Concurrent Transthyretin Cardiac Amyloidosis and Eosinophilic Myocarditis: A Case Report

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Eosinophilic myocarditis (EM) is a rare form of myocardial inflammation defined by eosinophilic infiltration with associated myocyte injury. Its clinical expression is heterogeneous, ranging from subtle symptoms of heart failure to fulminant cardiogenic shock. Because these features often overlap with other types of myocarditis and systemic conditions, establishing the diagnosis can be difficult. In such cases, endomyocardial biopsy (EMB) remains the reference standard.

Amyloid transthyretin (ATTR) cardiac amyloidosis is an infiltrative cardiomyopathy marked by amyloid fibril deposition in the heart's extracellular space. It usually presents with signs of heart failure, and echocardiography often shows concentric left ventricular hypertrophy (LVH), restrictive physiology, and a distinctive pattern of apical strain sparing. In recent years, the development of non-invasive diagnostic methods, as well as the availability of disease-modifying treatments, has significantly improved diagnosis and management.

To the best of our knowledge, the coexistence of ATTR cardiac amyloidosis and EM has not been previously reported. Such overlap presents distinct diagnostic and therapeutic challenges. These conditions may have synergistic effects on the structure and function of the myocardium. We describe a case of concurrent ATTR cardiac amyloidosis and EM, highlighting the role of multimodality imaging and multidisciplinary management of these overlapping pathologies.

PATIENT DESCRIPTION

An 81-year-old man with a history of type 2 diabetes mellitus, dyslipidemia, atrial fibrillation, and heart failure with preserved ejection fraction presented to the emergency department with a preliminary diagnosis of acute decompensated heart failure.

Four months before the current admission, transthoracic echocardiography revealed concentric LVH with features suggestive of infiltrative cardiomyopathy. Technetium-99m-pyrophosphate scintigraphy demonstrated grade 3 myocardial uptake, while serum immunofixation and free light chain analysis showed no evidence of monoclonal gammopathy. These findings confirmed the diagnosis of ATTR cardiac amyloidosis, and tafamidis therapy was initiated at that time.

During the current admission, the patient presented with gradually worsening dyspnea and signs of hypervolemia. Laboratory studies revealed elevated NT-proBNP at 19,299 pg/ml (reference < 300 pg/ml), increased troponin T at 125 ng/L (reference < 13 ng/L), and peripheral eosinophilia of 3.7 K/μL (reference < 0.7 K/μL). The electrocardiogram showed atrial fibrillation. A chest radiograph revealed signs compatible with pulmonary edema. The patient was treated with intravenous diuretics to achieve euvolemia, and a comprehensive evaluation for potential triggers was conducted. Thoracentesis of the pleural effusion confirmed a transudate, consistent with decompensated heart failure.

Transthoracic echocardiography showed an estimated ejection fraction of 55–60% with marked concentric LVH (interventricular septal thickness of 26 mm and a posterior wall thickness of 15 mm), biatrial dilation, and reduced global longitudinal strain to -10.9%, with a typical apical sparing pattern (findings consistent with those observed previously). The clinical and laboratory features were suspicious for EM, possibly as a manifestation of hypereosinophilic syndrome (HES), and cardiac magnetic resonance imaging (cMRI) was obtained to further evaluate myocardial involvement [Figure 1]. It showed

globally increased relaxation time in the basal segments on T1-weighted imaging, increased signal intensity in the mid-anterior and mid-inferoseptal segments on T2-weighted sequences, and diffuse and patchy late gadolinium enhancement (LGE) involving both mid-myocardial and subendocardial layers, suggesting a unique overlap of signs characteristic of amyloidosis and active myocardial inflammation. Further work-up focused on excluding primary and secondary causes of HES. ^{18}F-fluorodeoxyglucose positron-emission tomography/computed tomography (^{18}F-FDG PET/CT) demonstrated mild hypermetabolic activity in the distal third of the esophagus. Serologic testing for *Strongyloides*, *Toxocara*, and *Echinococcus* was negative, as were antineutrophil cytoplasmic antibodies (ANCA). Hematologic evaluation, including a peripheral blood smear, flow cytometry, and T-cell receptor studies, revealed no evidence of clonal proliferation.

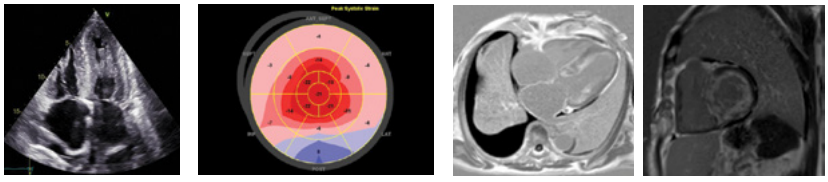
A presumptive diagnosis of acute EM in the context of HES was determined, and 60 mg prednisone therapy was initiated. The patient subsequently demonstrated marked clinical improvement, accompanied by a reduction in peripheral eosinophil count. He was discharged on prednisone 60 mg daily, with a plan for gradual tapering. Two months after initiation of corticosteroid tapering, the patient was hospitalized again for worsening heart failure. The eosinophil count increased to 8.8 × 10^9/L, prompting initiation of intravenous hydrocortisone 100 mg three times per day. An evaluation by an allergist confirmed HES, and treatment with anti-interleukin-5 therapy (mepolizumab) was initiated with a gradual reduction of steroids. Following treatment, the patient experienced modest clinical improvement; however, 6 months later he required one additional brief hospitalization for recurrent heart failure exacerbation. Eosinophil counts remained suppressed.

Figure 1. Multimodality imaging demonstrating transthyretin cardiac amyloidosis with concomitant eosinophilic myocarditis

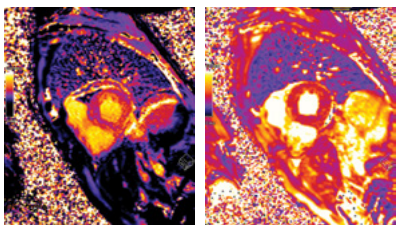
[A] Echocardiography in the apical four-chamber view shows concentric left ventricular hypertrophy with biatrial enlargement

[B] The strain bullseye plot demonstrates reduced global longitudinal strain (-10.9%) with relative apical sparing, characteristic of transthyretin amyloidosis

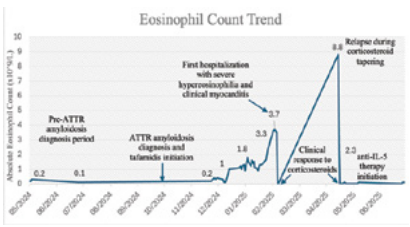
[E, F] Late gadolinium enhancement imaging demonstrates diffuse subendocardial and patchy mid-myocardial enhancement, a hallmark of eosinophilic myocarditis; these findings indicate transthyretin amyloidosis with coexistent eosinophilic myocarditis



[C] T1 and **[D]** T2 mapping reveal diffusely elevated values, consistent with amyloid infiltration and superimposed edema



[G] The trend in eosinophil count over the clinical course



COMMENT

An 81-year-old man presented with heart failure and marked hypereosinophilia, raising concern for EM. Although eosinophilia is common in EM, up to one-quarter of cases may present with normal counts, and in nearly one-third, the etiology remains unidentified. When secondary causes are detected, drug hypersensitivity is the most frequent, followed by eosinophilic granulomatosis with polyangiitis (EGPA), HES, infections, pregnancy, and malignancy [1].

Our patient had no history of atopy, asthma, or recent vaccination. In addition, tafamidis, the only recently initiated medication, has not been linked to eosinophilia [2]. Tafamidis therapy was initiated approximately 4 months prior to the index hospitalization. Eosinophil counts were within normal limits before and during the initial period following tafamidis initiation and began to increase approximately three months after treatment initiation, suggesting no immediate hypersensitivity reaction [Figure 1G]. Eosinophil counts dropped immediately after starting steroid therapy, surged again during tapering, and remained suppressed with anti-interleukin-5 therapy. Nevertheless, tafamidis therapy was discontinued to rule out a drug hypersensitivity reaction. The absence of asthma, sinusitis, neuropathy, or ANCA positivity made EGPA unlikely, and the negative parasitic serologies decreased the likelihood of an infectious etiology as the underlying trigger.

HES, defined by sustained eosinophilia >1.5 × 10^9/L with organ involvement, was strongly considered. HES may arise as a primary clonal disorder due to underlying hematologic malignancy, as a secondary (reactive) process in the setting of nonmalignant conditions, or as an idiopathic entity. Cardiovascular involvement occurs in 20–35% of patients, depending on HES phenotype [3]. In this case, ^{18}F-FDG PET/CT showed only mild, nonspecific distal esophageal uptake with no gross mass detected on CT, and no lymphadenopathy or marrow disease. Given the nonspecific nature of this finding, its absence on CT, the rarity of esophageal mass involvement in HES symptoms, and the patient's frailty, we decided not to proceed with gastroscopy.

The 2024 American College of Cardiology Expert Consensus Document on the Diagnosis and Management of Myocarditis [4] recommends EMB for patients with left ventricular dysfunction, symptomatic heart failure, arrhythmias, or peripheral eosinophilia. However, EMB is an invasive and high-risk procedure with multiple potential complications, including cardiac perforation with tamponade, ventricular arrhythmias, conduction blocks, and pneumothorax. Therefore, careful patient selection is essential.

cMRI has emerged as a valuable noninvasive diagnostic tool, demonstrating a sensitivity of 88% and a specificity of 96% for acute myocarditis when applying the updated Lake Louise criteria, particularly when performed within the first two weeks of symptom onset [5]. These criteria require at least one positive T2-based marker of myocardial edema and, ideally, one T1-based marker of myocardial injury, with the combination of both yielding the highest diagnostic specificity. In EM, cMRI typically demonstrates diffuse subendocardial LGE, a distinctive feature that differentiates it from other etiologies of myocardial inflammation. Additional findings, such as small epicardial aneurysms on cine imaging, have also been described [4].

In our case, the patient's advanced age and frailty, combined with the invasive nature and limited sensitivity of EMB, led to the decision to forego biopsy. The cMRI findings, including marked T2 signal hyperintensity, elevated T1 relaxation times, and diffuse subendocardial LGE, in conjunction with profound peripheral eosinophilia, strongly supported the diagnosis of EM.

Accordingly, our case represents a clinically probable EM rather than a biopsy-proven disease. Furthermore, the presence of diffuse and patchy mid-myocardial LGE suggested concomitant ATTR cardiac amyloidosis, highlighting a rare and distinctive overlap of imaging features indicative of both infiltrative and inflammatory cardiomyopathies. Repeat imaging was not performed during follow-up, primarily due to the patient's frailty and the decision to guide management clinically.

No prospective, randomized trials have established the efficacy of corticosteroid therapy in EM. However, a retrospective analysis of 179 case reports suggested an association between intravenous corticosteroid administration and reduced in-hospital mortality. The optimal dosing and taper strategy remain undefined [1]. In our case, the management approach was reviewed in a multidisciplinary team meeting, which led to the initiation of corticosteroid therapy.

CONCLUSIONS

To the best of our knowledge, this case describes the first documented coexistence of ATTR cardiac amyloidosis and eosinophilic myocarditis in the setting of hypereosinophilic syndrome. The sequence of events: diagnosis of amyloidosis, initiation of tafamidis, and the subsequent emergence of significant eosinophilia with myocardial injury, raises the possibility of interaction between processes that are usually considered distinct. Cardiac manifestations of HES are uncommon and rarely occur in isolation, making this overlap especially striking. We cannot prove causality, yet the findings broaden the clinical spectrum of ATTR cardiac amyloidosis and illustrate the potential for inflammatory overlap in infiltrative cardiomyopathy. Further research is required to better understand the mechanisms, clinical implications, and potential associations underlying this unusual overlap.

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