Significance of troponin I level as a marker of disease activity in the management of acute necrotizing eosinophilic myocarditis with normal peripheral eosinophil count: a case report

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Background
Eosinophilic myocarditis is characterized by myocardial eosinophilic infiltration and is largely associated with hypereosinophilia. However, eosinophilic myocarditis with a normal peripheral eosinophil count has been previously reported. Since the absence of eosinophilia poses a challenge for therapeutic management, we evaluated whether troponin I (TnI) levels can be used in the management of eosinophilic myocarditis where peripheral eosinophilia is absent.

Case summary
We report the case of a 77-year-old woman who developed cardiogenic shock due to acute necrotizing eosinophilic myocarditis, which required mechanical circulatory support. She did not have hypereosinophilia, but endomyocardial biopsy confirmed massive infiltration of eosinophils into the myocardium. We administered high-dose corticosteroids for 3 days and she dramatically improved. Along with this, the TnI level, which was elevated at the time of patient presentation, also decreased after steroid therapy. Troponin I level did not increase again without taking any oral prednisolone, and the follow-up biopsy after 6 months showed complete recovery of eosinophilic myocarditis.

Discussion
Troponin I-guided treatment is a useful tool in the management of eosinophilic myocarditis because it helps with therapeutic decisions, especially in the absence of eosinophilia.

Keywords
Acute necrotizing eosinophilic myocarditis • Troponin I level • Steroid therapy • Normal eosinophil count • Case report

Learning points
• Eosinophilic myocarditis is usually associated with hypereosinophilia. However, eosinophilic myocarditis with a normal peripheral eosinophil count has been previously reported, and it complicates not only diagnosis but also therapeutic decisions.
• Troponin I (TnI) levels reflect eosinophilic-related cardiac damage, therefore, TnI-guided treatment is a useful tool for the therapeutic management of eosinophilic myocarditis in the absence of hypereosinophilia.

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Introduction
Eosinophilic myocarditis is a relatively uncommon disease characterized by myocardial eosinophilic infiltration, based on peripheral hypereosinophilia (eosinophils >1500/μL). It can present as a spectrum ranging from asymptomatic myocarditis to acute necrotizing myocarditis, the latter frequently resulting in cardiogenic shock with a mortality rate of >50% and survival of only a few days. In some patients with eosinophilic myocarditis, peripheral eosinophilia may not develop during the clinical course, and heart failure could be mild and haemodynamics would be stable. However, as previously reported, acute heart failure, is mostly associated with hypereosinophilia. We present a rare case of ANEM involving a normal peripheral eosinophil count. Here, the patient’s condition suddenly deteriorated, finally resulting in cardiac arrest due to ANEM with the absence of hypereosinophilia. This absence poses a challenge for therapeutic management, as it raises a concern about parameters that can be used to guide appropriate treatment. Hence, we aimed to evaluate the significance of troponin I (TnI) level as a marker of disease activity in the management of ANEM with normal peripheral eosinophils.

Timeline

| Time | Procedure |
|------|-----------|
| 3 days prior to admission | Patient had a slight fever and general fatigue |
| Day 1 | Emergency pericardiocentesis for pericardial tamponade was performed |
| Day 2 | Patient’s haemodynamics suddenly deteriorated and mechanical circulatory support was needed for cardiogenic shock (left ventricular ejection fraction <10%) |
| Day 3 | Endomyocardial biopsy showed acute necrotizing eosinophilic myocarditis |
| Day 4–6 | Patient was treated by high-dose corticosteroids |
| Day 8 | Left ventricular ejection fraction dramatically improved and all the mechanical circulatory support devices were removed |
| Day 30 | Patient was discharged in a stable condition without taking any oral prednisolone |
| 6 months after discharge | Repeat endomyocardial biopsy revealed no recurrence of eosinophilic myocarditis |

Case presentation
A 77-year-old woman who developed general fatigue with a temperature of 36.8°C presented to our hospital. She had no previous history of cardiac disease. She was alert and had a blood pressure of 84/68 mmHg and a pulse rate of 109 b.p.m. She denied chest pain and dyspnoea. No rash was identified. Heart and lung sounds were indistinct. There were no murmurs or pericardial rubs, but her jugular vein dilatation was noted in the supine position. Electrocardiography (ECG) showed low voltage at the electrodes attached to all limbs (Figure 1). X-ray images revealed cardiomegaly. Echocardiography showed a moderate pericardial effusion with right atrial collapse. Left ventricular (LV) ejection fraction (EF) was preserved (≥60%). We diagnosed the pathological condition as pericardial tamponade with paradoxical pulse. Emergency pericardiocentesis yielded 200 mL of exudative fluid, and symptomatic relief was immediate. Systemic blood pressure increased from 84/68 to 163/86 mmHg. Blood analysis showed a leucocyte count of 8600/μL (normal range 3300–8600/μL) with 6.7% eosinophils of 576/μL (normal range 0–10%) and an elevated TnI value of 2.3 ng/mL (normal range <0.00156 ng/mL). Cytology of pericardial effusion showed 7.5% eosinophils of 1420/μL. Coronary angiography revealed no significant stenosis. Her body temperature increased above 39°C and blood pressure began decreasing on the 2nd day. The ECG monitor showed a ventricular rhythm of wide QRS complex. Eventually, she had pulseless electrical activity through complete atroventricular block in 20 min (Figure 2). Immediate cardiopulmonary resuscitation did not fully restore her spontaneous circulation and haemodynamics remained severely compromised. Thereafter, we inserted a temporary pacing catheter, an intra-aortic balloon pump, and veno-arterial extracorporeal membrane oxygenation after artificial ventilation. Left ventricular ejection fraction was extremely reduced (<10%) with 14-mm diffusely oedematous LV wall on echocardiography (Supplementary material online, Video S1). We suspected fulminant myocarditis and performed endomyocardial biopsy, while the patient was on the cardiopulmonary support devices on the 3rd day. Despite the lack of definite hypereosinophilia, the biopsy showed massive infiltration of eosinophils, which partially formed eosinophilic clusters (Figure 3). We diagnosed ANEM and initiated 1000 mg/day of IV methylprednisolone. Thereafter, high-dose corticosteroids administered for 3 days dramatically improved wall thickness and almost normalized LVEF on the 6th day. We no longer needed mechanical circulatory support and removed all the devices by the 8th day without any neurological sequelae. Troponin I level peaked at 17.8 ng/mL just before steroid therapy and rapidly decreased (Table 1). Thus, we completed the treatment with corticosteroids and conducted a careful follow-up to detect recurrence, while monitoring the TnI value. Fortunately, the TnI level did not increase again and no relapse of myocarditis was observed without taking any oral prednisolone. Conversely, peripheral eosinophil count remained normal throughout the clinical course. She was re-hospitalized 6 months later for endomyocardial biopsy. No inflammatory cells including eosinophils were identified (Figure 4). Echocardiography showed normal LVEF (≥72%, Supplementary material online, Video S2), indicating clinical and histological recovery of eosinophilic myocarditis.

Discussion
Acute necrotizing eosinophilic myocarditis has an exceedingly high mortality rate and could be fatal if a prompt diagnosis is not made. Nevertheless, the absence of eosinophilia complicates diagnosis and treatment. As shown in the previous reports, the cause of eosinophilic myocarditis is frequently associated with a hypersensitivity reaction...
**Figure 1** A standard 12-lead electrocardiogram on admission.

**Figure 2** Electrocardiographic findings of pulseless electrical activity and immediately-initiated cardiopulmonary resuscitation on 2th day.
to drugs or parasitic infections, allergic diseases and autoimmune disorders. However, the patient did not have any histories or symptoms that suggested those diseases. Then, we could not identify the cause of ANEM in this case. Although standardized therapy for ANEM has not been established, high-dose corticosteroids are initially recommended and, if necessary, immunosuppression or mechanical circulatory support should be considered, regardless of peripheral eosinophilia. The mechanism underlying eosinophilic infiltrate into the myocardium in the absence of eosinophilia is unclear; however, it is important to ensure that treatment involves preventing eosinophilic-related cardiac damage and subsequent ventricular dysfunction. In this sense, TnI-guided treatment is reasonable for determining the extent of cardiac impairment and the need to continue steroids or immunosuppressive therapy. A variety of pulse or taper

| Day | Procedure         | TnI (ng/mL) | Eosinophil (μL) |
|-----|-------------------|-------------|-----------------|
| 1   | Pericardiocentesis| 2.3         | 576             |
| 2   | IABP, VA-ECMO     | 14.5        | 205             |
| 3   | Biopsy            | —           | 541             |
| 4   | mPSL, 1000 mg     | 17.8        | 478             |
| 5   | mPSL, 1000 mg     | 2.9         | 12              |
| 6   | mPSL, 1000 mg     | —           | 14              |
| 7   |                   | 0.34        | 0               |
| 9   |                   | 0.28        | 101             |
| 16  |                   | 0.037       | 260             |
| 22  |                   | 0.022       | 279             |
| 72  |                   | 0.0062      | 218             |

IABP, intra-aortic balloon pump; VA-ECMO, veno arterial extracorporeal membrane oxygenation; mPSL, methyl-prednisolone.
Regimens have been advocated but the limited available data do not explicitly state the length of treatment.\textsuperscript{3,5,7,9} As shown above, monitoring TnI level can avoid administering unnecessary maintenance doses of steroids or immunosuppressive agents, which is favourable for avoiding their adverse effects. To our knowledge, this is the first case report showing that TnI level is a useful tool as a marker of disease activity for the therapeutic management of ANEM.

**Supplementary material**

Supplementary material is available at European Heart Journal - Case Reports online.

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**Slide sets**: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent**: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest**: none declared.

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