CASE REPORT

Eosinophilic myocarditis: an often subtle and potentially under-recognised phenomenon

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SUMMARY

A 34-year-old woman presented to our service with chest pain, a troponin rise and dynamic ECG changes. Of note, she had complained of fatigue, feeling constitutionally unwell and a generalised rash in the days prior to her presentation. Her echocardiogram showed normal wall motion and preserved ejection fraction. Her eosinophil count, normal at presentation, rose to a peak of $12.21 \times 10^5/L$. She was haemodynamically stable throughout with no evidence clinically of congestive cardiac failure. CT coronary angiogram showed no obstructive coronary artery disease. Cardiac MRI demonstrated areas of late gadolinium enhancement consistent with myocarditis. A diagnosis of eosinophilic myocarditis was made. No tissue biopsy was performed due to the patchy myocardial involvement and high potential for low-yield biopsy. Our patient was treated conservatively and has made an excellent recovery.

BACKGROUND

Eosinophilic myocarditis (EM) is a rare and potentially underdiagnosed condition that may present subtly.

Early recognition and identification of the condition allows appropriate management to be initiated and can improve the patient's prognosis.

CASE PRESENTATION

A 32-year-old woman presented to the emergency department of our centre with severe central chest pain radiating to both arms. This had lasted approximately 10 min in duration. The pain was sharp and central with an associated 'electric shock' sensation radiating down her arms bilaterally.

Her medical history was notable for a diagnosis of type 1 diabetes mellitus aged 14. Regular medications consisted only of insulin. She denied any food or drug allergies and had no history of atopy. Her social and family history was non-contributory.

In the week preceding her presentation, she described feeling fatigued and had developed a generalised rash 5 days beforehand which had since resolved. She reported temperature spikes of up to 38.2°C and felt constitutionally unwell with generalised myalgia.

On further questioning, our patient recalled a similar, less severe episode of generalised maculopapular rash approximately 6 months previously which had resolved without any medical intervention.

On examination, vital signs were stable with no documented fevers. Heart sounds 1 and 2 were present, there were no added sounds or murmurs. Her chest was clear to auscultation with normal vesicular breath sounds and she had no evidence of congestive cardiac failure. There was no rash present. Her abdomen was soft and non-tender and the patient was neurologically intact.

We proceeded with preliminary investigations to elucidate the underlying cause of this woman's symptomatology.

INVESTIGATIONS

Her initial ECG showed normal sinus rhythm with some dynamic T wave inversion over the precordial leads on serial ECGs.

Further telemetry showed normal sinus rhythm with no evidence of arrhythmia.

Her laboratory results are summarised below.

On admission, her eosinophil count was normal at $1.6 \times 10^5/L$; however this subsequently peaked at $12.21 \times 10^5/L$. Inflammatory markers were also raised with a C-reactive protein of 119 (ref: 0–5) and erythrocyte sedimentation rate of 80 mm/hour. Her IgE was also elevated at 174 kU/L (normal: 0–81 kU/L) and HbA1c indicated poor glucose control at 79 mmol/L.

Extensive autoimmune, viral and infectious screen was negative.

As mentioned above, high-sensitivity troponin T was raised on admission at 50 ng/mL, peaking at 100 ng/mL at 8 hours (normal <16 ng/mL).

Echocardiogram showed normal left ventricular function with an ejection fraction of >55% and no regional wall motion abnormalities. There was the impression of left inferolateral wall thickening and a small global pericardial effusion.

Cardiac MRI showed evidence of myocardial oedema involving the inferolateral wall at the base and inferior wall towards mid-cavity level (figure 1A). There was also some corresponding late gadolinium enhancement involving the inferolateral and inferior wall at the base; with transmural enhancement and subendocardial sparing (figure 1B).

DIFFERENTIAL DIAGNOSIS

Our patient had an initially vague presenting complaint of atypical chest pain with constitutional symptoms. Given her troponin rise, dynamic ECG changes and symptomatology, our initial differential was between an acute coronary syndrome and

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Figure 1 (A) Cardiac MRI in short axis oblique view. Bright blood technique demonstrates increased signal intensity in the inferolateral wall in keeping with myocardial oedema. (B) Cardiac MRI in short axis oblique view postgadolinium demonstrating late gadolinium enhancement in the inferior-inferolateral wall which is nearly transmural.

a myocarditis. Her rash and raised inflammatory markers raised the possibility of an underlying process related to the release of inflammatory mediators.

Differential included the following:

Acute coronary syndrome:

- ▶ plaque rupture
- ▶ coronary artery dissection
- ▶ Kounis syndrome¹: the concurrence of acute coronary syndromes with conditions associated with mast cell activation, involving interrelated and interacting inflammatory cells, and including allergic or hypersensitivity and anaphylactic insults.

Myocarditis:

- ▶ viral myocarditis
- ▶ EM-idiopathic hypereosinophilic syndrome (HES)
- ▶ drug reaction with eosinophilia and systemic symptoms (DRESS)
- ▶ toxocariasis.

CT coronary angiogram demonstrated no evidence of coronary artery disease and cardiac MRI also did not indicate infarct or ischaemia and was reported as consistent with myocarditis. This made an ischaemic event unlikely. With regard to Kounis syndrome, the presentation was not consistent with an anaphylactic or allergic reaction. The patient did not take any new medications to indicate a DRESS syndrome and toxocariasis was ruled out on serology.

Her subsequent rise in peripheral eosinophil count alerted us to the increasing likelihood of an underlying EM.

TREATMENT

While primarily under the care of the cardiology team, multi-disciplinary input was obtained from the rheumatology, haematology, dermatology and infectious disease services.

The patient was haemodynamically stable throughout her stay with no evidence of congestive cardiac failure. She was treated with high-dose corticosteroids and her chest pain and eosinophilia resolved.

OUTCOME AND FOLLOW-UP

Our patient was diagnosed with idiopathic EM secondary to a HES. This was based on both her raised peripheral eosinophil

count, absence of secondary causes and the clinical, biochemical and radiological evidence of carditis.

She made a good recovery with normalisation of her inflammatory markers and was discharged home well. Her eosinophil count has remained normal and she is continuing with steroid therapy, initially at a dose of 40 mg of oral prednisolone. Steroid sparing agents (mycophenolate or azathioprine) will be introduced in the near future. She will continue to be followed up as an outpatient by the cardiology and rheumatology services.

DISCUSSION

Hypereosinophilia is a disease state characterised by a marked increase in the number of eosinophils circulating in the bloodstream.²

Normally, eosinophilic cells constitute 0%–7% of leucocytes.² Persistent, markedly increased eosinophilia merits further diagnostic investigation and treatment. If left untreated, it can result in eosinophilic infiltration of tissues and potentially irreversible, life-threatening end-organ damage.

EM is a rare form of myocardial inflammation secondary to eosinophilic infiltration of the myocardium. The clinical course of the condition can vary considerably. Cases described in the literature extend across the entire spectrum of severity of cardiac disease; from patients presenting asymptotically to those with life-threatening cardiogenic shock.³

The first association in the literature between eosinophilia and myocardial disease was documented by Loeffler in 1936. Loeffler endocarditis is a form of restrictive cardiomyopathy, with fibrotic thickening of the myocardium secondary to eosinophilic infiltration and development of mural thrombi.⁴ Other forms of eosinophilic heart disease can include myocarditis, pericarditis and endomyocardial fibrosis. This spectrum may not represent separate disease entities but instead evolutionary phases of the same process.

A combination of a raised eosinophil count and cardiac symptomatology should always arouse suspicion for such a disorder. However, it should be noted that the condition can present with a normal peripheral eosinophil count, as it did initially in this case.² The exact prevalence of EM is unknown, with previous estimates of circa 1–2 cases per

Table 1 Results of comprehensive PubMed/PMC search for eosinophilic myocarditis cases

PubMed/PMC search for eosinophilic myocarditis cases	
Total cases	225
Hypereosinophilic syndrome spectrum	94
Idiopathic HES	72
Loeffler endocarditis	22
Secondary cases	131
Clozapine	42
Churg-Strauss syndrome	30
Drug induced (other)	17
Toxicaria	11
Pregnancy	8
Dobutamine	8
Parasite (other)	5
Leukaemia	4
Cancer	4
HIV	1

HES, hypereosinophilic syndrome.

million.⁵ Due to its variable clinical course and severity it may be underdiagnosed.

We conducted a PubMed and PMC literature search using the terms 'eosinophil' and 'myocarditis'. This resulted in identification of 105 papers describing a total of 225 cases of patients presenting with hypereosinophilia and myocarditis. Postmortem studies where it was not possible to ascertain whether the patients had presented with a clinical myocarditis syndrome were not included.

The cases identified were as follows: HES/idiopathic EM: 72 cases, Loeffler endocarditis: 22 cases, acute EM secondary to a defined precipitant: 131 cases. A breakdown of precipitants is detailed in [table 1](#).

The HES is defined as a persistently elevated eosinophil count ($>1500/\text{mm}^3$) for over 6 months with no identifiable cause and evidence of end-organ involvement. It is a diagnosis of exclusion after clonal eosinophilia (ie, due to leukaemia) and reactive eosinophilia (ie, due to infection, parasitic infection, drugs) have been ruled out.⁴

Diagnosis of EM was traditionally made on the basis of fulfilling two criteria⁶:

1. evidence of carditis (on ECG, Holter, telemetry, biochemical testing, echocardiogram, cardiac MRI)
2. histopathological evidence of eosinophilic infiltration of myocardium on cardiac biopsy.

However, tissue biopsy is not always necessary and may be reserved for cases where there is uncertainty regarding the definitive diagnosis.⁷ Treatment of the condition depends on the underlying aetiology.

If there is an obvious precipitant, this should clearly be avoided. Parasitic or infectious agents should also be treated with targeted therapy. For instance, myocarditis secondary to myeloproliferative disorders with fusion genes has been shown to respond to imatinib therapy.⁸

In idiopathic HES myocarditis, immunosuppression, primarily with corticosteroid therapy, has been reported to be effective and is used in the majority of patients initially.⁹ Given the rarity of the condition and the absence of randomised controlled trials, there is no good quality evidence to guide therapy beyond this.

Learning points

- ▶ Acute idiopathic eosinophilic myocarditis (EM) is a rare form of myocarditis, with less than 80 cases described in the literature.
- ▶ A raised eosinophil count and cardiac symptomatology should arouse clinical suspicion of the disorder.
- ▶ The diagnosis is made on the basis of evidence of carditis and a biopsy demonstrating eosinophilic infiltration of myocardial tissue.
- ▶ In idiopathic EM, immunosuppression with corticosteroids has been reported to be effective.

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