Incidental Late Stage Loeffler's Endocarditis in an Asymptomatic Patient

Trisha Gomez, MD, MBA, Sherilyn Munoz, DO, Eesha Purohit, MD, Christopher Madison, MD, Laura Franey, MD, and David McNamara, MD, MPH, *Grand Rapids, Michigan*

INTRODUCTION

Loeffler's endocarditis is a rare form of restrictive cardiomyopathy caused by endomyocardial infiltration of eosinophils. Patients typically become symptomatic when endomyocardial fibrosis ensues, causing restriction and subsequent heart failure symptoms. Presentation can vary from asymptomatic to advanced heart failure. We present a patient with no symptoms incidentally found to have Loeffler's endocarditis with evidence of fibrosis and apical thrombus on multimodality cardiac imaging.

CASE PRESENTATION

The patient is an asymptomatic 69-year-old woman with a history of hypertension, hypothyroidism, and gout who underwent preoperative evaluation and was found to have diffuse, anterior-predominant T-wave inversions on electrocardiogram (ECG; Figure 1) prompting further evaluation.

Workup included a transthoracic echocardiogram (TTE), which demonstrated preserved left ventricular (LV) systolic function and structurally normal cardiac valves without hemodynamically significant valve dysfunction. Using an ultrasound-enhancing agent, a filling defect in the apex was noted (Figure 2, Video 1) with complete cavity obliteration in this area. There was normal wall thickening and motion in the area adjacent to the filling defect. No prior TTE was available for comparison.

Based on the initial imaging, differential diagnoses included Loeffler's endocarditis, a prior apical myocardial infarction with an associated LV thrombus, and apical-variant hypertrophic cardiomyopathy (HCM).

Cardiovascular magnetic resonance (CMR) was pursued for further evaluation (Figure 3, Video 2), revealing normal LV chamber size and systolic function with an LV end-diastolic volume index of 59 mL/m^2 (normal, 52-86) and LV ejection fraction of 61%. This also demonstrated a mild increase in LV apical wall thickness and apical cap with evidence of a central, layered apical LV thrombus. There is associated apical subendocardial late gadolinium enhancement (LGE) in the corresponding segments. Myocardial tissue characterization at the level of the midventricle showed elevated native T1 (global, 1,055 msec [normal, 968-1,041]; anteroseptal, 1,086 msec [normal, 972-1,057]; inferoseptal, 1,078 msec [normal, 973-1,061]) consistent with diffuse myocardial fibrosis. Native T2 (global, 49 msec [normal, 42-52]; anteroseptal, 49 msec [normal, 43-55]; inferoseptal, 51 msec [normal, 42-53]) and extracellular volume (global, 26% [normal, <31%]) at the level of the midventricle were normal.

Typical CMR features of apical HCM such as wall thickness ≥15 mm, apical-to-basal wall thickness ratio ≥1.3-1.5, and LV apical aneurysm were not demonstrated. Overall, ECG, TTE, and CMR findings were thought to be most consistent with Loeffler's endocarditis.

Other workup including a complete blood count showed mild peripheral eosinophilia with an absolute eosinophil count of 530/uL (normal range, 0-500/uL). Extensive workup for hypereosinophilic syndrome (HES), including infectious (Strongyloides antibodies, stool culture for ova and parasites), autoimmune (erythrocyte sedimentation rate, antinuclear antibodies, C-reactive protein, antineutrophil cytoplasmic antibodies, creatine kinase), and hematologic (peripheral smear, serum protein electrophoresis, serum-free light chain assay, IgM, IgG, IgA, JAK2 mutation, B12, folic acid, complete metabolic panel, tryptase, and bone marrow biopsy with fluorescence in situ hybridization analysis) etiologies were unrevealing.

The patient was initiated on anticoagulation immediately following the TTE given the clinical suspicion for Loeffler's endocarditis. Multidisciplinary meetings with rheumatology and hematology teams occurred. Given the presence of cardiac end-organ dysfunction despite the mild degree of peripheral eosinophilia, the decision was made to start the patient on high-dose steroid pulse suppressive therapy with oral prednisone followed by a slow taper.

The patient remained asymptomatic with no evidence of clinical heart failure. Two months after initiation of steroids, there was complete resolution of peripheral eosinophilia. Follow-up CMR obtained after 3 months of oral anticoagulation and immunosuppression (Figure 4) demonstrated regression without complete resolution of the apical endomyocardial fibrosis and layered mural thrombus. Oral anticoagulation was continued while steroid was tapered.

Using shared decision-making, a repeat CMR was performed after the patient was off immunosuppressive therapy for 3 months. This demonstrated a mild increase in LV apical wall thickness with persistent layered mural apical thrombus (Figure 5) and complete resolution of apical LGE (Figure 6), suggesting successful treatment of the active endomyocardial fibrosis. Left ventricular chamber size and systolic function remained preserved. Myocardial tissue characterization at the level of the midventricle remained similar to baseline CMR with elevated native T1 and normal native T2 and extracellular volume values.

From the Department of Cardiovascular Medicine, Corewell Health/Michigan State University, Grand Rapids, Michigan.

Keywords: Restrictive, Thrombus, Fibrosis, Imaging, Hypereosinophilia

Correspondence: Trisha Gomez, MD, MBA, 100 Michigan Street NE, Grand Rapids, MI 49503. (E-mail: *trishamarie.gomez@corewellhealth.org*).

2468-6441
https://doi.org/10.1016/j.case.2023.09.009

VIDEO HIGHLIGHTS

Video 1: Contrast-enhanced TTE with apical 4-chamber view demonstrating echodense material in the LV apex, contiguous with the LV endocardium.

Video 2: Cardiovascular magnetic resonance steady-state free precession 4-chamber cine imaging demonstrating mild increase in LV apical wall thickness with LV mass adherent to the myocardium.

View the video content online at www.cvcasejournal.com.

Anticoagulation was continued and repeat imaging was recommended in 1 year. If there is evidence of fibrosis or thrombus progression while off of immunosuppressive therapy, treatment for eosinophilia will be reinitiated using either steroid or steroid-sparing therapy (e.g., mepolizumab).

DISCUSSION

Hypereosinophilic syndrome is a rare multisystem disease characterized by increased production of eosinophils, which could ultimately lead to end-organ damage.[1] Loeffler's endocarditis is the cardiac involvement of HES whereby the endomyocardium is infiltrated by eosinophils resulting in necrosis, toxic degranulation, thrombus formation, and eventual fibrosis.[2,3] Diagnosis typically occurs once patients become symptomatic from fibrosis causing a restrictive cardiomyopathy and subsequent heart failure symptoms or systemic embolism secondary to an associated thrombus formation due to the hypercoagulable inflammatory nature of the disease process[3,4] Although rare, patients can also be asymptomatic, as in this case, particularly when cases are identified early, challenging traditional treatment decisions.[5] Hence, high suspicion is necessary once characteristic imaging findings are observed.

The initial imaging modality of choice is echocardiography. Apical thickening and mural thrombi are characteristic, although diastolic dysfunction, valvular disease, and atrial enlargement may also be seen. The presence of a mural thrombi in the absence of associated wall motion abnormalities is highly suggestive of Loeffler's endocarditis, especially when there is concomitant peripheral eosinophilia. It is important to note, however, that the level of peripheral eosinophilia is not necessarily proportional to the degree of cardiac involvement and may not even be present during diagnosis.[1,6]

Not uncommonly, the apical thrombi and thickening can be confused with apical HCM. Electrocardiogram findings may be similar in apical HCM and Loeffler's endocarditis as both can present with T-wave inversions in the precordial leads, although greater degree of T-wave inversions and greater voltages may point toward apical HCM.

Endomyocardial biopsy remains the gold standard for diagnosis of Loeffler's endocarditis but is frequently deferred unless noninvasive imaging is inconclusive. Contrast-enhanced CMR has been used as the subsequent imaging modality of choice when ECG and TTE are suggestive of Loeffler's endocarditis as this can aid in thrombi visualization as well as identification of subendocardial LGE.[1,7]

A multidisciplinary approach should be undertaken and include hematology, rheumatology, and infectious disease specialists as it is important to exclude secondary causes of hypereosinophilia. Once secondary causes were excluded, our patient was started on immunosuppression—specifically, high-dose oral prednisone. This is the cornerstone of treatment, with a goal of reducing peripheral eosinophil levels. If necessary, steroid-sparing agents including monoclonal antibodies are used in cases of steroid nonresponders or those who would require prolonged duration of treatment.[3] Anticoagulation is indicated if a thrombus is identified. No clear guidelines exist regarding duration of therapy for immunosuppression and anticoagulation in Loeffler's endocarditis, both of which remain areas of investigation.

Once recognized, prompt treatment is warranted to avoid complications such as progressive heart failure, systemic embolism, fatal arrhythmias, valvular heart disease, and sudden cardiac death.[8]

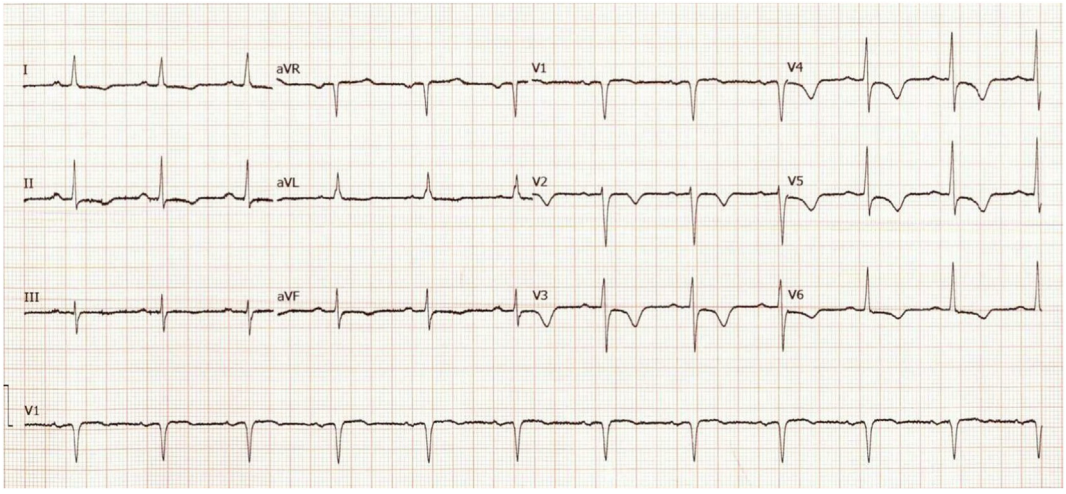

Figure 1 Electrocardiogram showing normal sinus rhythm, normal axis, prolonged QTc and diffuse T-wave inversions, predominantly in the anterior leads.

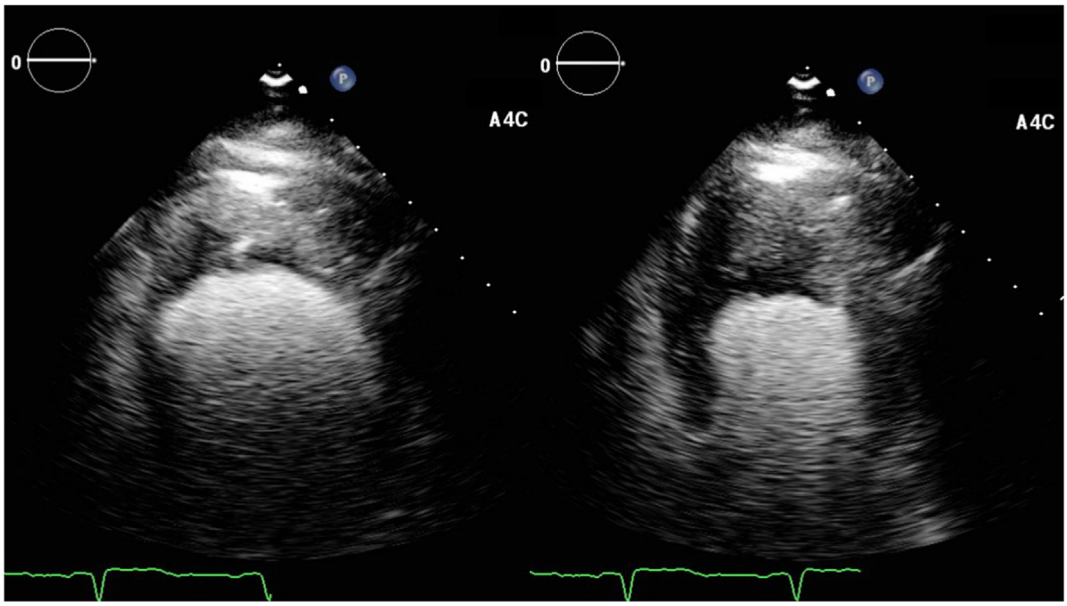

Figure 2 Transthoracic echocardiogram apical 4-chamber view in end diastole (*left*) and end systole (*right*) using an ultrasound-enhancing agent demonstrates echodense material in the LV apex, contiguous with the LV endocardium.

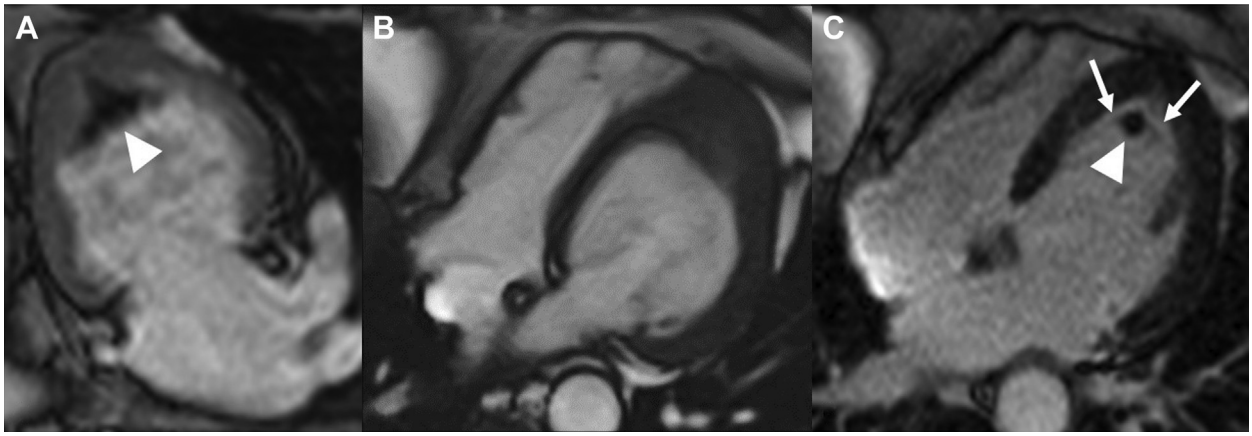

Figure 3 Cardiovascular magnetic resonance findings in Loeffler's endocarditis. **(A)** Cardiovascular magnetic resonance 2-chamber early postcontrast imaging showing a central, layered apical LV thrombus (*arrowhead*) with adjacent increase in LV apical wall thickness. **(B)** Cardiovascular magnetic resonance 4-chamber steady-state free precession cine imaging at end diastole demonstrates mild increase in LV apical wall thickness with LV mass adherent to the myocardium. **(C)** Cardiovascular magnetic resonance 4-chamber LGE imaging demonstrates subendocardial LGE (*arrows*) along the apical segments and apex with redemonstration of LV apical thrombus (*arrowhead*).

While the presence of LGE is typically associated with chronic, irreversible processes, previous studies have demonstrated that the presence of LGE does not always indicate irreversible myocardial fibrosis. A recent study evaluated the presence of LGE in an acute myocarditis population with findings showing complete resolution of LGE in a subset of patients on follow-up CMR.[9] Similar improvement in LGE distribution has been shown in amyloid patients following implementation of chemotherapy.[10] The above studies highlight that LGE is caused by myocardial pathology that increases the interstitial space, inclusive of edema or abnormal protein deposition, and not always indicative of irreversible replacement fibrosis. As with Loeffler's endocarditis, the presence of LGE is likely associated with a more acute process. In our patient, subendocardial LGE completely resolved after

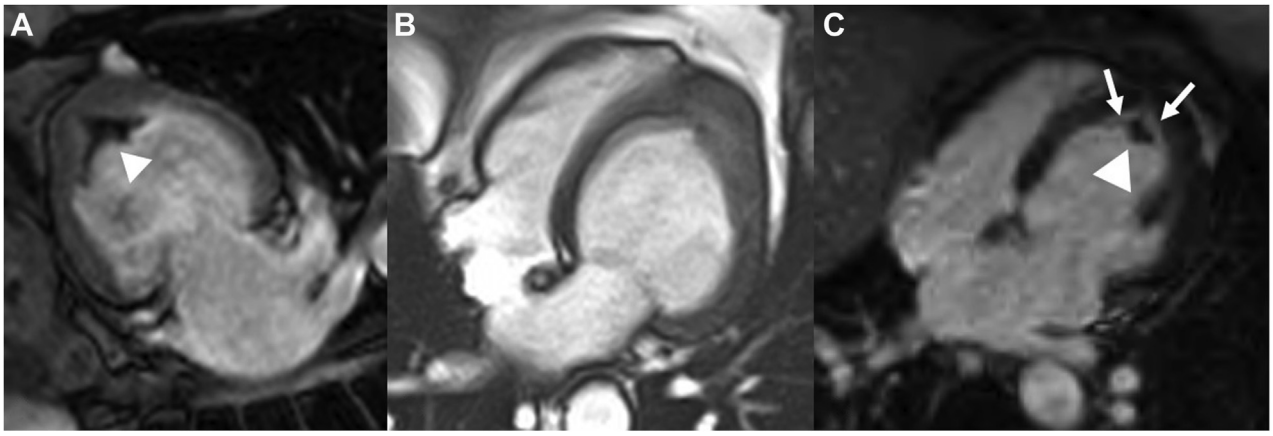

Figure 4 Follow-up CMR after treatment with anticoagulation and immunosuppression for 3 months. **(A)** Cardiovascular magnetic resonance 2-chamber early post–contrast imaging demonstrates persistence of central, layered apical LV thrombus (*arrowhead*). **(B, C)** Cardiovascular magnetic resonance 4-chamber steady-state free precession and LGE imaging showing regression without complete resolution of endomyocardial fibrosis (*arrows*) and persistent apical LV thrombus (*arrowhead*).

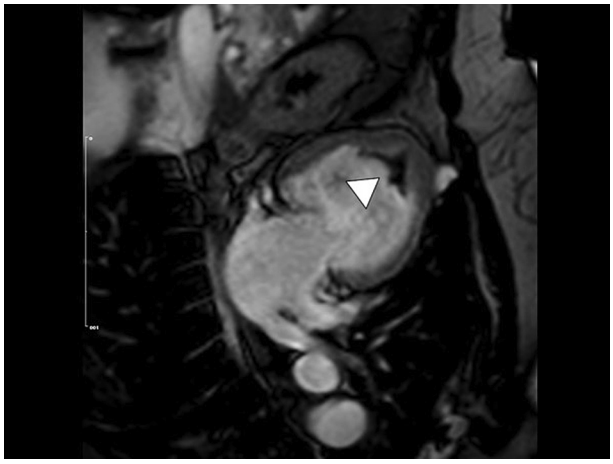

Figure 5 Cardiovascular magnetic resonance 2-chamber early post–contrast imaging on follow-up while off immunosuppressive therapy for 3 months demonstrating persistence of central, layered apical LV thrombus (*arrowhead*) with no significant interval change when compared to prior CMRs.

immunosuppressive therapy, suggesting reversibility once appropriate treatment has been instituted.

CONCLUSION

Loeffler's endocarditis is an uncommon sequela of HES. It is important to keep Loeffler's endocarditis in the differential despite its rarity as lack of prompt treatment can be life-threatening, even in asymptomatic cases. Without prompt treatment, complications could occur including systemic embolism, progressive heart failure, fatal arrhythmias, and valvular heart disease.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed consent was not required from the patient under an IRB exemption status.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

FUNDING STATEMENT

The authors declare that this report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

ACKNOWLEDGMENTS

We thank Katherine A. Couling, RDCS, RVT, for acquisition of images.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2023.09.009.

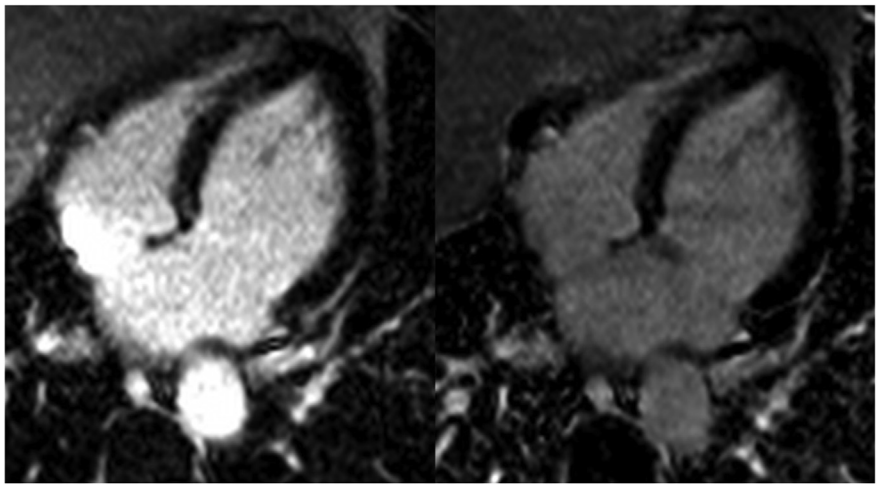

Figure 6 Cardiovascular magnetic resonance 4-chamber LGE imaging with magnitude image (*left*) and phase-sensitive inversion recovery image (*right*) demonstrating complete resolution of previously noted apical LGE/endomyocardial fibrosis.

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