Loeffler Endocarditis in Idiopathic Hypereosinophilic Syndrome Demonstrated by Magnetic Resonance Imaging Effectively Treated by Corticosteroids

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INTRODUCTION

Hypereosinophilia (HE) is diagnosed with persistent eosinophilia (absolute eosinophil count > 1.5 × 10^9/L) recorded on two occasions at least 1 month apart. If there is evidence of organ damage caused by HE and exclusion of other disorders as the main reason for organ damage, it is defined as hypereosinophilic syndrome (HES). Loeffler endocarditis is a subtype of HES in which the myocardium is involved and considered to be one of the major causes of morbidity and mortality in HES. The definite diagnosis of Loeffler endocarditis requires myocardial biopsy, an invasive procedure bearing certain risks, which may not always be available or consented by patients. Echocardiography can assess morphological and functional changes but not myocardial tissue composition. However, cardiac magnetic resonance imaging (MRI) is able to characterize different kinds of myocardial damage with satisfying resolution and can be a substitute of biopsy in the diagnosis of Loeffler endocarditis.

In this case, we report an interesting case of Loeffler endocarditis in idiopathic HES, which is demonstrated by cardiac MRI and effectively treated by corticosteroids.

CASE

A 47-year-old woman presented to the emergency room with a 3-week history of chest pain radiating to the back. She was afebrile and in no distress, with heart rate of 101 bpm and blood pressure of 110/78 mmHg; the rest of the physical exam was noncontributory. Laboratory tests revealed elevated NT-proBNP (5850 pg/mL; normal range, 0-100 pg/ml) and cTnT (1.27 ng/mL; normal range, 0-0.03 ng/mL) levels and HE (Table 1). Electrocardiography revealed 0.5-1 mm ST-segment depression in leads V_3-V_6. She was admitted to the department of cardiology for further evaluation.

Five months before admission, HE (Table 1) had been detected during a routine examination at the clinic but the patient had no chest pain. Three weeks before admission, she had a cold after which chest pain started accompanied by mild shortness of breath but no sweating, dizziness, nausea, vomiting, abdominal discomfort or orthopnea. Blood tests at that time in the other hospital revealed elevated cTnI (1.2 ng/mL; normal range: 0-0.5 ng/mL) and NT-proBNP (2620 pg/mL) levels and HE (Table 1). Both pulmonary artery chest computed tomography angiography and coronary angiography were negative, ruling out acute coronary artery syndrome and pulmonary embolism. With a presumptive diagnosis of myocarditis, she was treated with prednisone (10 mg/d), which she discontinued after discharge. Ten days before admission, the patient returned to the clinic of our hospital with worsening chest pain. Electrocardiogram revealed no changes, which together with chest pain pattern rendered acute coronary syndrome unlikely, and echocardiography was normal. Coenzyme Q10 was prescribed but she developed a pruritic rash, and after stopping coenzyme Q10 for 3 days, she restarted it without rash recurrence. However, chest pain persisted.

On admission, the patient was treated with diuretics, beta-blockers, trimetazidine and coenzyme Q10.
Further blood testing revealed increasing eosinophil count (up to $24.83 \times 10^9/L$, Table 1). She denied any travel history or exposure to new drugs, and neither anti-parasite antibodies in serum nor parasite eggs in stool were detected. In peripheral blood smear, eosinophils accounting for 47.5% of granulocytes were morphologically normal; no clonal proliferation or presence of primitive cells was apparent. Bone marrow biopsy demonstrated proliferative change without abnormal cellular morphology or distribution. No autoantibodies were detected. No abnormalities in lymphocyte immunophenotype were detected by flow cytometry. Tests for FIP1L1-PDGFRα, ETV6-PDGFRβ, BCR-ABL fusion genes, chromosomal rearrangements and JAK2 V617F or MPL W515L mutations were negative. Gadolinium enhanced cardiac MRI revealed left ventricular edema and striated delayed enhancement between the apex and papillary muscles restricted to the endocardium with decreased contractility, independent of coronary arterial supply (Figure 1A, 1B), indicating endocardial inflammation. Endocardial biopsy was recommended as an essential tool to verify the pathological change and the cause of chest pain. However, the patient refused considering the risks of this invasive procedure.

Based on the laboratory test results and clinical symptoms, she was diagnosed with Loeffler endocarditis of idiopathic HES. Although the patient had no pruritic rash after taking coenzyme Q10 again but surging eosinophil was recorded after that, which made drug allergy a possible precipitating factor. Coenzyme Q10 were discontinued and prednisolone (1 mg/kg/d, i.e., 50 mg/d) was started. Two days later, blood tests revealed dramatically decreased eosinophil count and percentage, which after another 2 days normalized along with white blood cell count (Table 1). cTnT and NT-proBNP levels dropped significantly.

<table>
<thead>
<tr>
<th>Date</th>
<th>Cardiac enzyme (ng/ml)</th>
<th>NT-proBNP (pg/ml)</th>
<th>WBC ($\times 10^9/L$)</th>
<th>Eosinophil count ($\times 10^9/L$)</th>
<th>The percentage of eosinophil to WBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017/12/6</td>
<td></td>
<td></td>
<td></td>
<td>6.64</td>
<td>2.75</td>
</tr>
<tr>
<td>2018/3/29</td>
<td>1.20 (cTnI)</td>
<td>2620</td>
<td></td>
<td>5.86</td>
<td>2.66</td>
</tr>
<tr>
<td>2018/4/10</td>
<td>0.05 (cTnI)</td>
<td>288</td>
<td></td>
<td>11.39</td>
<td>1.59</td>
</tr>
<tr>
<td>Admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2018/4/25</td>
<td>1.270 (cTnT)</td>
<td>5820</td>
<td></td>
<td>18.95</td>
<td>13.08</td>
</tr>
<tr>
<td>2018/4/28</td>
<td>0.538 (cTnT)</td>
<td>2753</td>
<td></td>
<td>32</td>
<td>24.83</td>
</tr>
<tr>
<td>Prednisolone initiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2018/5/1</td>
<td>0.420 (cTnT)</td>
<td>4993</td>
<td></td>
<td>9.81</td>
<td>1.38</td>
</tr>
<tr>
<td>2018/5/3</td>
<td>0.397 (cTnT)</td>
<td>2911</td>
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<td>6.82</td>
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<td></td>
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<td>2018/6/14</td>
<td>0.022 (cTnT)</td>
<td>863</td>
<td></td>
<td>4.75</td>
<td>0.04</td>
</tr>
</tbody>
</table>

The normal range of cTnI was 0-0.5 ng/ml. The normal range of cTnT was 0-0.03 ng/ml. The normal range of NT-proBNP was 0-100 pg/ml. The normal range of eosinophil count and percentage was 0.02-0.52 $\times 10^9/L$ and 0.4-8.0%, respectively. cTnT, cardiac troponin T; NT-proBNP, N-terminal Pro-B-type natriuretic peptide; WBC, white blood cell.
also decreased (to 0.4 ng/mL and 2911 pg/mL, respectively). Chest pain resolved and the patient was discharged. The dosage of prednisolone was gradually decreased by 5 mg/week. One month after discharge blood test revealed decreased NT-proBNP level with normal cTnT level, eosinophil count and percentage (Table 1). Cardiac MRI demonstrated alleviated endocardial edema and delayed enhancement (Figure 1C, 1D).

**DISCUSSION**

HES, defined as persistent HE (i.e., absolute eosinophil count > 1.5 × 10^9/L recorded on two occasions at least 1 month apart) leading to organ damage, can be caused by: reactive eosinophilia secondary to allergy, parasitic infections, drugs, and tumors, among others; myeloid disorder with clonal proliferation of eosinophils, in which fusion genes, chromosomal rearrangements or gene mutations can be detected; abnormal lymphocytes producing excess cytokines such as interleukin-5 that stimulate eosinophil proliferation. It can also be idiopathic as in the present case.

Unfortunately, the patient refused to undergo recommended endocardial biopsy which did not allow us to ascertain whether myocardial eosinophilic infiltration was the major cause of the presentation at admission. Gadolinium enhanced cardiac MRI findings were consistent with the first stage of HES involving endocardium, i.e., the acute necrotic stage with endocardial damage, which precedes thrombus formation and myocardial fibrosis (Figure 1). Because of negative genetic testing, absence of clonal proliferation in bone marrow biopsy, normal lymphocyte immunophenotype, and absence of evidence of other reactive eosinophilia, the patient was diagnosed with Loeffler endocarditis of idiopathic HES. However, this patient had a transient rash and surging eosinophil count after taking coenzyme Q10, which made coenzyme Q10 likely a deteriorating factor for endomyocardial injury.

Although HES is a rare condition that can affect various organs with symptomatology determined by the affected organ and damage extent, the heart is involved in over 50% of the cases as a major cause of morbidity and mortality. Histological evidence is essential for the definitive diagnosis of Loeffler’s endocarditis, however, endocardial biopsy, which the patient refused, is an invasive procedure bearing certain risks and sampling errors. Negative histological finding can not completely rule out the possibility of Loeffler endocarditis. Moreover, endocardial biopsy could cause severe mechanical complications which made the risks outweigh the benefits. Gadolinium enhanced cardiac MRI may detect various stages of eosinophil-mediated cardiac damage, and has a typical endocardial late enhancement pattern in Loeffler endocarditis, which made cardiac MRI an promising method in diagnosis and treatment response monitoring. For the management of HES, if fusion genes are detected, tyrosine kinase inhibitors can be tried; otherwise, corticosteroids may be the preferred option, which in the present case effectively relieved symptoms, and reduced eosinophil count and cardiac enzyme levels.

**LEARNING POINTS**

The management of Loeffler endocarditis requires thorough laboratory and auxiliary examination to ascertain the cause of HE. Myocardial biopsy is needed for the definite diagnosis of Loeffler endocarditis. With the ability to characterize different pathological changes, Gadolinium enhanced MRI is an promising alternative method without sampling error and invasive complications.

**ACKNOWLEDGEMENTS**

All the authors declare no conflict of interest.

**CONFLICT OF INTEREST**

All the authors declare no conflicts of interest.

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