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Eosinophilic myocarditis: Gardia lamblia infestation and Garcinia cambogia – coincidence or causality? (RCD code: III-1B.1.o)

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Abstract

Eosinophilic myocarditis is a rare form of myocardial inflammation that may lead to heart failure and death, if left untreated. A previously healthy 26-year-old man was admitted to the department with chest pain and dyspnoea, that started two days before. Few days prior to the onset of symptoms he started to take weight-loss supplement with Garcinia cambogia. On laboratory tests myocardial necrosis markers were positive and blood hypereosinophilia was noted. Left ventricular ejection fraction was slightly decreased to 45% with regional wall motion abnormalities and significantly thickened left ventricle walls. Coronary angiography did not show any abnormalities. Endomyocardial biopsy revealed eosinophil infiltration of the myocardium. Stool cultures were positive for Giardia lamblia. The patient initially received standard heart failure therapy and then due to eosinophil infiltration of the myocardium, systemic steroids and antiparasitic treatment were added. His general condition and ejection fraction improved after a week and he was discharged home on standard heart failure treatment and prednisone. In the setting of acute coronary syndrome symptoms in patients without atherosclerotic lesions and decreased ejection fraction myocarditis should be suspected. Blood hypereosinophilia may raise suspicion of the eosinophilic myocarditis. The proper diagnosis should be supported by endomyocardial biopsy results as it plays key role in the initiation of steroid therapy which leads to heart failure symptoms relieve and improvement of left ventricle function. JRCD 2016; 2 (7): 1–1

Key words: rare disease, heart failure, cardiomyopathy, hypereosinophilia, electrocardiogram, echocardiography, endomyocardial biopsy

Introduction

The incidence of biopsy-proven myocarditis ranges from 9 to 16% in adult patients [1,2] with non-ischaemic dilated cardiomyopathy. Although often the aetiology of the myocarditis remains unknown, a broad spectrum of infectious, systemic diseases or toxins and drugs can be the cause of the disease. The most common aetiologies are either viral or autoimmune. Eosinophilic myocarditis (EM) is a rare form of myocardial inflammation, which may be fatal if left untreated. The incidence of EM in unselected autopsy cases is reported at 0.5%, however, studies on the explanted hearts from heart transplant recipients showed that the actual frequency may be as high as 20% [3]. EM is characterized by eosinophilic infiltration of myocardium and in the vast majority of cases it is associated with peripheral blood hypereosinophilia [4,5]. At the cellular level, the degranulation of eosinophils and release of cytotoxic cationic proteins are observed, which ultimately lead to the increase cellular membrane permeability and induce of myocytes necrosis and apoptosis [6].

Case report

A previously healthy 26-year-old man acutely presented in the Emergency Department with chest pain, dyspnoea and general malaise, that started two days before. He underwent a flu-like infection two weeks before, which completely resolved, but also admitted taking a weight-loss supplements with Garcinia Cambogia for a few days before symptoms onset. On physical examination the patient was afebrile, without symptoms of heart failure with blood pressure of 140/90 mmHg and heart rate of 100 bpm. Twelve-lead electrocardiogram showed sinus tachycardia and negative T waves in III and aVF leads (Figure 1).

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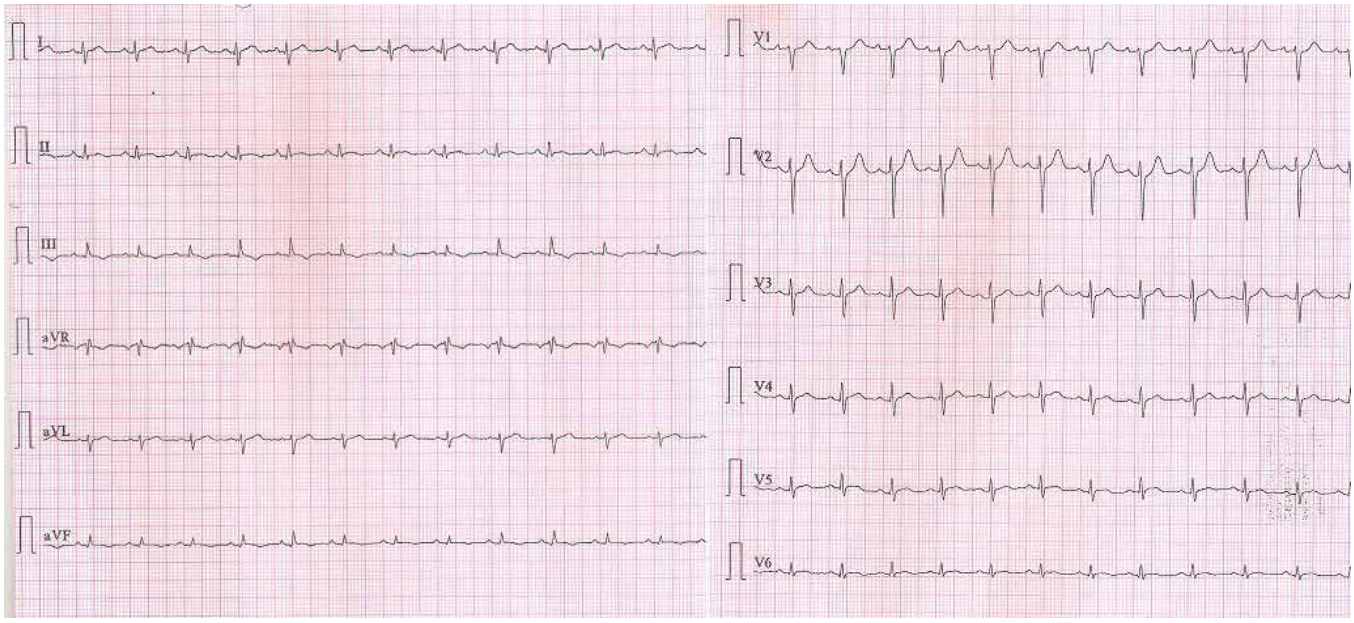

Figure 1. 12-lead electrocardiogram performed upon admission. Negative T waves in leads III and aVF

On laboratory tests myocardial necrosis markers were significantly increased with high-sensitive troponin T level of 0.963 ng/ml (upper limit of normal [ULN] <0.014 ng/ml] and CK-MB of 36 U/l (ULN <24 U/l), C-reactive protein was negative and white blood cells of 11 340/µl (ULN <10 000/µl), with slight increase of eosinophils 740/µl (ULN <700/µl). The initial echocardiogram showed mildly impaired left ventricular systolic function with ejection fraction (EF) of 45% with significantly thickened septum of 16 mm [ULN <12 mm] and posterior wall of 14 mm [ULN <12 mm] as well as regional wall motion abnormalities – hypokinesis of inferolateral wall and mild pericardial effusion (Figure 2).

Due to rapid symptom onset, chest pain and elevated cardiac markers and a suspicion of acute coronary syndrome it was decided to perform urgent coronary angiography, which showed normal coronary arteries (Figure 3).

The patient was started with routine heart failure (HF) pharmacological therapy, consisting of angiotensin converting enzyme inhibitor (perindopril of 2.5 mg q.d.), beta blocker (carvedilol of 3.125 mg b.i.d) and mineralocorticoid receptor antagonist (eplerenone of 25 mg q.d.). Serum cardiotropic viruses IgM antibodies titers were negative. On the fourth day of hospital stay, an increase of eosinophil count was observed to 2380/ µl with a stable value of white blood cells of about 11 000/µl. Stool cultures for Giardia lamblia cysts were positive. Due to persisting dyspnoea a chest X-ray was performed and revealed 10 mm nodule in the right lung. On further computer tomography evaluation of the lungs multiple nodules of 5–9 mm diameter with ground glass opacification in both lungs were present (Figure 4).

Because of persisting symptoms and impaired EF, it was decided to perform an endomyocardial biopsy (EMB). Cardiac bioptates

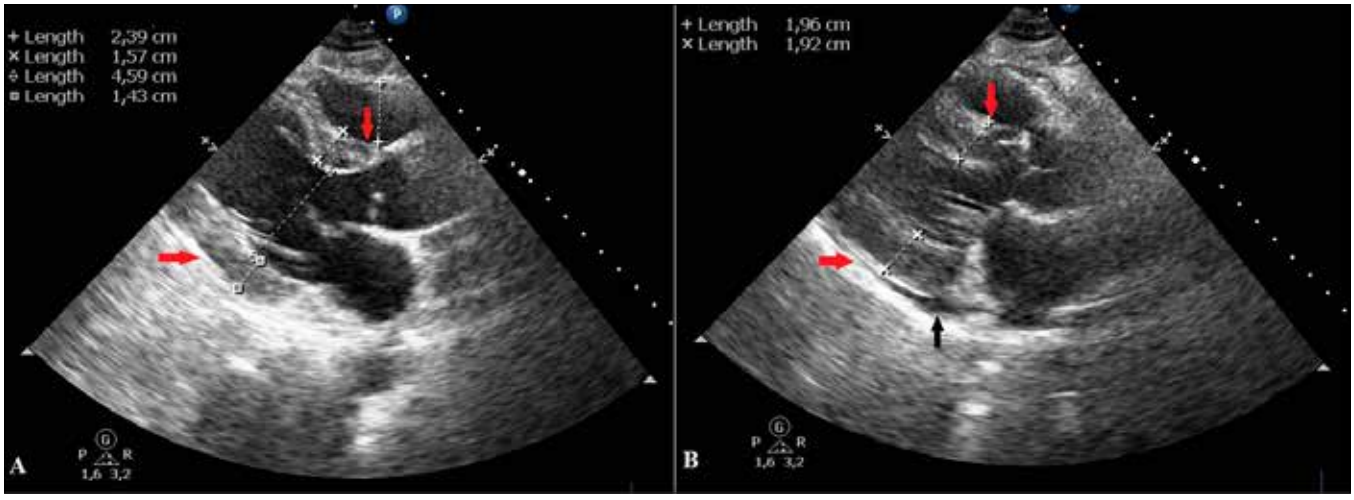

Figure 2. Echocardiography performed on admission: Parasternal long axis (PLAX) view in diastole (A) and systole (B) shows significantly thickened left ventricle posterior wall and septum (red arrows) and minor pericardial effusion (black arrow)

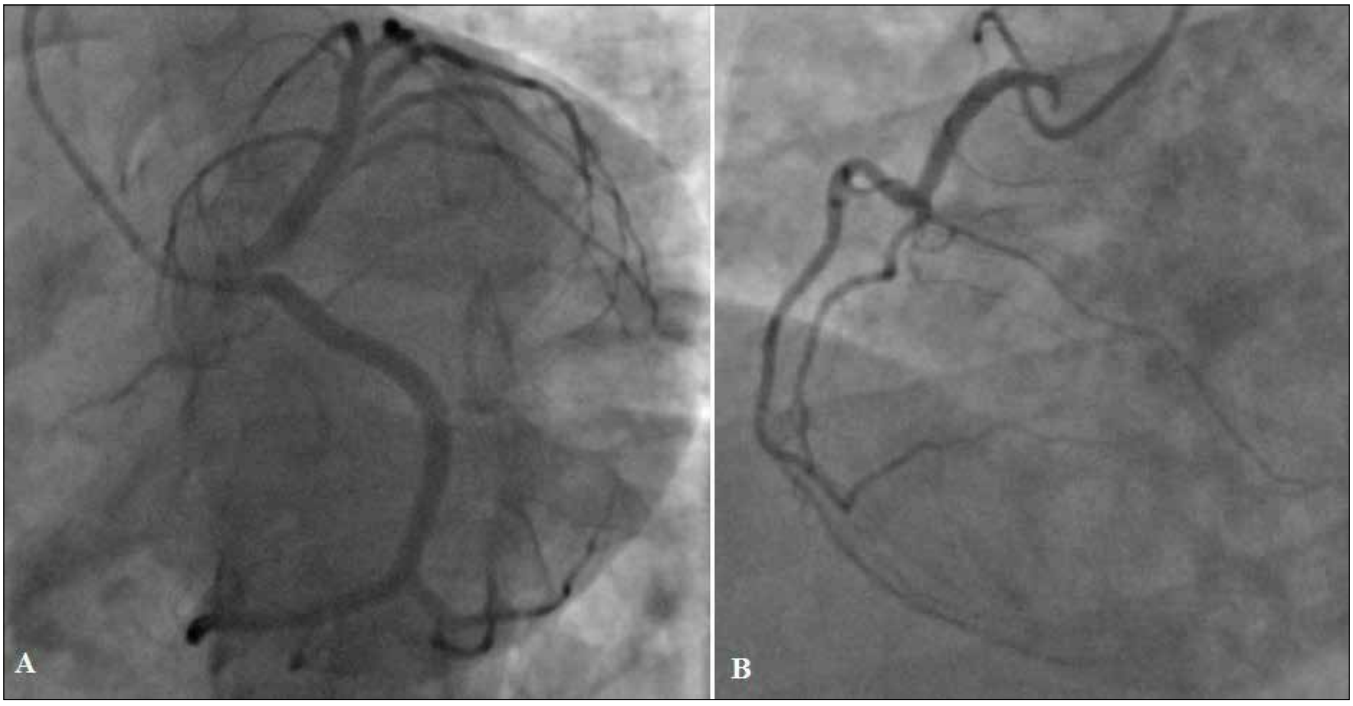

Figure 3. Coronary angiography showing a normal left coronary artery (A) and right coronary artery (B)

were harvested from the right ventricular septum. On histo-pathology, massive eosinophil infiltration of the myocardium was revealed (Figure 5).

Based on the biopsy results, the diagnosis of eosinophilic myocarditis was established. In addition to the standard HF treatment, an oral steroids – prednisone of 1 mg/kg/day was initiated. Moreover, the treatment of giardiasis with metronidazole 250 mg t.d.s was started. A week later patient was doing well. On the follow up echocardiography a marked increase of EF to 55% was noted and previously observed regional wall motion abnormalities were not seen. Furthermore, a decrease of the septum and posterior wall thickness (12 mm and 11 mm, respectively) was noted (Figure 6).

On the 13th day since admission, patient was discharged home in good clinical condition on a standard HF treatment and prednisone with 5 mg tapering doses per day. On 30-day follow-up the patient remained asymptomatic with EF of 55% on echocardiography.

Discussion

EM, a rare form of myocardial inflammation can be caused by various hypereosinohilic disorders, which include:

- drug hypersensivity reactions (probably most common) [3] especially to antibiotics, antituberculotic drugs [7], anticonvulsants (carbamazepine) [8], anti-inflammatory, diuretics and inotropes (dobutamine) [9] and also antipsychotic clozapine [9, 10] and toxins
- parasitic infestations – toxocara canis [11, 12], ascariasis [13], schistosomiasis, trichinosis, amoebiosis [6], toxoplasmosis [9]
- idiopathic hypereosinophilic syndrome [9],
- malignancies (T cell lymphoma, acute or chronic eosinophilic leukemia) [9, 14]
- paraneoplastic events (lung andenocarcinoma [15] or biliary tract cancers [9]
- vasculitic and granulomatous disease (Churg – Strauss syndrome) [6, 9]
- tropical endomyocardial disease [6]
- transplant rejections [6]

In the case described above two possible aetiologies of EM might be suspected, which are Giardia lamblia infestation and Garcinia cambogia supplements admission prior to the hospitalization. The active agent of Garcinia cambodia is hydroxycitric acid, which plays a role in the inhibition of fatty acids synthesis. The potential side effects of Garcinia cambodia may include hepatotoxicity and

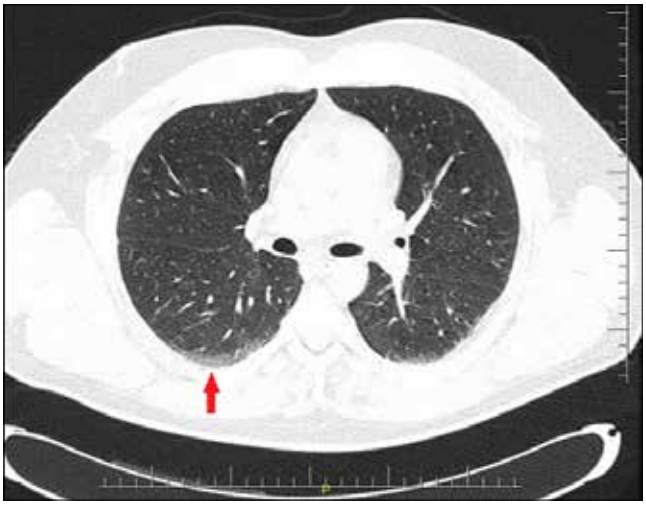

Figure 4. Computed tomography of the chest. Ground glass opacification in both lungs (arrow)

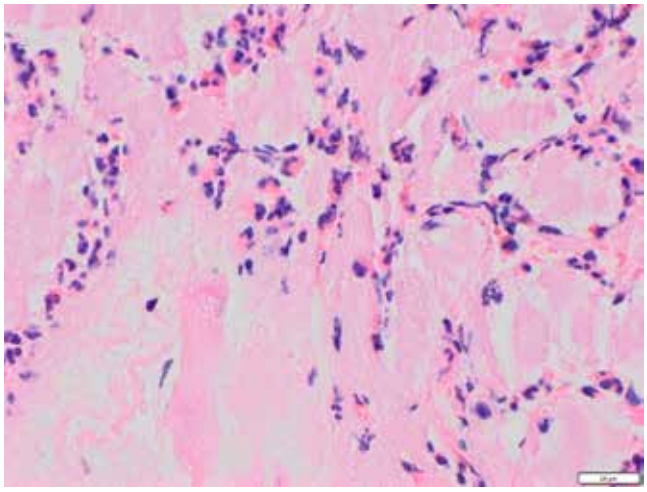

Figure 5. Histological findings showing eosinophil infiltration of the myocardium

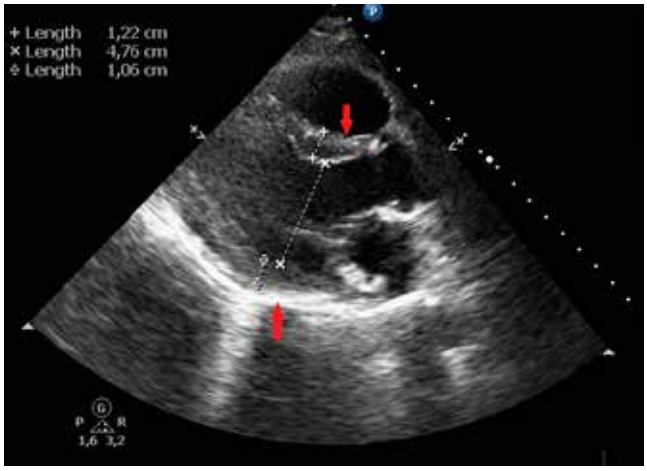

Figure 6. Echocardiography performed at discharge: Parasternal long axis view in diastole. Normal thickness of the septum and posterior wall

rhabdomyolysis, but are not well confirmed, as they were described in patients taking multicomponent weight-loss herbal supplements [16]. However, the temporal relationship of the Garcinia cambodia administration with acute necrotizing eosinophilic myocarditis and the lack of any other precipitating factors was recently described [17]. The association of Giardiasis (hypereosinophilia caused by parasitic infection) and myocarditis is also known [18]. Clinically EM can manifest with various symptoms such as fever, chills, malaise, acute coronary syndrome, acute HF, cardiogenic shock, arrhythmias and sudden death. The final diagnosis is based on EMB results, as the eosinophil count may be sometimes within normal limit [4]. In the case described above initially eosinophilia was slightly elevated, but later a marked increase in the eosinophil count was observed. According to the Japanese Circulation Society Task Force Committee on Acute and Chronic Myocarditis, EM has its specific features, such as: eosinophilia > 500/μl, cardiac symptoms (dyspnea, chest pain), elevated cardiac markers (CK-MB, troponin), ECG changes, transient hypertrophy or abnormal wall motion on echocardiography; coronary angiography is recommended to exclude myocardial infarction [19]. The definite diagnosis should be based on EMB studies, which are recommended as the diagnostic gold standard [1, 2, 19]. In the presented case all clinical and echocardiographic criteria were fulfilled and the final diagnosis was confirmed by biopsy findings.

The initial therapy of EM depends on HF severity. Some patients can even require temporary left ventricle mechanical support. First-line therapy consists of systemic administration of corticosteroids to reduce organ damage induced by eosinophils [19, 20]. Suggested doses are: initial 1 g methylprednisolone pulse dose for patients with cardiac tamponade, cardiogenic shock or pulmonary oedema; prednisolone or prednisone 1 mg/kg/day with gradual tapering is suggested for more stable patients [5]. Little is known about the duration of corticosteroid maintenance therapy [5]: some describe a year-long therapy [3], the others 6 month therapy [5, 21]. This therapy should be accompanied by treatment of underlying cause of eosinophilia, if known [3, 5]. In this case it was anti-parasitic treatment.

Conclusion

In the setting of acute coronary syndrome symptoms and decreased EF without atherosclerotic lesions on coronary angiography a myocarditis should always be suspected. The presence of co-existing eosinophilia may raise the suspicion of EM. The proper diagnosis, confirmed by EMB plays a key role as the early administration of corticoid therapy may restrict eosinophil inflammation, which leads to heart failure symptoms relieve and improvement of left ventricle function.

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