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Case Report

Unexplained cardiac hypertrophy as a clue to plasma cell tumour: a case study

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Abstract: Initial diagnosis: A 60-year-old male presented with initial diagnosis chest tightness, fatigue, and arrhythmia. Indications for plasma cell tumour: Initial imaging suggested amyloidosis due to myocardial thickening. Left ventricular hypertrophy and delayed enhancement on Magnetic Resonance Imaging (MRI), along with an elevated κ:λ ratio, raising suspicion for a plasma cell tumour. Confirmation of the plasma tumour: Further diagnostic tests, including immunofixation electrophoresis and myocardial biopsy, confirmed a plasma cell tumour. The patient was diagnosed with light chain (AL) amyloidosis, a subtype of plasma cell tumor, confirmed by bone marrow biopsy and immunohistochemistry. Treatment: Treatment with bortezomib, dexamethasone, and daratumumab resulted in significant symptomatic improvement. Conclusion: This case underscores the importance of considering plasma cell disorders in unexplained cardiac hypertrophy and highlights the need for early diagnostic strategies and targeted therapies.

Keywords: Cardiac hypertrophy, plasma cell tumour, myocardial amyloidosis, heart failure, case report

Introduction

Myocardial hypertrophy, unexplained thickening of the heart muscles, is associated with several conditions such as hypertension, vascular disease, and chronic heart failure [1]. First identified by Donald Teare in 1958, this condition can lead to heart dysfunction and is a leading cause of illness and death, especially among older adults [2]. Chronic pressure or volume overload on the heart often drives hypertrophy, activating harmful genetic pathways and pro-hypertrophic signals. In adults, external factors influence its progression [2].

Plasma cell dyscrasias, including multiple myeloma, solitary plasmacytoma, and light chain amyloidosis, can also manifest with cardiac involvement. Light chain amyloidosis, a common complication of multiple myeloma, often leads to restrictive cardiomyopathy but can also cause unexplained cardiac hypertrophy. Recent studies have highlighted that while restrictive patterns are common in amyloidosis, isolated cardiac hypertrophy can occur, making diagnosis challenging [3, 4].

This case study presented a patient whose initial symptom of unexplained cardiac hypertrophy led to the diagnosis of a plasma cell tumour. A literature review highlights the need to consider systemic malignancies when diagnosing unexplained cardiac hypertrophy and the importance of developing precise diagnostic and therapeutic approaches.

Case presentation

Demographic characteristics and main complaint

A 60-year-old male was admitted to Affiliated Hospital of Hebei University, Baoding, Hebei, China on January 22, 2024. He complained of chest tightness, fatigue, and shortness of breath that had been worsening over the past six months, with a significant increase in symptoms the day before admission. He also report-

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ed sweating, nausea, vomiting, and orthopnea. His medical history included untreated hypertension for one month, a 45-pack-year smoking history, and social alcohol consumption.

Past medical history

The patient had been diagnosed with renal failure 15 days before coming to the hospital. His blood pressure was approximately 160/80 mmHg when he was first seen.

Family history

No relevant family history was reported.

Present illness

The patient's symptoms had progressively worsened over the past six months, finally reaching an acute point the day before admission. He experienced ventricular tachycardia while at a local hospital and required electrical cardioversion before being transferred to our emergency department.

Physical examination revealed a grade II/VI systolic murmur heard in the left third and fourth intercostal spaces, with radiation to the neck. There were no other abnormal physical findings.

Laboratory findings

a) Myocardial Enzymes: CKMB 16.87 ng/ml, cTnI 1.45 ng/ml, Myo 79.6 ng/ml, BNP 28177 pg/ml. b) Routine Laboratory Tests: Urea 11.46 mmol/L (elevated), Creatinine 158 μmol/L (elevated). c) Lipid Profile: Total cholesterol 7.13 mmol/L, Triglycerides 1.94 mmol/L, LDL cholesterol 4.91 mmol/L, VLDL cholesterol 1.03 mmol/L. d) Urinalysis: Occult blood 1+, Urinary protein 3+, Urinary microalbumin >0.15 g/L. e) Serum Free Light Chains: κ (kappa) 687.5 mg/L, λ (lambda) 31.0 mg/L, κ:λ ratio 22.177. f) Immunofixation Electrophoresis: Urine IgG, IgA, and IgM were negative; κ-light chain was positive, λ-light chain was negative. Serum fixed protein electrophoresis was negative. g) 24-hour Urinary Quantification: Creatinine 5.01 mmol/24 hours. No abnormalities in κ-LC and λ-LC.

Imaging findings

a) Cardiac Ultrasound: Left ventricular hypertrophy was observed, accompanied by valvular regurgitation. b) Coronary Angiography: Coronary arteries were clear, but there was a pressure difference of 24 mmHg. Ischemic cardiomyopathy was excluded. c) Cardiac MRI: Mild biatrial enlargement and diffuse myocardial thickening with delayed gadolinium enhancement were present, suggestive of amyloidosis. Valvular regurgitation was also noted. d) Myocardial Tomographic Imaging: This test did not suggest ATTR amyloidosis.

Abdominal Biopsy: κ+++ and λ- (**Figures 1**-**3**).

Diagnosis

The patient presented with progressive shortness of breath and chest tightness, with a medical history of untreated hypertension and renal failure. Cardiac ultrasound revealed left ventricular hypertrophy, leading to further evaluation. Cardiac MRI confirmed diffuse myocardial thickening with delayed enhancement, suggestive of amyloidosis. Laboratory tests showed elevated free light chains (κ:λ ratio of 22.177) and immunofixation electrophoresis confirmed a κ-light chain plasma cell tumour. Bone marrow biopsy further confirmed the presence of monoclonal plasma cell proliferation. The patient was diagnosed with myocardial amyloidosis (κ+++, λ-, and TTR-), which is linked to a plasma cell tumour (AL-CA). Flow cytometry confirmed the presence of a plasma cell tumour (~10%) (**Figure 4**). The patient was diagnosed with light chain (AL) amyloidosis, a subtype of plasma cell tumor, confirmed by bone marrow biopsy and immunohistochemistry.

Treatment

The patient was treated with a weekly regimen of bortezomib (1.1 mg subcutaneously), dexamethasone (20 mg intravenously/intramuscularly), and daratumumab (1800 mg subcutaneously). Subsequent follow-up revealed significant clinical improvements, including reduced fatigue, improved exercise tolerance, and decreased BNP levels. Repeat echocardiography demonstrated partial regression of myocardial hypertrophy.

Follow-up and survival

The patient is still receiving treatment, and we will continue to monitor his progress and manage any problems that may arise.

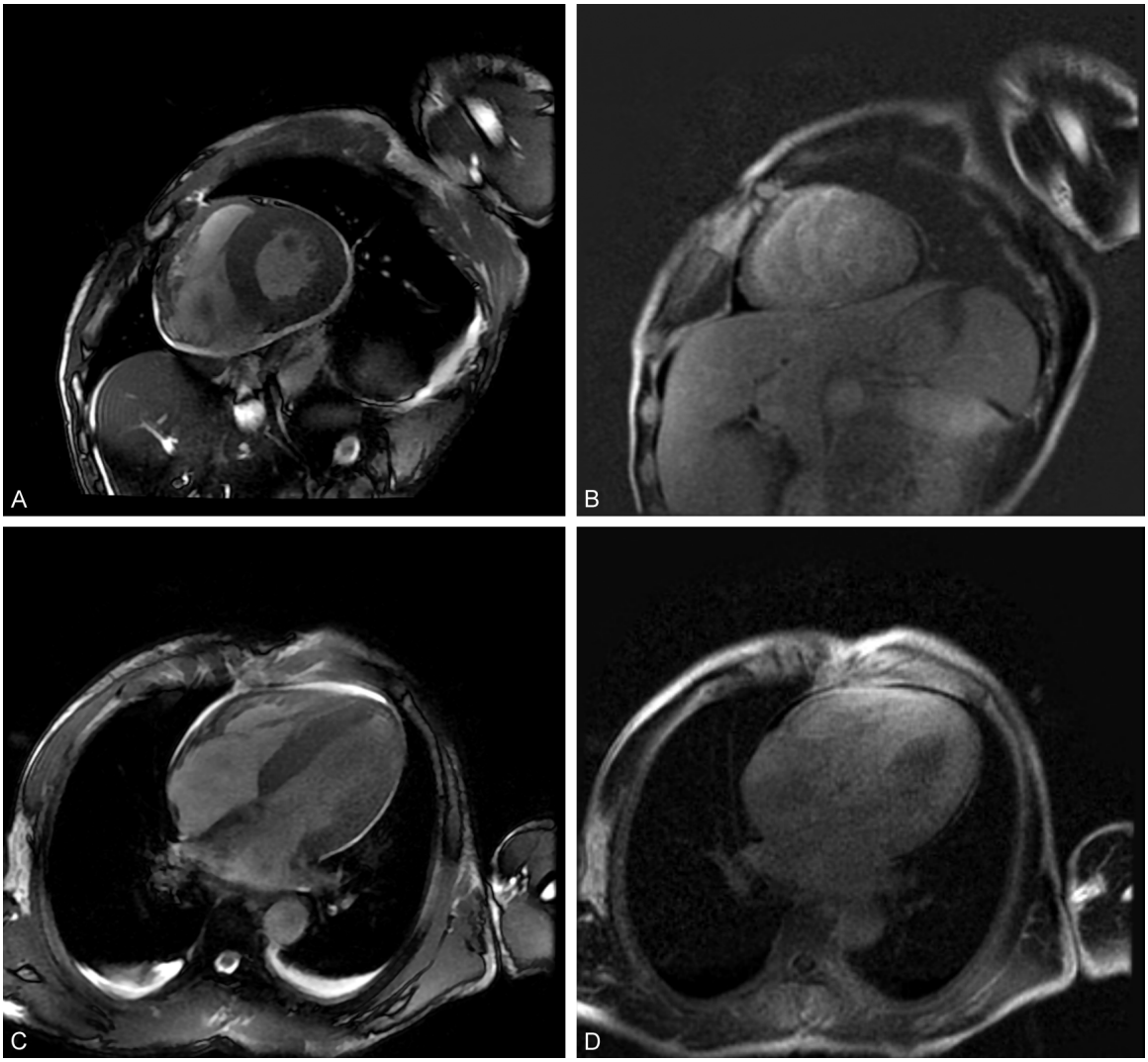

Figure 1. Multimodality cardiac imaging revealing diffuse myocardial thickening and enhancement consistent with infiltrative cardiomyopathy. A. This echocardiographic image demonstrates increased left ventricular myocardial thickness in the short-axis view. The concentric hypertrophy is suggestive of an infiltrative cardiomyopathy, requiring further evaluation. B. Diffuse Myocardial Enhancement in the Left Ventricular Short Axis View (Cardiac MRI with late gadolinium enhancement (LGE) reveals diffuse subendocardial enhancement in the left ventricular myocardium. This pattern is characteristic of cardiac amyloidosis and helps distinguish it from other hypertrophic cardiomyopathies). C. Cardiac Abnormalities (Myocardial Thickening, Pericardial Effusion, and Pleural Effusion) Evident on Four-Chamber Heart Imaging (A four-chamber view of the heart obtained via echocardiography illustrates myocardial thickening, pericardial effusion, and pleural effusion. These findings are consistent with advanced cardiac amyloidosis and systemic involvement). D. Four-Chamber Heart Displaying Diffuse Myocardial Enhancement in the Left and Right Ventricles (Late gadolinium-enhanced cardiac MRI in a four-chamber view shows diffuse myocardial enhancement in both left and right ventricles. This suggests amyloid infiltration, which is a hallmark of light-chain (AL) amyloidosis).

Discussion

Unexplained cardiac hypertrophy requires careful evaluation due to its varied etiologies. While hypertrophic cardiomyopathy and hypertensive heart disease remain common causes, infiltrative disorders such as cardiac amyloidosis, particularly light-chain amyloidosis (AL amyloidosis) secondary to plasma cell dyscrasia, should be considered. This case highlights the importance of including AL amyloidosis in the differential diagnosis of unexplained myocardial thickening.

Novosad et al. (2023) reported a case of cardiac amyloidosis presenting with dyspnea and

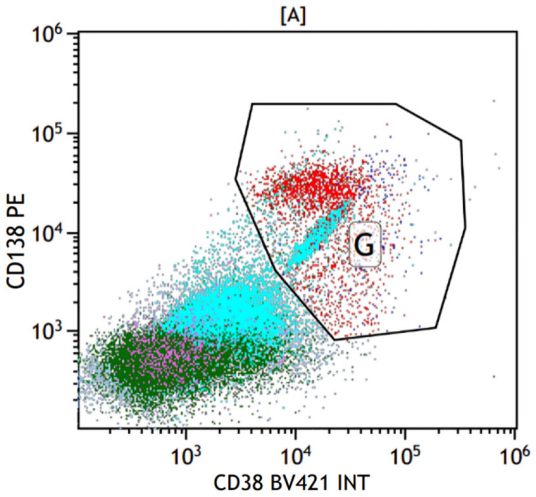

Figure 2. Immunoassay analysis of a plasma cell tumour (The immunohistochemical analysis of the bone marrow biopsy demonstrates monoclonal plasma cell proliferation. The cells express CD38 and CD138 markers, supporting the diagnosis of plasma cell dyscrasia).

syncope. Diagnostic evaluation, including cardiac MRI and biopsy, confirmed the diagnosis. Treatment with bortezomib, cyclophosphamide, and autologous hematopoietic stem cell transplantation resulted in improved cardiac function. These findings are consistent with our results, where bortezomib-based therapy yielded positive outcomes and cardiac MRI played a crucial role in early diagnosis [5]. Similarly, another case report described a patient presenting with fever and left ventricular hypertrophy, where myocardial biopsy confirmed amyloidosis. Corticosteroid therapy led to improvement in left ventricular function. The present study also underscored the significance of early diagnosis via biopsy in preventing heart failure [6]. However, Ohara et al. (2019) described a patient with palpitations and lower limb edema, diagnosed with left ventricular hypertrophy and subsequently succumbing to sudden cardiac arrest. This case underscores the risks associated with diagnostic delays [7]. Despite promising therapeutic advances, AL amyloidosis remains a condition with variable prognosis. As reported by Ohara et al. (2019), some patients may experience rapid disease progression despite early intervention. Our case highlights the importance of regular follow-up and serial imaging to monitor disease course and treatment response [7].

The favourable outcome observed in our patient further contributes to the growing body of evidence supporting the efficacy of bortezomib-based regimens in cardiac amyloidosis associated with plasma cell tumours. Zhang et al. (2020) reported a case of cardiac amyloidosis presenting with fatigue, bilateral lower limb edema, dyspnea, and symmetric left ventricular hypertrophy. Despite treatment with bortezomib, dexamethasone, and thalidomide, the patient died due to cardiorenal failure. This case underscores the variable prognosis of AL amyloidosis, even with standard therapies, and highlights the need for early diagnosis and new combination therapies [8]. Hirata et al. (2019) reported a case of amyloidosis with shortness of breath and anemia, where multiple biopsies confirmed the diagnosis. Treatment with bortezomib, dexamethasone, and autologous stem cell transplantation led to improved cardiac function, reinforcing the efficacy of bortezomib-based regimens in this disease [9]. Zhu et al. (2019) studied a patient with bilateral lower limb edema diagnosed with amyloidosis through multiple biopsies. Treatment with thalidomide, bortezomib, cyclophosphamide, and dexamethasone led to complete symptom resolution. This study showed the efficacy of multiagent chemotherapy in improving symptoms, similar to the positive therapeutic results in the present study [10].

Guan et al. (2020) described a case of extramedullary plasmacytoma associated with myocardial amyloidosis, successfully treated with bortezomib, consistent with the therapeutic approach employed in the present study [11]. Holcman et al. (2021) found that more than one-third of patients with unexplained cardiac hypertrophy had amyloidosis, underscoring the importance of advanced biochemical tests and imaging, such as cardiac MRI, for early diagnosis [12]. Early detection and intervention remain crucial in improving survival outcomes in cardiac amyloidosis. Recent studies emphasize the need for standardized screening protocols in patients with unexplained cardiac hypertrophy, particularly those with concurrent renal dysfunction or abnormal serum free light chains. The findings in our study align with research by Holcman et al. (2021), who suggested that multimodal imaging combined with hematologic markers can facilitate earlier diagnosis and targeted treatment [12]. The present study also emphasizes the use of modern imaging and advanced techniques for early detection of cardiac tumours [13, 14]. These studies collective-

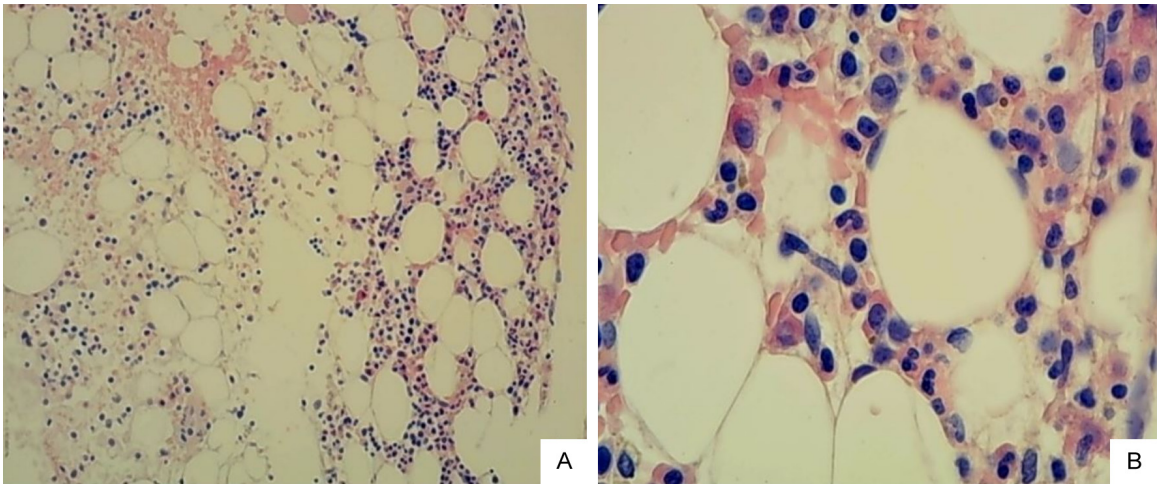

Figure 3. Comparison of monoclonal cell proliferation; 6a: Monoclonal cell proliferation at a magnification of 0.4 cm × 0.2 cm × 0.2 cm, ×4; 6b: Monoclonal cell proliferation at a magnification of 0.7 cm × 0.2 cm × 0.2 cm, ×40. Immunohistochemistry results: CD38+ and CD138+ (~10%), κ+, λ-. (A) Low-power magnification (4×) and (B) high-power magnification (40×) of a bone marrow biopsy specimen. Immunohistochemistry confirms the presence of plasma cells with positive staining for κ-light chains and negative staining for λ-light chains, confirming monoclonal proliferation.

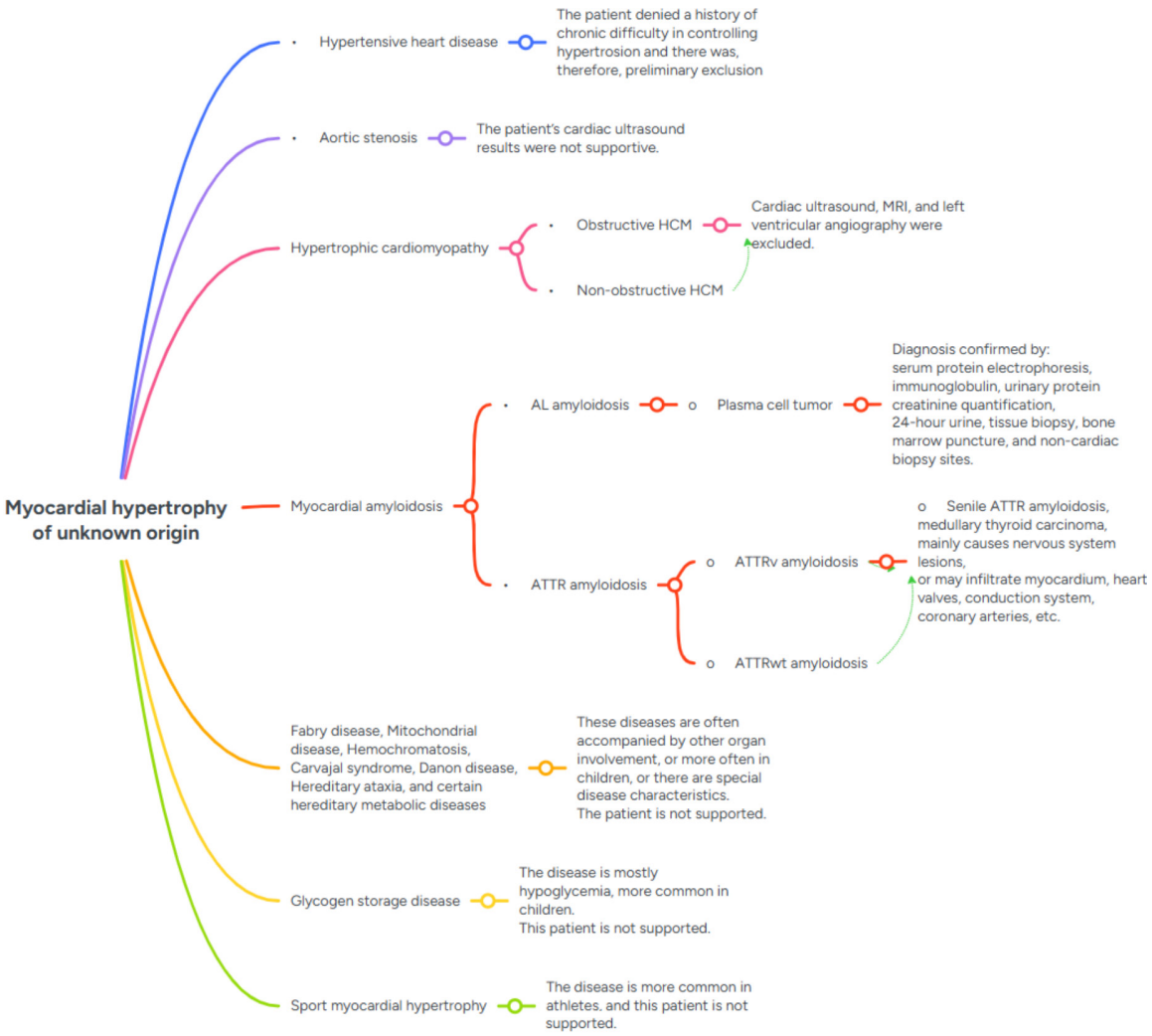

Figure 4. Rapid diagnostic mind map for unexplained cardiac hypertrophy. A flowchart illustrating the stepwise diagnostic approach to unexplained cardiac hypertrophy. It includes key imaging modalities, biochemical markers, and histopathological evaluations used to differentiate cardiac amyloidosis from other causes of hypertrophy.

ly emphasize the vital role of early diagnosis in unexplained cardiac hypertrophy, especially when amyloidosis or plasma cell tumours are underlying causes. Using advanced imaging tools, biochemical tests, and a thorough clinical examination is essential for timely diagnosis. Garcia-Pavia et al. (2021) emphasized the direct correlation between early diagnosis and improved prognosis in cardiac amyloidosis and rare cardiac tumours. They also underscored the importance of combining modern biochemical tests and imaging, such as cardiac MRI and PET, in achieving accurate diagnosis of amyloidosis, a finding consistent with the present study [15]. Waldmeier et al. (2022) discussed using advanced imaging techniques like MRI, SPECT, and CMR to diagnose cardiac amyloidosis, showing that these methods can help identify amyloid fibrils early and distinguish different cardiomyopathies [16]. New treatments, like bortezomib, as used in this and other studies, have demonstrated high efficacy in treating plasma cell tumours and cardiac amyloidosis. Kastritis et al. (2020) demonstrated that using a combination of bortezomib, melphalan, and dexamethasone led to increased survival and reduced mortality in patients [17]. Although hypertension is a well-known cause of left ventricular hypertrophy, the degree and pattern of myocardial thickening observed in this patient were atypical - especially considering the diffuse delayed gadolinium enhancement on cardiac MRI, which is not characteristic of hypertensive cardiomyopathy. Furthermore, the markedly abnormal κ:λ ratio, together with the imaging findings, raised suspicion for an infiltrative cardiomyopathy such as AL amyloidosis secondary to plasma cell dyscrasia. This diagnosis was confirmed by immunohistochemistry and bone marrow biopsy. Similar diagnostic challenges have been described in case reports by Xuan Guan et al. (2020) [11] and Mousavizadeh et al. (2023) [18], where cardiac plasmacytomas led to myocardial thickening that initially mimicked hypertensive or idiopathic cardiomyopathies. In a case reported by Andrea et al. [19], a patient presented with a right atrial mass, and imaging studies, including CT and PET-CT, were instrumental in identifying the lesion as a primary cardiac plasmacytoma, highlighting the importance of multimodal imaging in such rare presentations. Further supporting this, Vrettou et al. [20] described a case where echocardiography and cardiac magnetic resonance imaging revealed a cardiac mass, and subsequent biopsy confirmed it as a plasmacytoma, emphasizing the role of imaging in conjunction with histopathological analysis for accurate diagnosis.

In our patient, flow cytometry was conducted on myocardial biopsy tissue, revealing a clonal population of plasma cells, confirming the diagnosis of a primary cardiac plasma cell tumour. This approach aligns with the diagnostic strategies employed in the aforementioned cases, where tissue biopsy and immunophenotypic evaluation were pivotal. Given the rarity of primary cardiac plasmacytomas, it's crucial to consider them in differential diagnoses when imaging reveals atypical myocardial thickening, especially when accompanied by laboratory findings indicative of plasma cell dyscrasia.

Conclusion

This case highlights the presentation of unexplained cardiac hypertrophy as an initial sign of a plasma cell tumour, posing a diagnostic challenge in differentiating amyloidosis-related cardiac hypertrophy from other etiologies. Using advanced diagnostic techniques, such as imaging and biopsies, we could identify myocardial amyloidosis early and start treatment quickly, which significantly improved the patient's symptoms. This case emphasized the importance of considering systemic malignancies, such as plasma cell tumours, in cases of unexplained cardiac symptoms. Early diagnosis and treatment are vital for enhancing patient outcomes. Regular follow-up is essential for monitoring the effectiveness of treatment and managing any potential complications.

Disclosure of conflict of interest

None.

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