Cardiac MRI findings of endomyocardial fibrosis (Loeffler’s endocarditis) in a patient with rheumatoid arthritis

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Loeffler’s endocarditis and cardiac manifestations of the hypereosinophilic syndrome (HES) are rare and difficult to diagnose. We report a case of in a 36 year-old female with a history of rheumatoid arthritis with disabling dyspnea. The transthoracic echocardiogram demonstrated normal systolic cardiac functions and a left ventricular apical thrombus. However, using cardiovascular magnetic resonance (CMR) with inversion-recovery (IR) delayed enhancement, and cine steady-state free precession (SSFP) sequences, we were able to clearly demonstrate endocardial fibrosis, tissue inflammation, apical ventricular hypertrophy, and LV thrombus that correlate with clinical findings. We believe cardiac MRI is more useful than transthoracic echocardiography in the diagnosis and management of HES and ultimately it obviated the need for biopsy to confirm the diagnosis.

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Introduction

Epidemiologic data of endomyocardial fibrosis (EMF) continues to be scarce, despite the fact that EMF is considered the most common form of restrictive cardiomyopathy [1]. Most studies of EMF occur in tropical regions such as Uganda where there is a high prevalence of the disease.

Loeffler’s endocarditis was first described as a component of a multi-system disease in 1968, when Hardy and Anderson published a paper titled The hypereosinophilic syndromes [2] (HES). Thereafter, Parrillo et al. [3] studied 26 patients with hypereosinophilic syndrome. The data provided a correlation between hypereosinophilic syndrome and Loeffler’s endocarditis. It also showed that about 40–50% of patients with hypereosinophilic syndrome have cardiac involvement.

Previous studies reveal that about 10% of patients with rheumatoid arthritis (RA) have hypereosinophilia (HE). They show that HE might occur either due to a reaction from the RA drug therapy or in relation to the RA process as a result of extra-articular vasculitis [4].
In idiopathic HES, treatment includes glucocorticoids and myelo-suppressive drugs. The latter is used in cases that are resistant to glucocorticoids and in severe forms of HES. Glucocorticoids inhibit many chemical mediators and are known to be the most effective therapy. In addition to the above mentioned treatment, treatment of the cause will be added in cases of secondary HES [5,6].

In this case report, we describe a patient with rheumatoid arthritis under treatment, and suffering from eosinophilia. We also describe the typical cardiac magnetic resonance (CMR) findings of Loeffler's endocarditis.

**History:** We report the case of a 36-year-old female patient known to have rheumatoid arthritis and referred for CMR to investigate disabling dyspnea:

- **Lab findings**
  - Rheumatoid factor (latex = positive 1/16 = 192 IU/ml).
  - CRP: positive (8 mg/L).
  - Anti CCP: positive = 990 u/ml.
  - Microcytic hypochromic anemia (hemoglobin = 8.3 g/dl, MCV = 69.5 fl).
  - Mild thrombocytopenia (121 · 10^3/cmm).
  - Eosinophil count = 12%, increased to 28% with three-month interval between both blood counts.

- **Clinical chemical analysis** including liver enzymes, bilirubin and renal functions were within the normal ranges.
- **Stool analysis:** Negative for parasitic infestation.

- **Immunology report**
  - Anti-PR3 hs = 1.4 U/ml (normal).
  - Anti-MPO IgG (p-ANCA) = 1.5 U/ml (normal).
  - Anti-B2-glycoprotein 1 IgM = 2.4 MPL U/ml (normal).
  - Anti-cardiolipin IgGAM screen = 4.7 U/ml (normal).
  - Anti-nuclear abs = negative.
  - Anti ds DNA = 18 U/ml (normal).

- **Doppler lower limbs**
  - Moderate to sever lower limb ischemia.

- **Echo findings**
  - Obliteration of the left ventricle (LV) apex with possible LV apical thrombus.
  - Good ventricular systolic functions.

- **Mitral valve**
  - Mildly thickened leaflets with restricted posterior leaflet and diastolic doming of the anterior leaflet.
  - Leaflet excursion is adequate.
  - Eccentric mitral regurge.
  - Regurgitate jet is directed extremely posterior swirling over the left atrial wall 5.5 cm², PISA radius: 0.8 cm.

- **Dilated left atrium:**
  - **CT chest:** Widespread mosaic appearance in both lung fields.
  - **U/S Abdomen:** Fatty liver.

**Materials and methods**

- **CMR:** The study was performed using a 1.5 T Magnet (Philips-MRI, Achieva).
- **CMR sequences and protocols** were performed as previously described [7,8].

1. **A. Sequences**
   - Cine steady state free precession (SSFP): in short axis, 2-chamber, 4-chamber and axial views in order to assess cardiac volumes and functions. Slice thickness was 8 mm. Acquisition was during breath hold commands. TE:1.7 ms and TR:3.3 ms. Stacks of slices in the axial and short axis views covered both ventricles from the atrioventricular (AV) junction to the apex.

2. **Dark blood sequences:** T1 Turbo spin echo (TSE) and T2 TSE were acquired for tissue characterization before and after contrast injection in breath hold mode.

3. **Inversion recovery (IR) images:** These were acquired using the phase sensitive inversion recovery (PSIR) and FLASH sequences. Acquisition was 10 min after intravenous injection of MRI gadolinium (Magnevist) contrast material to detect the pattern of the late gadolinium enhancement (LGE). Slice thickness was 10 mm. Views were acquired mid-ventricular in short axis, 2-chamber and 4-chamber views.

4. **Velocity encoding phase contrast (VENC):** Blood flow was measured as previously described. In brief, a double oblique through plane in the vessel of interest was carefully planned. The physician responsible for the visit carefully screened the ECG along the entire sequence. Usually, if more than three untriggered pulses occurred, the sequence was aborted and repeated, [9] as the policy of our center is to have no flow...
measurements rather than faulty flow measurements. Slice thickness 8 mm, VENC: 200 cm/s in 30 cardiac phases. Measurements were performed in the aorta, pulmonary artery, and mitral valve.

5. Indirect method of calculating the mitral regurgite (MR) was aorta stroke volume – stroke volume of LV.

B. **Contrast material:** MRI gadolinium (Magnevist) contrast material. Dose injected was 0.14 mmol/kg. Renal functions were checked before injecting the contrast material.

C. **Data assessment:** The images were viewed and post-processed by the author. In order to calculate the cardiac volumes and functions, the end diastolic and end systolic volumes were identified visually as the cardiac phase showing the largest and smallest ventricular volumes respectively. Endomyocardial contouring was traced semi-automatically. The papillary muscles were excluded from the ventricular volumes.

**Results**

The acquisition extended for 60 min. Amount of injected contrast was about 16 ml. The ventricular volumes and functions were calculated using the available workstation in the Philips MRI. Ventricular volumes and functions were normalized to body surface area.

The CMR showed the following findings:

- Diffuse subendocardial late gadolinium enhancement involving both the left ventricle (LV) and the right ventricle (RV) (blue arrows) (Fig. 1).
- An apical RV and LV wall thickening with almost total obliteration of the RV apex (Fig. 2).
- LV apical dark signal thrombus showing no evidence of contrast material in the LGE (red circles) (Fig. 1).
- Preserved bi-ventricular systolic functions.
- Normal bi-ventricular volumes.
- Mild MI: 12–13% (Fig. 3). Mild Pericardial effusion (Fig. 4).
Discussion

CMR is a key tool for diagnosing and monitoring, and for the prognostic stratification of most cardiomyopathies. It provides a full assessment of systolic and diastolic functions, and tissue characterization, particularly of fibrosis, using delayed-enhancement sequences (DE) [3,10].

Endomyocardial fibrosis is characterized by the deposition of fibrous tissue in the endocardium, predominantly in the apices of the right and left ventricles, and considered to belong to the group of restrictive cardiomyopathies [11,12].

Endomyocardial fibrosis lesions in Loeffler’s endocarditis are probably secondary to hypereosinophilic syndromes. This is due to the role played by the increased eosinophil count and serotonin secretion in the pathological process, causing damage and necrosis of the endocardium [13,14]. Blood picture in our case was performed twice with a six-month interval showing a rise in the eosinophil percentage.

In practice, transthoracic echocardiography is the first examination to be performed and provides an accurate evaluation of systolic and diastolic functions. The advantages of echocardiography is its non-invasiveness and relatively low-cost. In our case, it showed an apical thrombus and evaluation of the systolic cardiac functions. However, the limitations of echocardiography can be summarized in its tissue characterization and differential diagnosis of restrictive cardiomyopathies [15].

CMR plays an important role in the diagnosis and prognosis of this condition. It provides precise morphological evaluation, usually characterized by restriction with non-dilated or small ventricles, with an element of hypertrophy, more in the apical regions. In the current case, ventricles were not dilated but apices of both ventricles were hypertrophied with obliteration of the RV apex.

Among typical CMR findings, described in literature [13] and which are present in the current case
report, are the often increased atria size due to severe diastolic dysfunction with a restrictive disorder. IR sequences after contrast injection confirm diagnosis by showing typical subendocardial enhancement extending from the subvalvular regions to the apices of the two ventricles. Thrombi are frequently described at the apex of the LV and/or RV.

The disadvantages of cardiac MRI are its costs, which are higher than echocardiography. However, the emergence of new techniques and software have allowed rapid acquisitions, and in turn, a shorter scan time as well as decreased use of contrast material in some scenarios. Moreover, in today’s case the cost benefit is considered relatively high, since cardiac MRI saved the costs of a performing biopsy.

In our current case, medical treatment included diuretics and anti-rheumatic medication, which were used to improve dyspnea. Initially, the patient received low molecular weight heparin (Clexane) treatment. It was withdrawn under cover of the warfarin anticoagulant (Marevan). The patient was advised to continue on Marevan treatment and dismissed from the hospital. A follow-up MRI was recommended after one year to assess the patient’s cardiac functions and the delayed enhancement, and hence the efficacy of the treatment.

The utility of endomyocardial biopsy is currently being reviewed in consideration of new advances in diagnostics [16]. A myocardial biopsy in our case was avoided after the provision of a competent CMR diagnosis, which highly correlated with clinical findings.

Conclusion

CMR yielded significant diagnostic information, which was not found with a transthoracic echocardiography. CMR is non-invasive, and can competently assist in the diagnosis of endomyocardial fibrosis.

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