A Case of Loeffler Endocarditis That Showed Endomyocardial Systolic Dysfunction Detected by Layer Specific Strain Analysis

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Summary
Loeffler endocarditis is a rare comprehensive cardiac manifestation caused by eosinophilic cell infiltrations and is present in 50%-60% of patients with hypereosinophilic syndrome (HES). Left ventricle (LV) endocardial systolic dysfunction is a major cause of morbidity and mortality in HES and Loeffler endocarditis. We present a case of Loeffler endocarditis, whose left ventricular (LV) systolic dysfunction and endocardial systolic dysfunction were first neglected by conventional transthoracic echocardiography (TTE), but were later pointed out by layer-specific longitudinal strain analysis. With timely initial therapeutic management, the patient’s outcome was remarkable. Thus, we strongly recommend strain analysis as a necessary supplementary test of conventional TTE in all patients with Loeffler endocarditis.

Key words: Longitudinal strain

Loeffler endocarditis is a rare cardiac manifestation secondary to endomyocardium damage by eosinophilic cell infiltrations, characterized by progressive subendocardial fibrosis and restrictive dysfunction with marked peripheral eosinophilia. Conventional echocardiography is one of the most common initial imaging modalities in Loeffler endocarditis diagnosis. However, it is impossible to solely rely on left ventricular ejection fraction (LV EF) for precise evaluation of LV systolic function and detection of endocardial systolic dysfunction. Compared with this, two dimensional-speckle tracking echocardiography (2D-STE) can quantify myocardial mechanics through a layer-specific longitudinal strain, which not only can detect early subtle LV systolic dysfunction and even more specific LV endocardial systolic dysfunction, but also provides more precise follow-up cardiac assessments to patients with Loeffler endocarditis.

In this report, we present a typical case of Loeffler endocarditis with remarkable prognosis, and interpret the significant role that layer-specific strain analysis plays.

Case Report
A 53-year-old man was admitted for progressive dyspnea, with fatigue for more than half a year, which was aggravated within a month prior to arrival. On arrival, he was in functional class III according to New York heart association (NYHA). His vital signs and physical exams were normal. Complete blood counts (CBC) showed elevated eosinophils (4.80 x 10^9/L), and blood analysis of Brain Natriuretic Peptide (BNP) was elevated (1,048 pg/mL). Fluorescence in situ Hybridization (FISH) for the FIP1L1-PDGFRα gene was positive. Further work-up for secondary causes of hypereosinophilia were excluded. An electrocardiogram revealed non-specific ST-segment changes. Transthoracic echocardiography (TTE) demonstrated wall thickening in both ventricles, obliteration of left ventricle apex by thrombosis formation (2.6 cm² in size, Figure 1A) with preserved left ventricle ejection fraction (LVEF 52%), and bi-atrium enlargements with moderate tricuspid valve regurgitation. Trans-mitral flow showed a restrictive filling pattern (Grade III) with E/A ratio 2.2, E wave-deceleration time (EDT) 78 ms. Furthermore, layer-specific longitudinal strain (LS) was analyzed on the QLAB (8.0 software, IE33 ultrasound system), and LV peak values of global LS (GLS), endocardial LS (GLS_endo), epicardial LS (GLS_epi) were respectively averaged from the apical 4-, 3- and 2-chamber views. In a normal population, peak LV GLS is expected in the range of -20%, and the absolute value below -20% is considered abnormal. Overall LV GLS was reduced to -10.96%, indicating LV systolic dysfunction, which was overlooked by single LV EF evaluation. LV GLS_endo and GLS_epi were -14.16% and -15.89% respectively, and LS transmural gradient was -1.73%, calculated as the difference between LV GLS_endo and GLS_epi, further indicating much more remarkable LV endomyocardial systolic dysfunction (Figure 2A). Since LV endocardial LS value should be higher than that of LV epicardial LS in normal population.
The hypereosinophilia syndrome (HES) and Loeffler endocarditis were diagnosed based on the above findings and endomyocardial biopsy results. Therefore, corticosteroid, warfarin, furosemide, spironolactone, beta-blocker and imatinib were initiated.

Six months later, the patient came back with significant improvements in NYHA class I. His CBC and eosinophils (0.39 × 10^9/L) came back within normal range and BNP decreased to 348 pg/mL. Follow-up TTE demonstrated the decrease of left ventricle apical thrombosis to 1.76 cm² in size (Figure 1B), improvements of diastolic function to Grade II with a decrease of the E/A ratio to 1.5, and no significant change to LVEF (54%). However, remarkable changes were detected by layer-specific LS analysis (Figure 2B). First of all, overall LV GLS increased to -16.47%, even though still considered abnormal below -20%. Secondly, LV GLSendo and GLS epi increased to -18.79% and -16.21%, respectively, and the LS transmural gradient increased to 2.53%, which indicated significant recovery of endomyocardial systolic function, therapeutic efficiency and, further, a favorable clinical outcome.

**Discussion**

HES is a rare systemic disease with persistent peripheral blood eosinophilia (> 1,500/mm³ for > 6 months) with unknown causes. Cardiac involvement, especially LV endocardial layer dysfunction, is a major cause of morbidity and mortality for HES patients. Loeffler endocarditis is one of main cardiac manifestations complicated with HES and is present in 50% - 60% of HES cases.

Conventional echocardiography has been one of the mandatory and most versatile imaging modalities in Loeffler endocarditis diagnosis, characterized with apical obliteration by wall thickness and thrombosis formation, and development of diastolic dysfunction. Preserved LV systolic function is common in Loeffler endocarditis. However, it is likely that systolic function evaluated by LV EF...
was underestimated in most previous studies, since LV EF reflects only global LV volumetric changes, rather than true myocardial contractility.2) Besides, precise evaluation of myocardial contractility should be considered equally as significant as evaluation of diastolic dysfunction. In this regard, 2D-STE-derived GLS, which represents relative myocardium length changes during cardiac cycles, seems to be more representative of true myocardial contraction and offers more precise diagnostic and incremental prognostic data over LV EF in a variety of conditions, including Loeffler endocarditis.2) Like the case above, we successfully used LV GLS to detect myocardial systolic dysfunction and recovery masked by LV EF evaluation. However, LV GLS has a limited role in providing comprehensive diagnostic and prognostic data in Loeffler endocarditis, since LV GLS reflects LV global systolic function instead of systolic function of LV endocardium layer, which, as a matter of fact, is a major cause of morbidity and mortality in Loeffler endocarditis. Thus, to confirm the precise endomyocardial systolic dysfunction involvement, layer-specific deformation quantification is needed.5)

Under normal conditions, the left ventricle is non-homogenously composed of three myocardial layers1) (endoocardial, middle, and epicardial layer). Layer-specific LS in a normal population should have a higher peak value of LV endocardial LS than that of the LV epicardial LS, which makes the transmural gradient.1) Nevertheless, in Loeffler endocarditis, endocardium impairments may lead to a significant decrease of the endocardial longitudinal strain value, with relative sparing of the longitudinal strain value in the epicardial layer, attributing to significant decrease in transmural gradient, and vice versa. Therefore, close detection of LS transmural gradient evolution in Loeffler endocarditis not only benefits in observation of disease progression, but also helps to predict the prognosis. Like the case reported above, close follow-up with layer-specific LS analysis helps us monitor significant improvement in endocardial systolic function, which is matched with favorable clinical outcomes of the patient.

Thus, we highly recommend 2D-STE, particularly layer-specific longitudinal strain analysis as a necessary supplementary test with conventional TTE for all patients with suspected and confirmed Loeffler endocarditis. Since precise and comprehensive evaluations of systolic function should be considered equally significant.

To our best knowledge, this is the first case report of Loeffler endocarditis where endocardial systolic dysfunction was detected with layer-specific longitudinal speckle tracking analysis.

Disclosures
Conflicts of interest: None.

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