

## Is Recurrent Myopericarditis Recurrent Viral Myopericarditis?

### Tekrarlayan Myoperikarditler Tekrarlayan Viral Myoperikarditler midir?

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#### ABSTRACT

Myopericarditis is an illness with normally favorable prognosis and mostly seen in young adults. It is known that myopericarditis can be recurrent. However, it cannot be clarified why it is recurrent. We are presenting two cases including a 16-year-old and a 17-year-old patients gone through myopericarditis for 3 times. We did a detailed research to introduce etiological reasons in two patients. We studied infectious reasons, autoimmune diseases, immunological and rheumatic diseases including mainly viral pathogens. During the myopericarditis attacks of patients, no pathological finding was identified other than being monocytosis in full blood counts, moderate sedimentation, CRP increase and raised troponin in laboratory data. We determined all viral pathogens known as agent as negative in both patients of ours. We think that patients particularly with more than one recurrent myopericarditis should be evaluated with a different perspective.

**Key Words:** Recurrent Myopericarditis, Viral infections, Etiology

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#### ÖZET

Myoperikardit daha çok genç erişkinlerde görülen ve prognozu genellikle iyi seyirli olan bir hastalıktır. Myoperikarditin tekrarlayıcı olabildiği bilinmektedir. Ancak neden rekürrens olduğu açıklanamamıştır. Biz biri 16 diğeri 17 yaşında olan ve üçer kez myoperikardit geçiren iki ayrı hastamızı sizlere sunuyoruz. Her iki hastada da etyolojik nedenleri ortaya koymak için detaylı bir araştırma yaptık. Başta viral patojenler olmak üzere enfeksiyöz nedenleri, otoimmün hastalıkları, immünolojik ve romatolojik hastalıkları araştırdık. Hastaların myoperikardit atakları sırasında laboratuvar verilerinde ılımlı sedimentasyon ve CRP artışı, troponin yüksekliği ve tam kan sayımlarında monositoz olması dışında patolojik bulgu saptanmadı. Her iki hastamızda da etken olarak bilinen tüm viral patojenleri negatif saptadık. Özellikle birden çok tekrarlayan myoperikardit geçiren hastaların farklı bir bakış açısıyla değerlendirilmesi gerektiğini düşünüyoruz.

**Anahtar Sözcükler:** Tekrarlayan Myoperikardit, iral enfeksiyon, Etiyoloji

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**INTRODUCTION**

Myopericarditis is used as a clinical definition that pericardial inflammation includes myocardial (1,2). In patients with pericarditis, this diagnosis is thought together with emergence of raised troponin and protection of left ventricular systolic functions (1,2). Myopericarditis autoimmune diseases can be related to many viral or bacterial infections (3,4,5,6,7). The prognosis of the disease is quite well and it normally gets better without any sequela with nonsteroid anti-inflammatory treatment and relaxation (11). However, myopericarditis can display recurrence in approximately 13% of patients (11). The disease can manifest itself with chest pain, ECG changes and increase in cardiac enzymes (8,9,10). The reasons or risk factors of recurrence are unknown in the disease. Most recently, "seasonal recurrent myopericarditis" definition was used for the patient gone through myopericarditis in the same months every year (12). Myopericarditis repeated itself in two different patients for three times in our clinic. We aimed to present these patients and discuss the reasons of recurrent myopericarditis.

**CASE REPORT***Patient 1 (US)*

A 16-year-old male patient applied to emergency service of our hospital firstly with chest pain complaint on February 2016. In his ECG, troponin I level was determined as 464 ng/mL though no pathological finding was identified. His left ventricular (LV) systolic functions were evaluated as normal in his electrocardiography. Minimal pericardial effusion was determined. In the patient's full blood count, the following was determined: hemoglobin (Hb) 14.2 gr/dL, leucocyte (WBC)  $14.5 \times 10^3 / \mu\text{L}$  (normal range 3.84-9.84  $10^3 / \mu\text{L}$ ). Sedimentation was established as 43 mm/h (normal range 0-15 mm/h). The patient was evaluated as myopericarditis and hospitalized and initiated ibuprofen 30 mg/kg/day (divided 3 doses equally). Troponin level increased to 1180 ng/mL. As of the second day of the treatment, chest pain disappeared, troponin levels began to decrease and after 4 days, troponin decreased to normal levels. Undergone upper respiratory infection history was not present in the patient.

After the patient had gone through 7 months without any complications, he applied to emergency service again with the same complaint on September 2016. Troponin levels were identified, ECG and echocardiography were evaluated as normal. Coronary arteries were assessed as normal in coronary angiography. Ibuprofen treatment was applied to the patient by hospitalizing for 5 days. Clinical and laboratory findings ameliorated totally. Finally, he referred to us with chest pain complaint on September 2017 and similar clinical and laboratory findings were identified. ECG and echocardiography were evaluated as normal. His findings totally got better with antiinflammatory treatment. Laboratory data of the patient obtained during myopericarditis attacks for three times.

*Patient 2 (MKI)*

A 17-year-old male patient applied to our hospital with chest pain complaint for three times including October 2015, July 2016 and January 2018. In three references of the patient, after upper respiratory tract infection findings such as sorethroat, fever and weakness had initiated, chest pain complaint emerged 2-3 days later. In the last physical examination of the patient performed on January 2018; it was seen that oropharynx was hyperemic and tonsils were hypertrophic. Micro lymphadenopathy in anterior cervical was palpated. Blood pressure was 110/70 mmHg, heart rate was 77/min. Heart auscultation findings were evaluated as normal. The patient described his chest pain as astringent, distinct in the left breast and spreading to the left arm. ECG findings of the patient were evaluated as normal. In his echocardiography, however, it was observed that there was a mild impairment in the left ventricle (LV) systolic functions (EF: %48 FS: %24). In his full blood count, the following were determined: Hb 12.8 gr/dL, WBC  $9.7 \times 10^3 / \mu\text{L}$  (normal interval 3.84-9.84  $10^3 / \mu\text{L}$ ), sedimentation 48 mm/h (normal interval 0-15 mm/h). In the throat culture, there was no reproduction. The evaluation of the patient applied to the hospital with the same symptoms for the third time was also carried out with advanced imaging methods. His coronaries were assessed as normal with coronary CT angiography. In cardiac MR evaluation, small focal pathological contrast involvement was established in the left ventricular inferolateral wall. Ibuprofen treatment was commenced for the patient who had been hospitalized with myopericarditis diagnosis in his three applications. Both his symptoms and troponin elevations got better in 5-7 days. LV systolic function impairment follow up diagnosed in his last hospitalization ameliorated in the early period. There was no complaint of the patient during the periods between the applications. Laboratory data of the patient in the course of his three attacks were given in Table 1 at full detail.

**Table 1.** Two patients had laboratory data during the myoperikardit attacks.

	Patient 1			Patient 2		
	February 2016	September 2016	September 2017	October 2015	July 2016	January 2018
Peak Troponin (ng/mL)	1180	1240	2200	980	1205	2180
Sedimentation (mm/h)	43	44	44	33	42	48
CRP (mg/L)	16	8	14	28	30	22
Hb (gr/dL)	14.2	13.6	13.1	12.1	11.5	12.8
WBC ( $10^3 / \mu\text{L}$ )	14.5	11.4	10.8	14.8	12.6	9.7
Platelets ( $10^3 / \mu\text{L}$ )	268	195	244	175	266	288
Lymphocyte (%)	28	32	30	26	40	34
Monocytes (%)	24	20	18	14	22	20
Eosinophils (%)	1	0.5	1	2	1	1
*Disease duration (day)	4	5	5	5	7	5

CRP: C reactive protein, Hb: hemoglobin, WBC: white blood cell

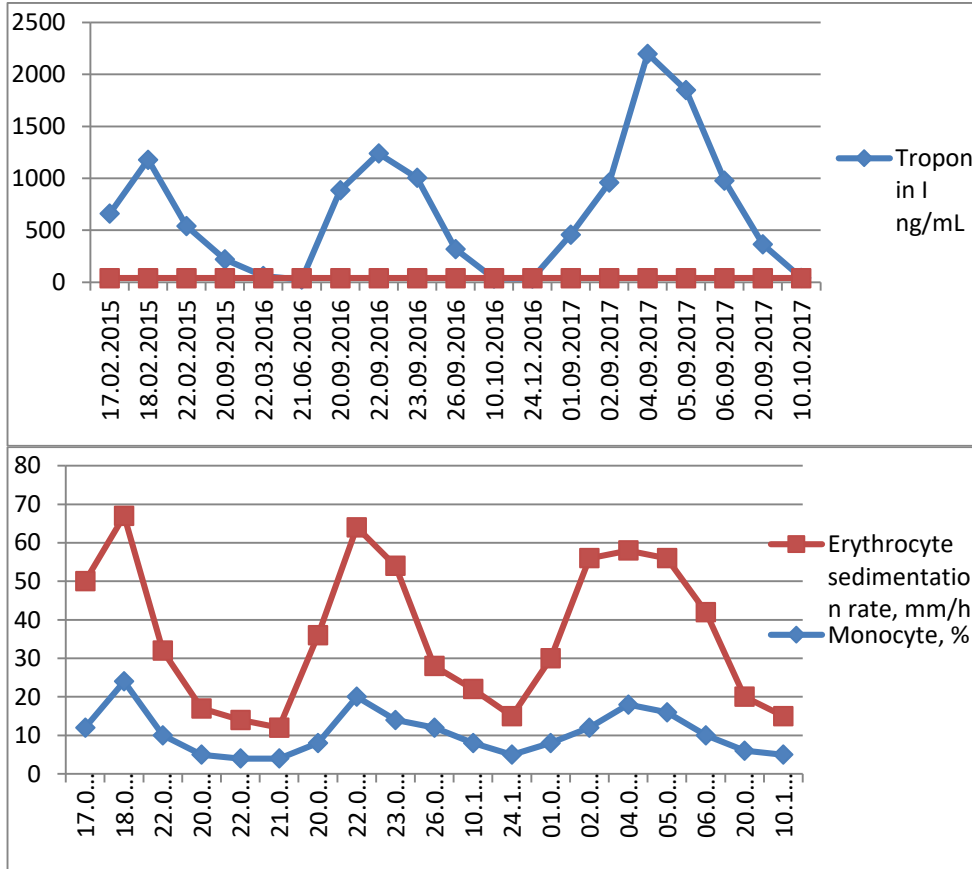
\*Disease duration; between the day when troponin height was detected and the day when troponin levels returned to normal

**DISCUSSION**

It is reported in the literature that there is a myopericarditis recurrence changing between 10% and 28.6% (13,14). When all publications were evaluated, average recurrence rate was identified as 13% (11). Nevertheless, recurrence reasons were not explained mostly.

Since two patients that we present had gone through myopericarditis for three times, a comprehensive pathogen agent scanning was performed in the last hospitalization. Epstein-barr virus (EBV), cytomegalovirus (CMV), coxsackievirus, salmonella, brucella, adenovirus, influenza, parainfluenza virus, parvovirus, toxoplasma, herpes virus, echovirus, hepatitis B serology, HIV serology and respiratory virus panel scanings were identified as negative. No reproduction was determined in throat, stool and urine cultures.

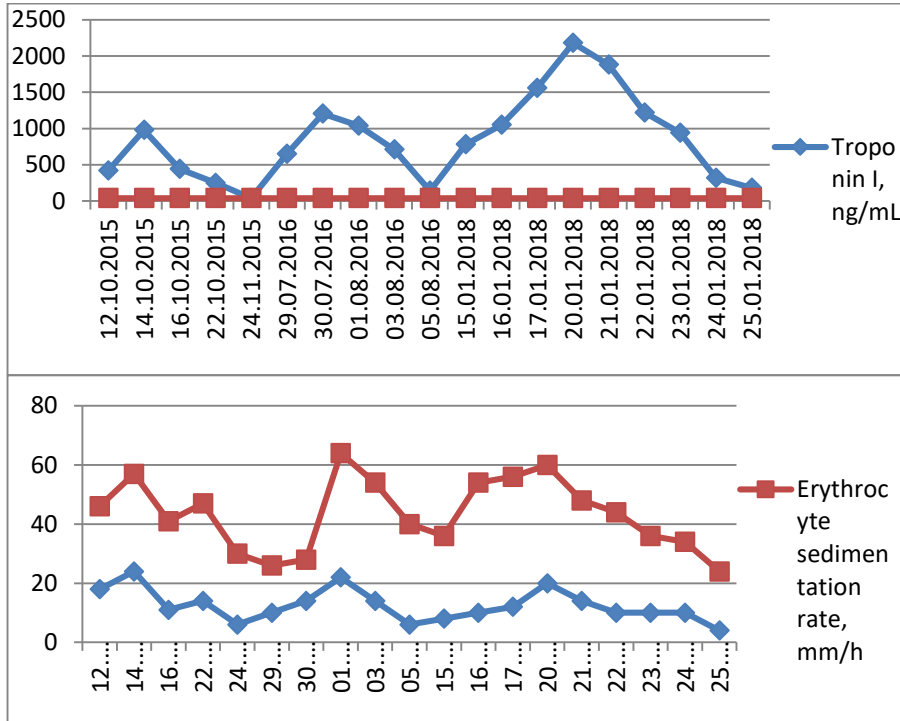
The patients were also evaluated in terms of collagen tissue and autoimmune diseases. Anticardiolipin antibody, antimitochondrial antibody, anti-Ro, anti-La, anti scl70, anti histone antibody, anti phosphatidylserine, anti-PMscl, anti nuclear antibody, C-ANCA, P-ANCA, anti-dsDNA, anti- cathepsinG antibody levels were established as negative. Gene analysis for familial mediterranean fever (FMF) obtained from patients was identified as negative. HLA-B5 was determined as negative. Celiac antibodies were established as negative. No clinical data was determined that made us think the presence of ulcerative colitis or Chron disease (15,16). Gene analysis for TRAPS (Periodical Sydrome related to TNF Receptor) was determined as negative. In the workups of the patients, we did not establish any infectious, immunological or rheumatic factors that could explain etiology.



**Graph 1.** Monocyte, ESR and Troponin course of patient 1 during myopericarditis attacks.

During the myopericarditis attacks of both of our patients, other than mild elevation in sedimentation and CRP values and troponin increase, no pathological laboratory data was identified. Another common conspicuous characteristic of them was that in complete blood counts, they had monocytosis emerging during the myopericarditis attacks. Although monocyte levels were normal except for attacks, it attracted attention that monocyte levels increased with sedimentation and troponin levels interrelatedly (Graphic 1 and 2). The most frequent reason of myopericarditis has been accepted as viral (17).

It is not always possible to determine viral pathogen. It has been pointed out in the literature that there is a seasonal pattern for both recurrent myopericarditis and acute myopericarditis (12,18). This feature has been linked to increasing viral infection in some seasons (12,18). However, no specified pathogen has been presented. In the full blood count of a patient who had gone through myopericarditis attacks for 4 times in the same months every year, attention was drawn that there was monocytosis (12).



**Graph 2.** Monocyte, ESR and Troponin course of patient 2 during myopericarditis attacks.

This situation was linked with a viral pathogen, however, no pathogen was specified. Monocytosis observed during the attacks of our both patients shows similarity. We do not find seasonal myopericarditis and viral myopericarditis definitions and explanations adequate for our patient who had undergone myopericarditis attacks. If the reason for these attacks is viral pathogen, then it must be a pathogen apart from that we know as an agent. Nonetheless, the attacks were observed in different months and seasons. Additionally, we studied all viral agents known as a pathogen for pericarditis, myocarditis and myopericarditis in our patients and we did not determine any. However, it is difficult to explain how recurrent attacks can occur after a long time intervals with the same pathogen. In these patients, the common characteristics of genetic or immunological factors can be examined. Evaluation with respect to common gene alleles can be helpful in patients with myopericarditis together with monocytosis.

As a result; it is worrisome for both doctors and patients that myopericarditis is recurrent in some patients. It is not always possible to associate this clinical table to another systemic disease that can accompany or viral reasons. The patients that myopericarditis is recurrent should be evaluated with a different point of view involving rheumatic, immunologic and genetic review.

#### Conflict of interest

No conflict of interest was declared by the authors.

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