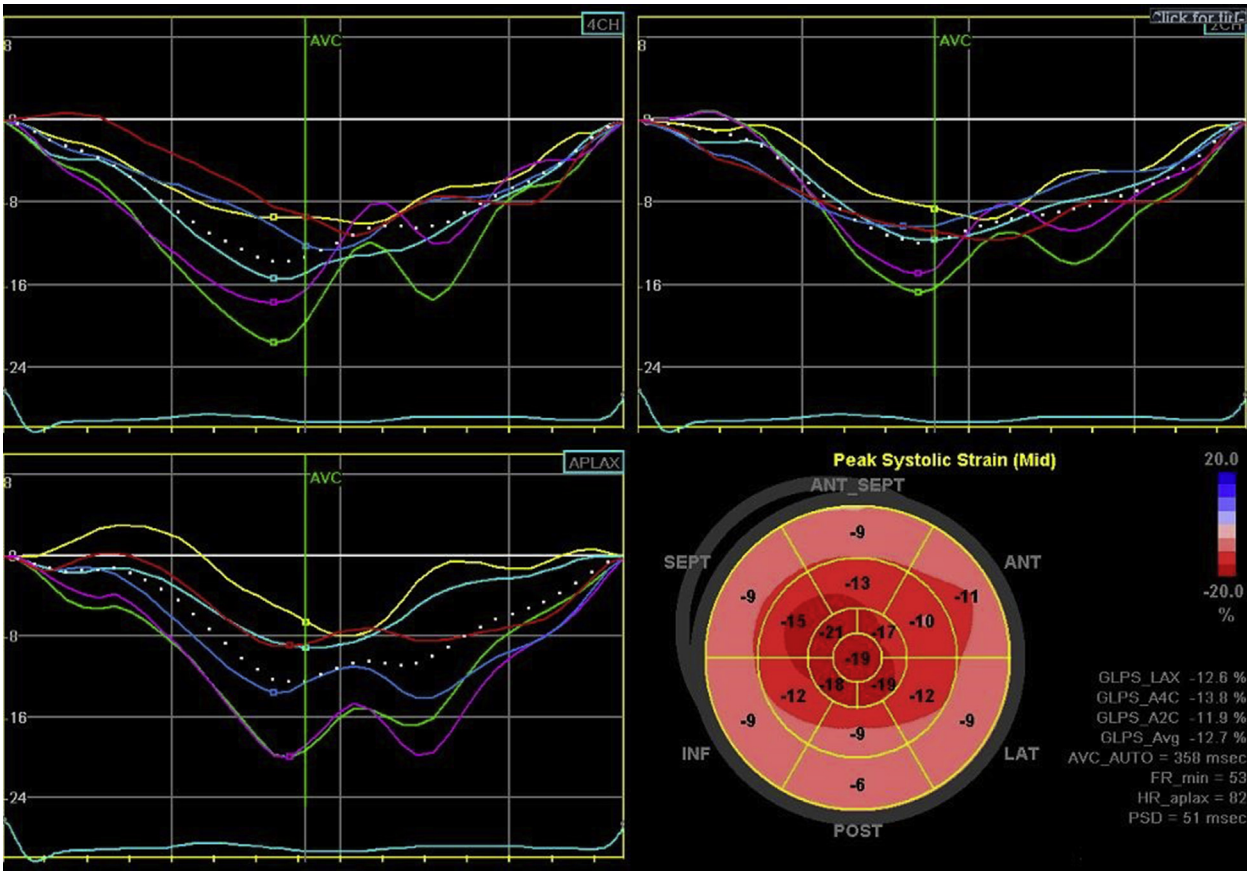

Figure 3 LV longitudinal strain by speckle-tracking echocardiography shows prominent apical sparing and decreased global longitudinal strain of −12.7%.

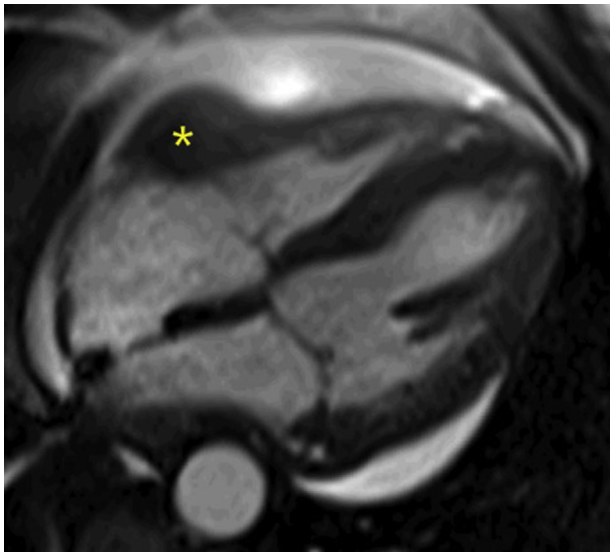

Figure 4 CMR four-chamber cine images with balanced steady-state free precession pulse sequence. Moderate, circumferential pericardial effusion and epicardial mass (*yellow asterisk*) are seen in the right atrioventricular groove. No LV hypertrophy was present, and myocardial mass was normal.

infiltration detected on TTE (including strain) or CMR imaging is rare but has been described.[2] Soft tissue deposition of amyloid as an amyloidoma is also unusual and may occur in the mediastinum.[1] It has also been reported to occur on serous membranes such as the pericardium.[3] There have also been case reports of plasmacytomas that can occur at the same location as in our patient, the atrioventricular groove.[4,5] Plasmacytomas have also been associated with neuropathy.[6] Although the patient had achieved hematologic remission, given the location of the mass and his progressive neurologic symptoms, systemic AL amyloidosis remained a consideration. Thus, a surgical biopsy was pursued for a definitive answer in this situation.

Classical features of cardiac amyloid were not present on TTE or CMR imaging, other than the presence of a pericardial effusion and the relative apical sparing on longitudinal strain. Compared with transthyretin amyloid, AL amyloid is associated with a smaller increase in LV mass and less LV hypertrophy.[7] Although underrecognized, cardiac infiltration is common in patients with AL amyloidosis, even with normal LV wall thickness.[8] CMR imaging allows myocardial characterization such as detection of extracellular volume expansion due to amyloid deposition, which may occur earlier than late gadolinium enhancement and holds prognostic value.[7,9] Relative apical sparing on longitudinal strain by speckle-tracking echocardiography is specific for cardiac amyloid and may

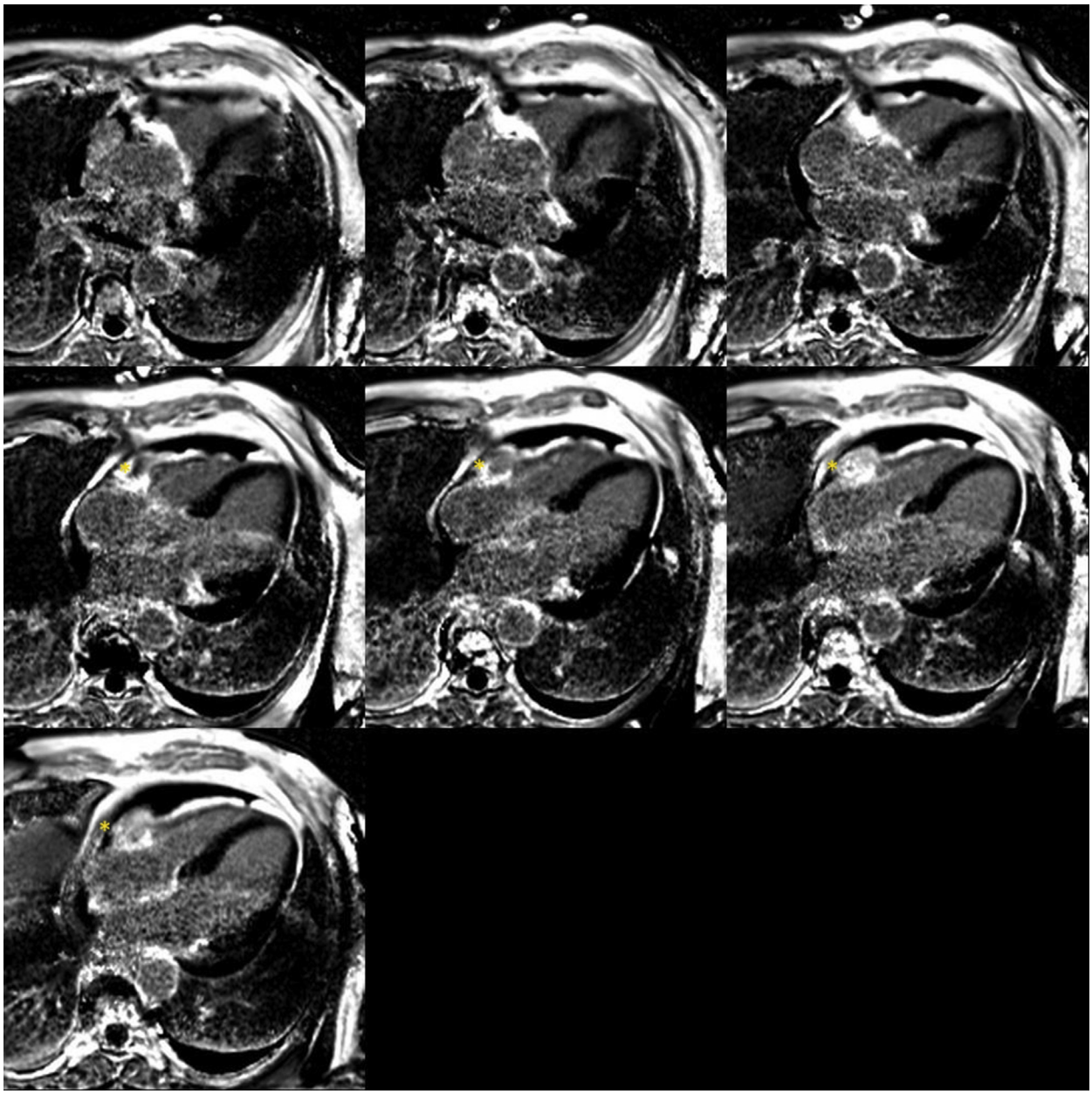

Figure 5 CMR late gadolinium enhancement imaging. There was no delayed enhancement in the myocardium to suggest scar or infiltrative disease. Heterogeneous delayed enhancement was noted in the epicardial mass (*yellow asterisk*).

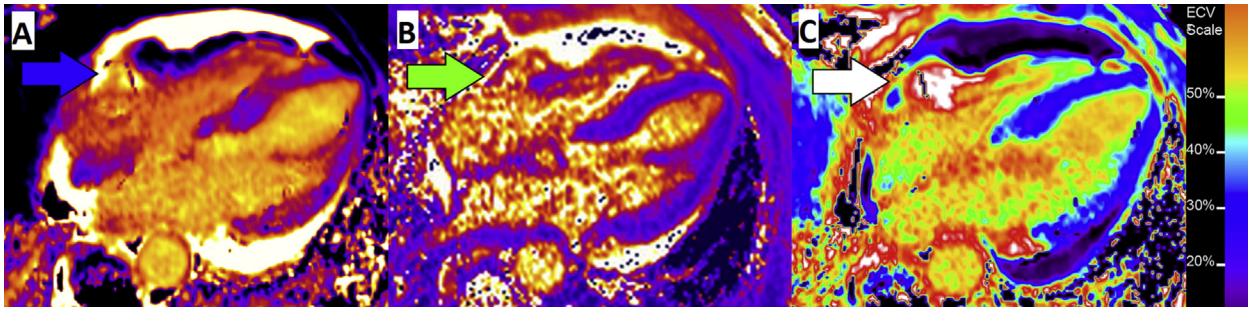

Figure 6 CMR parametric mapping. **(A)** Native (precontrast) T1 map using modified Look-Locker imaging showing uniform T1 values in the myocardium of about 1,050 msec (upper limit of normal) and about 1,474 msec in the epicardial mass (*blue arrow*). **(B)** The epicardial mass (*green arrow*) had high T2, about 180 msec, which is elevated. The T2 value of the myocardium was 52 msec, which is within the normal range. **(C)** Extracellular volume (ECV) map showing normal ECV fraction of 27.7% in the myocardium and 89.6% for the epicardial mass (*white arrow*), consistent with amyloidoma.

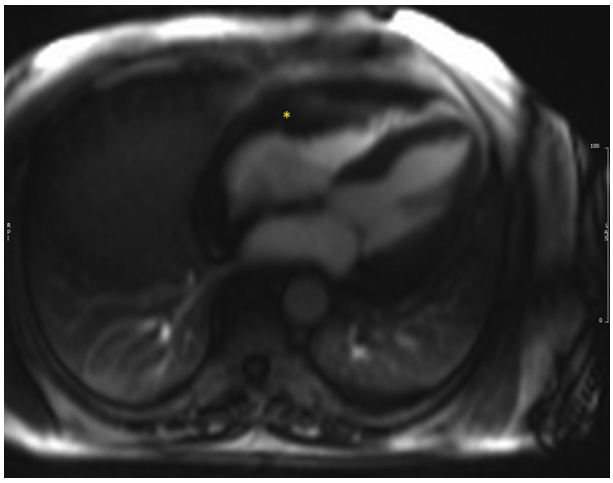

Figure 7 CMR first-pass perfusion with injection of gadolinium contrast. There is no significant contrast perfusion of the epicardial mass (*asterisk*).

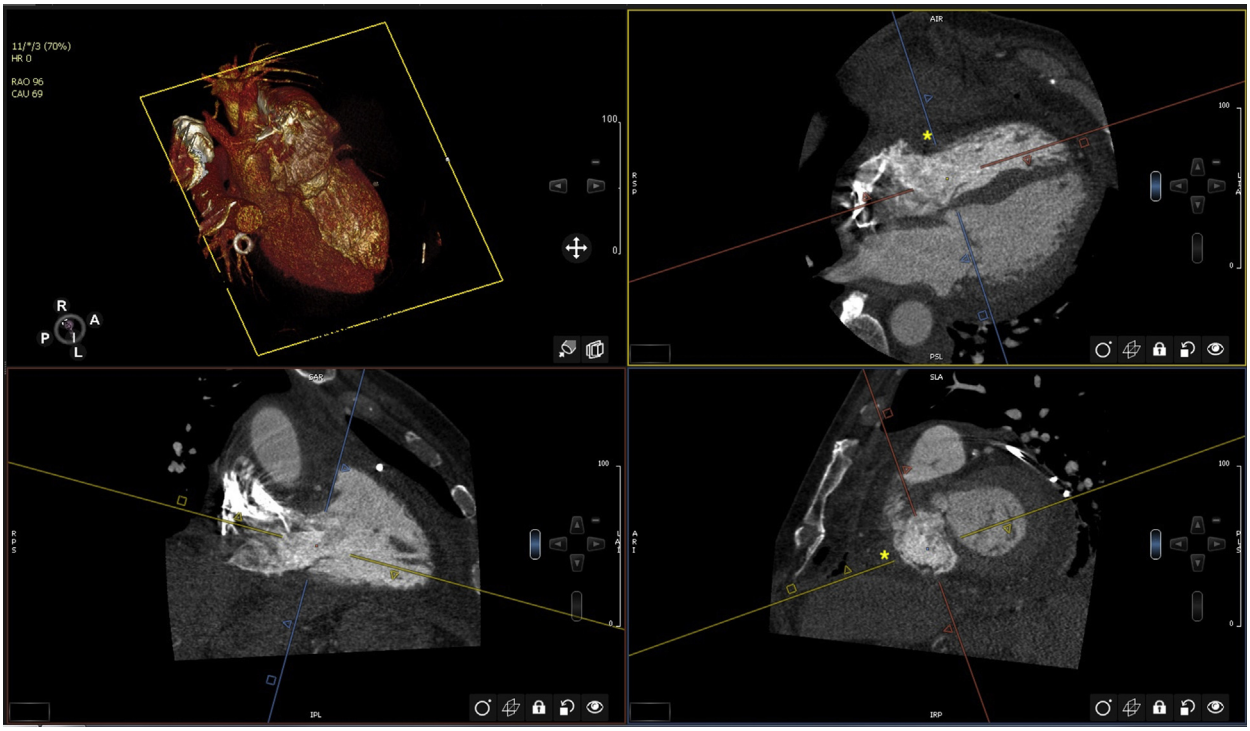

Figure 8 Cardiac computed tomographic (CT) angiography. The epicardial mass (*asterisk*) is ill defined and has similar CT attenuation (+40 Hounsfield units) to the adjacent pericardial effusion. A pericardial drain was in place at the time.

be detectable early in the disease process.[7,10] Although the strain pattern is subjectively suggestive of cardiac amyloidosis the relative apical sparing is <1.0. With this in mind, it is possible that our patient had early-stage cardiac amyloid, before the development of supportive findings on CMR imaging.

Early diagnosis is crucial in amyloidosis because of the poor prognosis, particularly when there is cardiac involvement. Median survival time from onset of heart failure because of cardiac amyloid is approximately 6 months.[7] Furthermore, novel therapies have increased the potential for mitigating symptoms and prolonging remission from both AL and transthyretin subtypes. In this case, the underlying cause of the patient's dysautonomia and polyneuropathy was initially uncertain, although amyloid was suspected. There was no other systemic sign of amyloid deposition, such as liver, renal, gastrointestinal, or cardiac involvement. Because echocardiography and other cardiac imaging revealed an epicardial mass that served as a target for biopsy, histologic diagnosis of amyloid could be established. This ultimately led to the patient's receiving chemotherapy, with improvement of his functional status, such that he may be considered for potential autologous hematopoietic stem cell transplantation.

CONCLUSION

This is the first described case of an epicardial amyloid mass without myocardial involvement in cardiac amyloidosis. Echocardiography and multimodality imaging were critical to making the correct diagnosis for this patient. He was started on novel treatment for AL amyloidosis, with alleviation of symptoms.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2019.12.003.

REFERENCES

1. Urschel JD, Urschel DM. Mediastinal amyloidosis. Ann Thorac Surg 2000;69:944-6.
2. Georgin-Lavialle S, Guellich A, Deux JF, Buob D, Damy T. Isolated pericardial infiltration without myocardial involvement in light-chain–related amyloidosis. Ann Thorac Surg 2017;103:e255-7.
3. Cicco S, Racanelli V, Vacca A, Ria R, Leone P, Battaglia S, et al. Suspected pericardial tuberculosis revealed as an amyloid pericardial mass. Case Rep Hematol 2018;2018:8606430.
4. Vigo F, Ciammella P, Valli R, Cagni E, Iotti C. Extraskeletal multiple myeloma presenting with an atrial mass: a case report and a review of the literature. J Med Case Rep 2012;6:236.
5. Ooi GC, Chim JCS, Au WY, Khong PL. Radiologic manifestations of primary solitary extramedullary and multiple solitary plasmacytomas. AJR Am J Roentgenol 2006;186:821-7.
6. Read D, Warlow C. Peripheral neuropathy and solitary plasmacytoma. J Neurol Neurosurg Psychiatry 1978;41:177-84.
7. Falk RH, Alexander KM, Liao R, Dorbala S. AL (light-chain) cardiac amyloidosis: a review of diagnosis and therapy. J Am Coll Cardiol 2016;68:1323-41.
8. Lee GY, Kim K, Choi JO, Kim SJ, Kim JS, Choe YH, et al. Cardiac amyloidosis without increased left ventricular wall thickness. Mayo Clin Proc 2014;89:781-9.
9. Petrie A, Moon JC, Maestrini V, Banypersad SM, Wechalekar AD, Sado DM, et al. T1 mapping and survival in systemic light-chain amyloidosis. Eur Heart J 2014;36:244-51.
10. Thavendiranathan P, Phelan D, Collier P, Popović ZB, Thomas JD, Hanna M, et al. Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. Heart 2012;98:1442-8.