Letter to the Editor

Myocardial acoustics-assisted diagnosis of right ventricular Loeffler endocarditis

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Introduction

Loeffler endocarditis is a rare type of endocarditis secondary to eosinophilia (1). The main injuries include subendocardial thrombosis in the early stage and myocardial invasion in the middle and advanced stages. Currently, endocardial biopsy is still the gold standard for the diagnosis of Loeffler endocarditis, but because of its invasiveness, it is of limited application in clinical setting (2). We here present a case of a patient with a large occupation of the right ventricle, resulting in limited returned blood volume, with hypovolemic shock as the first manifestation. Myocardial contrast echocardiography confirmed the nature of the space-occupying lesion, and despite puzzling additional examination results and medical history data, a diagnosis of Loeffler endocarditis was eventually made. Based on this diagnosis, he underwent appropriate medical treatment with positive results. The efficacy of the treatment confirmed the previous diagnosis.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the relevant institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

On May 1, 2021, the patient, a 58-year-old male, had symptoms of with recurrent diarrhea with no apparent cause. On May 3, 2021, these symptoms were accompanied by shortness of breath and perspiration after activity, which could not be relieved by rest, and the patient lost consciousness. He was found by his family and taken to the emergency room in Chengdu First People's Hospital on May 4, 2021. His previous medical history included symptoms of gastritis and duodenitis, and a routine blood test in January 2021 showed an elevated eosinophil count (percentage of eosinophils was 52.1%, and the absolute value of eosinophils 6.59×10^9/L). He denied a history of diabetes, hypertension, coronary heart disease, infectious disease, allergy, and surgery.

At admission, the physical examination showed the following: body temperature 36.0 ℃, pulse 97 times/min, respiratory rate 21 times/min, and blood pressure 73/56 mmHg (1 mmHg =0.133 kPa). He was conscious, but looked unwell and pale. His skin and sclera were not yellowed, and there was no edema of the superficial lymph nodes in any area of the body. Edema was present on both legs, and many red spots and skin lesions were visible on the skin surface. The borders of the heart were enlarged, the sounds of the heart were distant, the rhythm of the heart was uniform, and no murmur could be heard in any region of the valves. No abnormality was seen in the thorax, and no abnormal sound was detected in either lung percussion or auscultation. The physical examination shows: the entire abdominal was without tenderness, rebound pain,

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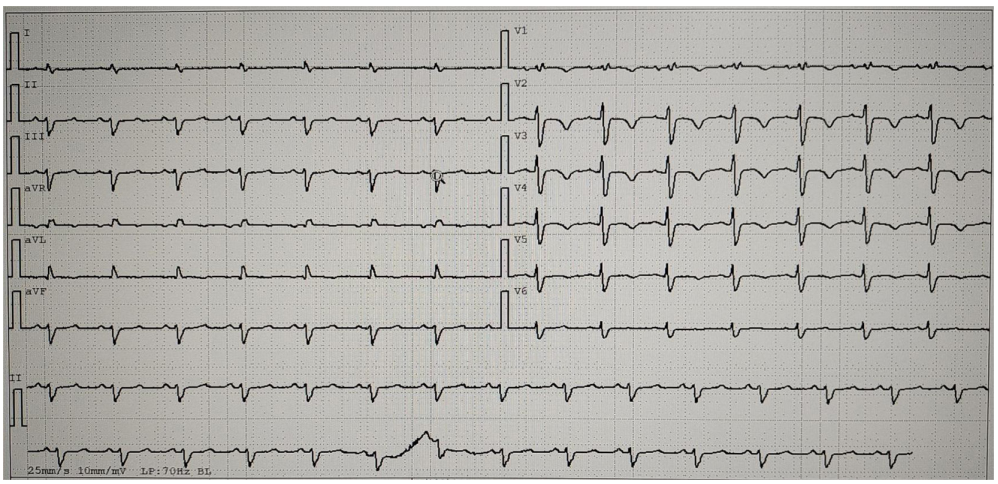

Figure 1 The ECG of the patient showed normal sinus rhythm, left posterior fascicular block, complete right bundle-branch block, and T-wave shift. ECG, electrocardiograph.

abdominal cramps, and percussion pain in the liver and kidney areas.

The electrocardiograph (ECG) showed normal sinus rhythm, left posterior fascicular block, complete right bundle-branch block, and T-wave shift (*Figure 1*).

Blood routine examination included the follow results: eosinophil count, 14.39×10^9/L; eosinophil percentage, 61.2%; white blood cell count, 23.48×10^9/L; neutrophil count, 6.52×10^9/L; C-reactive protein count, 27.64 mg/L. The myocardial enzyme results included a creatine kinase-MB level of 6.5 μg/L and a troponin level of 0.25 μg/L. The kidney function results were as follows: urea, level of 15 mmol/L; creatinine, level of 160 μmol/L; and uric acid, level of 505 μmol/L.

Chest and abdominal computed tomography (CT) showed mild inflammation in both lungs and a slight pleural effusion in the right chest. Cardiac chamber dilatation and pericardial effusion also were detected on CT scans. There were also local swelling and thickening of the gastrointestinal wall, ascites in the whole abdominal cavity and pelvis, and enlarged lymph nodes.

Echocardiography revealed right heart enlargement (the right ventricle end-diastolic diameter was 36 mm, and the right atrium diameter was 51 mm) and a diffuse moderate echogenic mass filling the right ventricle, occupying a space about 37 mm × 44 mm × 68 mm in size; the echogenicity of the mass was uneven, the boundary was irregular, and the boundary between the mass and the ventricular wall was unclear (*Figure 2*). The mass caused a narrowing of the right ventricular inflow and outflow tract, the inner diameter of the narrowest part was 15 mm, a small amount of tricuspid regurgitation was present, and the systolic function of the right ventricle was reduced [tricuspid annular plane systolic excursion (TAPSE) 12 mm]. The measured value of left atrium and ventricle decreased (the left ventricle end-diastolic diameter was 30 mm, and the left atrium diameter was 23 mm), with normal left ventricular systolic function (left ventricular ejection fraction was 58%) and inadequate cardiac output (the left ventricular stroke volume was 18.5 mL). There was also moderate pericardial effusion in the pericardial cavity.

Given the all aforementioned data, the admission diagnosis was hypovolemic shock, acute gastroenteritis, atrophic gastritis, and renal insufficiency. The nature of the right ventricle occupancy remained to be determined. Empirical treatment was administered, which included fluid therapy to correct hypovolemic shock and electrolyte and acid-base imbalances.

A myocardial acoustic contrasting procedure was also applied. A total of 1 mL of SonoVue was slowly injected into the vein in the left elbow. In the right ventricle, a markedly solid echo was visible, which had spread widely over the surface of the endocardium and extended to the tricuspid valve (*Figure 3*). No significant enhancement was noted in the inner part of the solid on the post-contrast image. Compared with conventional ultrasound, the boundary between the space-occupying area and their right ventricular myocardial layer was clear after imaging, with smooth edges (*Figure 3*). An additional 1 mL of the contrast agent was added. Real-time perfusion imaging (RTPI) was

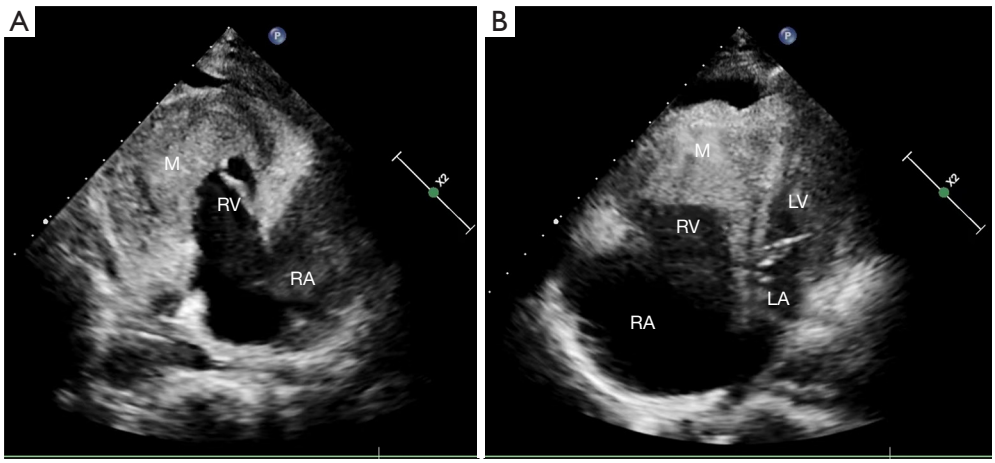

Figure 2 Transthoracic echocardiography. (A) Mass in the right side of the heart; (B) comparison of left and right sides of the heart in terms of size. M, mass; RV, right ventricle; RA, right atrium; LV, left ventricle; LA, left atrium.

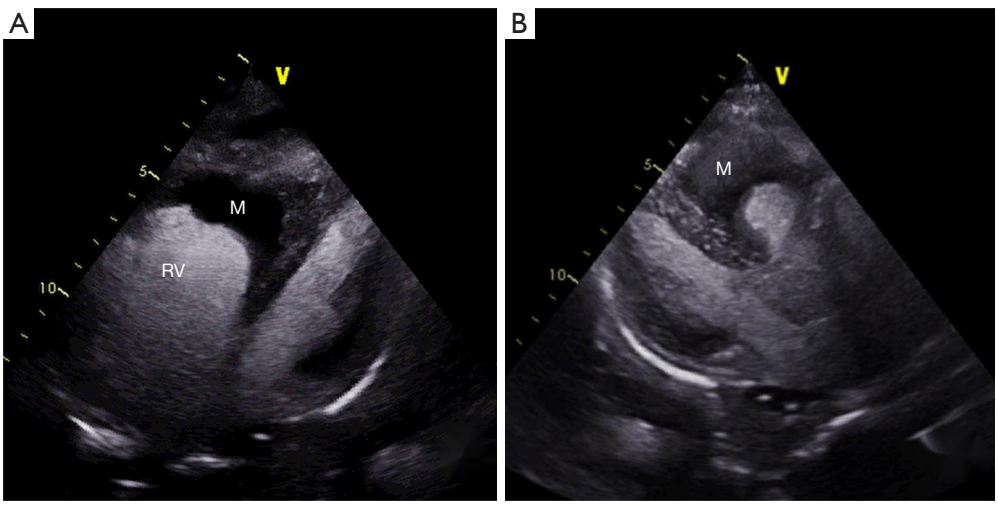

Figure 3 Left ventricular contrast medium. M, mass; RV, right ventricle.

performed via blasting for 10 consecutive frames with a high mechanical index (MI) (MI =1.2), and the contrast agent signal in the space occupied did not increase (*Figure 4*). The final angiographic results suggested that the right ventricular mass was irregular in shape, had a clear boundary with the endocardium, and lacked a blood supply; it was therefore diagnosed as thrombosis.

The diagnosis and treatment plan were devised as follows. Based on medical history, laboratory tests, and cardiac, bone marrow, and genetic test results, the patient was diagnosed with Loeffler endocarditis. A treatment plan, including integration and prednisone, was devised. The patient received 5,000 IU of low-molecular weight heparin (twice a day), subcutaneous injection of anticoagulants, and 60-mg prednisone (once a day) oral treatment. Additional cardiac occupation was continuously observed and surgical intervention could not yet be ruled out.

Within 2 months, the patient's hypovolemia was relieved, the peak blood pressure was 113/79 mmHg, and a routine blood test showed a normal eosinophil count. Echocardiography showed that the right side of the heart was enlarged (*Figure 5*) (the right ventricle end-diastolic diameter was 33 mm, and the right atrium diameter was 62 mm) as was the mass under the endocardium of the right heart; compared with the previous examination, the space-occupying area was significantly reduced (the maximum

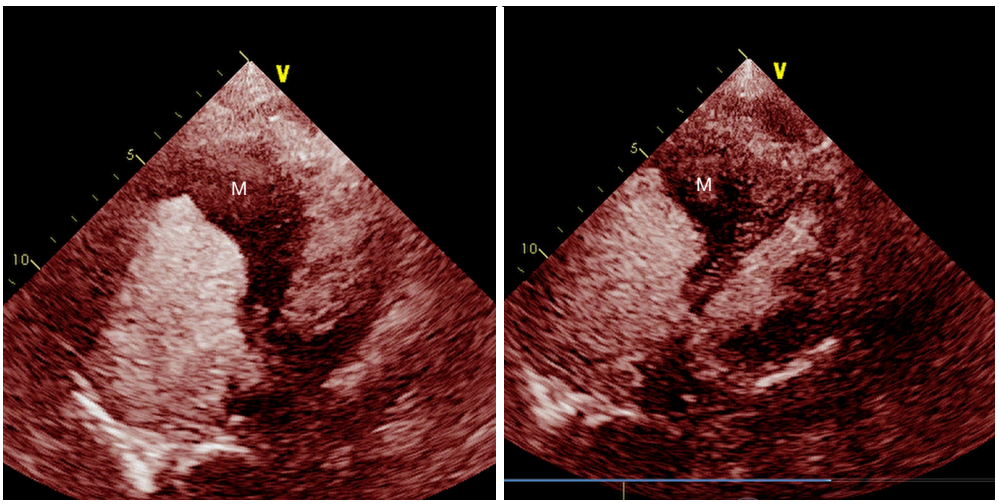

Figure 4 Angiographic in RTPI. M, mass; RTPI, real-time perfusion imaging.

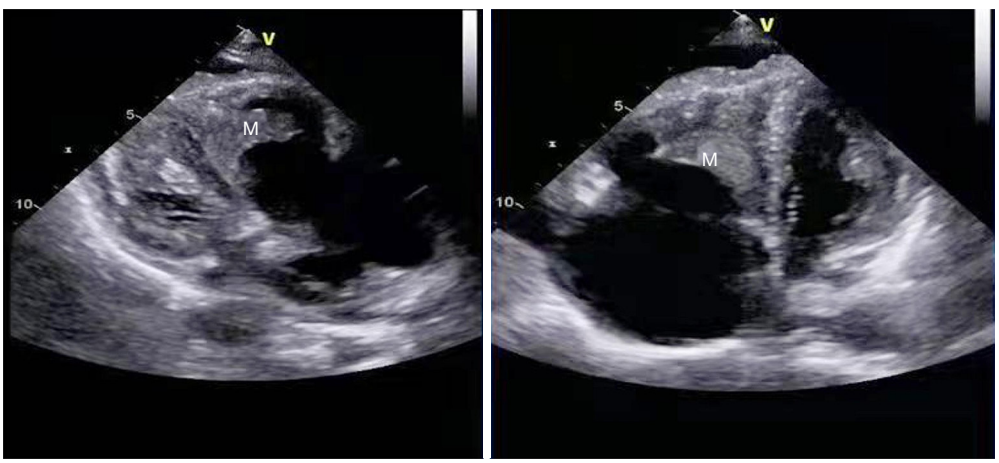

Figure 5 Echocardiography for 2 months after the patient's discharge. M, mass.

diameter was about 24 mm × 30 mm), with a large amount of tricuspid regurgitation and decreased right ventricular systolic function (TAPSE 7 mm). The measured value of left atrioventricular anteroposterior diameter was normal (the left ventricle end-diastolic diameter was 42 mm, and the left atrium diameter was 30 mm), with normal left ventricular systolic function (left ventricular ejection fraction was 72%) and normal left ventricular stroke volume (the left ventricular stroke volume was 44.5 mL). A moderate amount of pleural effusion was found.

Discussion

Loeffler endocarditis is a type of endocardial disease, which includes two subtypes, Loeffler endocarditis and Davis disease. These two subtypes have similar phenotypes, both showing endocardial fibrosis at the apex of the ventricle and in the ventricle region (3). Loeffler endocarditis was first proposed by Loeffler in 1932 (4). Most patients with this disease were from poor tropical and subtropical regions and were around 40–50 years old. He reported that the incidence of Loeffler endocarditis was associated with filarial infection and abnormal immune function. This case presented in this report was classified as a subtype of Loeffler endocarditis. Compared with the short-term onset of endocardial fibrosis in Davis disease, the onset of the Loeffler endocarditis subtype has a slow and protracted development process.

The long progression of Loeffler endocarditis can be divided into three phases: the initial phase, characterized by eosinophil infiltration and myocardial intima necrosis, starts with an increase count in eosinophils for more than 5 weeks and lasts for 10 months; the second stage is the thrombotic phase, in which subendocardial thrombosis appears in the damaged area and is followed by occupation of the ventricles, which lasts for 24 months; the final stage of fibrosis occurs after 24 months, in which fibrosis forms and heals the inflammation, but fibrosis causes restrictive cardiomyopathy; this stage is difficult to treat and has a significant mortality rate, with heart transplantation being the only treatment (5).

The diagnosis of Loffler endocarditis consists of a sustained increase count in eosinophils. To identify the cause of increased eosinophils, direct evidence of myocardial damage is required, and a myocardial biopsy is the gold standard. Eosinophilia may be secondary to tumors, parasitic infections, and allergic reactions. After the above factors are excluded, the patient's condition can be attributed to idiopathic eosinophilic syndrome. Treatment of Loeffler endocarditis is based on the diagnosis and analysis of the disease. It is necessary to take into account the cause of eosinophilia and the stage and extent of cardiac damage in the patient. The goal of the therapy is to reduce the heart damage caused by eosinophils. The treatment can be divided into two parts: normalizing eosinophilic counts and reducing heart damage caused by eosinophilic cells. Currently, patients with Loeffler endocarditis are routinely treated with anti-heart failure, myocardial cell-protection drugs upon admission, depending on their condition. Warfarin or heparin can be administered to patients with ventricular thrombus. However, corticosteroids remain the most widely used and effective first-line agents for rapid reduction of eosinophil-mediated heart damage. In patients diagnosed with Loeffler endocarditis, the response to corticosteroid therapy is usually rapid. Several studies have reported that patients treated with cortisol were able to receive improvements in cardiac ejection fraction, with peripheral eosinophil counts returning to normal after a few days (6-10).

The presently discussed case should have been diagnosed as an intermediate stage of Loffler endocarditis, characterized by thickening of the endocardium with numerous clots. In this case, the diagnosis process lacked the support of a myocardial biopsy and the imaging diagnosis was limited by the patient's condition. However, when the patient was in a critical condition, we opted for quick and easy imaging-assisted diagnosis, boldly postulating the possibility of Loeffler endocarditis, and treated him quickly with cortisol in combination with anticoagulant drugs. Finally, we achieved positive therapeutic results in a short period of time. The therapeutic effect of this case confirmed our speculation. In the context of eosinophilia, simplifying the diagnosis process and adopting immunosuppressive therapies could quickly alleviate the disease when the patient's relevant condition is critical. It should also be noted that Loffler endocarditis is commonly complicated by multiple organ damage in addition to cardiac disease (1). In this case, in addition to heart disease, skin lesions, pleural effusion, and gastrointestinal inflammation were apparent upon admission, and these conditions were alleviated after eosinophil reduction. Unfortunately, we did not perform additional biopsies for skin lesions or gastroenteritis. In addition, follow-up of patients with Loffler endocarditis is also necessary, as the long-term development of Loffler endocarditis can lead to dilated cardiomyopathy, which also occurred in our case. The patient later returned to the hospital for a reexamination. The results showed that the eosinophil count had returned to normal and that the thrombus in the heart was reduced. However, the patient's right-side heart failure did not subside, the right ventricular systolic function continued to decrease, the chambers of the heart continued to expand, and significant regurgitation of the tricuspid valve occurred. We considered that the advanced state of this patient was associated with the irreversibly invasive damage of the myocardium and valves via eosinophils. The surgeon hoped to offer a tricuspid valve replacement, but the patient refused additional treatment due to family financial reasons and has since lost contact.

The diagnosis of Loeffler endocarditis includes laboratory examination to confirm that eosinophils continue to increase and imaging examination or myocardial biopsy to determine certain morphological changes, such as subendocardial thrombosis, eosinophil infiltration, or even myocardial fibrosis (11). Corticosteroids are preferred for the treatment of Loeffler endocarditis, followed application of cytotoxic drugs, such as hydroxyurea and azathioprine, or immunomodulatory drugs, such as interferon. In addition, of diuretic β-blockers and anticoagulants can treat intracardiac thrombosis and embolism (12). Beedupalli *et al.* searched the case reports of 32 cases of Loeffler endocarditis and found that 30 cases were caused by eosinophilia while 2 cases were caused by eosinophil leukemia. Of these, 12 cases involved only the left ventricle, 11 involved only the right ventricle, and 9 involved only the right ventricle.

Involvement of the right ventricle is associated with a higher fatality rate. In Beedupalli *et al.*'s study, 2 patients had thrombectomy surgery and the rest were treated with medication. Most patients were sensitive to glucocorticoids, and 3 were treated with imatinib in combination with glucocorticoids (13).

It is also worth noting that the imaging test used for patients with Loeffler endocarditis in our case was myocardial contrast echocardiography. In patients with severe illness who cannot tolerate lying down and have decreased renal function (contraindication of enhanced CT), myocardial acoustic contrast may be preferable; first, this may facilitate bedside examination, and second, myocardial acoustic contrast agent is a type of sulfur hexafluoride microbubble preparation and via pulmonary metabolism, may be tolerable to patients with abnormal liver and kidney functions. Myocardial contrast echocardiography is a relatively new technology. Its basic principle involves enhancing the nonlinear echo signal generated by contrast agent microbubbles based on a variety signal processing technologies under a low MI to suppress the linear echo signal generated by tissues and thus achieve microcirculation-enhanced imaging; this ultimately provides a means of evaluating the microcirculation perfusion of the myocardium and cardiac space-occupying lesions (14). In the study by Guo *et al.*, 36 cases of cardiac space-occupying lesions were evaluated with myocardial contrast echocardiography (15). The sensitivity and specificity of myocardial contrast echocardiography in diagnosing cardiac space occupancy lesions were 100% and 91%, respectively.

Conclusions

The incidence of Loeffler endocarditis is low, and its clinical manifestations vary considerably among individuals. These patients usually develop restrictive cardiomyopathy at a later stage. Thus, early diagnosis and effective treatment can reduce mortality. Moreover, the treatment of the disease is based on the cause. If it is caused by eosinophilia syndrome, most patients are sensitive to treatment with glucocorticoids in combination with imatinib. In patients with severe valve insufficiency, surgical valve replacement with removal of excessive fibrotic tissue and mural thrombosis is feasible, and anticoagulants will be helpful in the prevention and treatment of thromboembolism. But treatment with a heart transplant is the only effective treatment for patients who end up with severe cardiac fibrosis. Clinicians currently have an inadequate understanding of the disease, and greater attention in this area is needed.

Acknowledgments

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Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1371/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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