

# A concerned clinical situation in pediatric cases: Acute myopericarditis, experience of a center from Anatolia

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## Abstract

**Aim:** Myopericarditis/Perimyocarditis is an inflammation in the heart muscle. There is an increase in cardiac biochemical markers with echocardiographic (ECHO) and/or electrocardiographic (ECG) changes in patients. We aimed to investigate the demographic, clinical, laboratory and imaging features and follow-up results of patients diagnosed with acute myopericarditis in our clinic.

**Materials and Methods:** In this study, demographic and laboratory data and physical examination findings of 15 pediatric patients diagnosed with myopericarditis between December 2017-September 2020 were retrospectively recorded.

**Results:** Five (33.3%) of the patients were girls, 10 (66.6%) were boys. The first presentation complaint was chest pain in 11 (73.3%) patients, palpitations in two (13.3%) patients, respiratory distress, abdominal pain and vomiting in two (13.3%) patients. Troponin values were increased in all cases. N-terminal prohormone brain natriuretic peptide (NT-ProBNP) level was >100 pg/ml in seven patients. In treatment, nine patients received ibuprofen, and three patients received inotrope and anticongestive therapy support as well as intravenous immunoglobulin (IVIG). In the follow-up, heart functions normalized within four months in all cases.

**Conclusion:** Myopericarditis should be considered especially in adolescent boys who present with complaints such as chest pain, palpitations, respiratory distress, and cardiac enzyme elevation and ECG changes. Although the prognosis is good in most of myopericarditis cases, the risk of morbidity may be high in patients with high initial cardiac enzyme values, delayed cardiac enzyme return to normal, and systolic dysfunction on ECHO, so long-term follow-up of these patients should be done by pediatric cardiologists.

**Keywords:** Ibuprofen; myopericarditis; N-terminal prohormone brain natriuretic peptide; troponin

## INTRODUCTION

Myocarditis is inflammation of heart muscle diagnosed with clinical, histological, immunological or immunohistological criteria representing structural and functional effect after inflammation, cell injury or loss in heart muscle (1). Whether or not there are systemic symptoms accompanying myocarditis or endocardium or pericardium involvement, it may occur due to many infectious, connective tissue, granulomatous, toxic or idiopathic processes affecting the myocardium (2). Acute pericarditis is inflammation of the pericardium as a result of viral infections and in clinical practice is mostly observed with myocarditis. The anatomical proximity and common etiological agents cause the association of these two clinical situations. Myopericarditis or pericarditis syndrome are names used for situations with pericarditis involvement at the fore dominantly and myocardial involvement included in the process. Perimyocarditis is used for situations with myocarditis clinic at the fore (3,4).

The etiology of myopericarditis consist of infections, autoinflammatory situations, neoplasm, trauma, metabolic causes and idiopathic (4). Most cases are idiopathic, with no definite cause identified even after comprehensive studies (5). The most common cause among identifiable reasons is infection. Infections usually are linked to with viruses (4,5).

The definite incidence and prevalence of myopericarditis is unknown (6). Among those attending hospital 0.1% are given acute pericarditis diagnosis. Myocarditis incidence is estimated to be from 1 to 10 cases per 100,000 people (5). In this study, the aim was to assess patients with acute myopericarditis diagnosis in our clinic in terms of demographic features, clinical findings, laboratory and imaging features and follow-up outcomes.

## MATERIALS and METHODS

From 1 December 2017-1 September 2020, the records of 15 patients with myopericarditis monitored by the Ministry

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of Health Ordu University Education and Research Hospital Pediatric Cardiology Department were retrospectively investigated. Demographic features, complaints at attendance, physical examination and laboratory findings and ECG and ECHO findings were assessed in patients with acute myopericarditis diagnosis. Information related to forms of treatment and surveillance were recorded.

Acute pericarditis diagnosis was placed with the presence of at least two findings of typical chest pain, pericardial rubbing sound and ECG variations (ST segment elevation, sinus tachycardia). The presence of myocardial involvement was diagnosed with high cardiac biomarkers (Creatine kinase-MB fraction or troponin I), left ventricular systolic dysfunction on ECHO, and identification of reduced ejection fraction (EF). Before beginning the study, permission was granted by Ordu University Clinical Research Ethics Committee (2020/140).

### Statistical Analyses

Statistical analyses were assessed using the SPSS (Statistical Package for Social Sciences) Windows 15.0 program. Continuous variables are given as median (minimum-maximum), while categorical variables are expressed as percentage.

### RESULTS

A total of 15 patients with myopericarditis diagnosis from December 2017-September 2020 were included in the study. Five of the patients were girls (33.3%) and 10 were boys (66.6%). Median age of cases was 12 years (1-17 years), and median weight was 28 kg (13-70 kg). Complaints on first attendance were chest pain in 11 cases (73.3%), palpitations in two (13.3%), and respiratory distress, abdominal pain and vomiting in two (13.3%) patients. Troponin values in all cases were above normal values when they attended.

**Table 1. Demographic, laboratory and treatment characteristics of the patients**

Number of cases	Age (year)	Gender	Initial ECG	Initial troponin	NT-ProBNP (pg/ml)	ECHO	Troponin return to normal (day)	Treatment	Intervention type	Final situation
1	1	M	Sinus tachycardia, VES	0.5	2850	LV systolic dysfunction, MY (middle), EF:%30	12	Inotrope	-	LV dilation, EF:%58
2	6.5	F	Sinus tachycardia, VES	1.2	5684	LV systolic dysfunction, MY (mild), EF:%35	10	ETE, inotrope (milrinone, dopamine), IVIG	-	MY (mild) EF:%64
3	9	M	Diffuse ST elevation	0.7	580	MY (mild), EF:%48	7	Anticongestive therapy, IVIG	-	Normal
4	9	F	Sinus tachycardia	1.6	156	MY (mild), EF:%65	2	Ibuprofen	-	Normal
5	10	F	Diffuse ST elevation, Sinus tachycardia	3.1	104	Hyperechogenicity? MY (mild), EF:%60	4	Ibuprofen	-	Normal
6	10.5	M	Diffuse ST elevation, Sinus tachycardia	1.2	84	Hyperechogenicity? EF:%72	3	Ibuprofen	-	Normal
7	11	M	Diffuse ST elevation	0.6	32	Normal EF:%72	5	-	-	Normal
8	12	M	Diffuse ST elevation	0.9	45	Hyperechogenicity? EF:%68	4	Ibuprofen	-	Normal
9	12	F	Diffuse ST elevation	3	76	Normal, EF:%74	6	-	-	Normal
10	13	F	Diffuse ST elevation	1.5	75	Hyperechogenicity? EF:%64	5	Ibuprofen	-	Normal
11	14	M	Diffuse ST elevation	1.1	68	Normal EF:%66	4	-	-	Normal
12	16	M	Diffuse ST elevation	1.2	48	Normal, EF:%64	3	Ibuprofen	-	Normal
13	16	M	Diffuse ST elevation, Sinus tachycardia	2.5	43	Hyperechogenicity? MY (very mild) EF:%72	3	Ibuprofen	-	Normal
14	16	M	Diffuse ST elevation	0.8	180	Normal, EF:%68	5	Ibuprofen	-	Normal
15	17	M	ST elevation in inferior leads	14	120	Normal, EF:%64	8	Ibuprofen	Coronary angiography	Normal

M: Male, F: Female, ECG: Electrocardiography, VES: Ventricular extrasystole, LV: Left ventricle, BNP: Brain natriuretic peptide, ECHO: Echocardiography, MY: Mitral regurgitation, ETE: Endotracheal intubation, IVIG: Intravenous Immunoglobulin

Electrocardiographic were taken and 12 cases (80%) were identified to have widespread ST elevation, with six cases (40%) having sinus tachycardia. Additionally, two cases with low EF value were observed to have rare ventricular extra systole (VES) on ECG. The cases with VES did not have more advanced arrhythmia during 24-hour ECG Holter recordings. Cases did not have ventricular tachycardia (VT), atrioventricular block, or supraventricular tachycardia (SVT) observed on ECG and during intensive care follow-up. Seven cases (46.6%) had NT-ProBNP levels >100 pg/mL. The three cases with low ejection fraction values had NT-ProBNP levels >100 pg/mL.

Echocardiography identified EF <50% in three cases, with mild and above MY in five cases. There was no segmentary wall motion disorder on the ECHO, mostly left ventricular systolic dysfunction. Pericardial effusion was not observed in any case. Due to technical and infrastructure inadequacy, no case had cardiac magnetic resonance imaging (MRI) or endomyocardial biopsy (EMB) procedures performed. One case with family history of atherosclerosis at young age had ST elevation in inferior derivations on ECG and long continuation of pain, so coronary angiography was performed. Coronary pathology was not identified as a result of coronary angiography. Etiologic assessment measured high viral antibody titers in three patients (1 adenovirus, 1 echovirus, 1 Epstein-Barr virus). Two cases diagnosed with myopericarditis during the corona virus disease 2019 (COVID-19) pandemic had swab tests negative for COVID-19. All cases were admitted to intensive care on first attendance for surveillance and bed rest. For two cases with low EF, in addition to inotrope [dopamine (n=1), milrinone (n=2)] support due to heart failure, they also had anticongestive treatment (loop diuretic, angiotensin-converting enzyme inhibitor) and IVIG treatment administered. The 3<sup>rd</sup> case with low EF began anticongestive treatment and IVIG treatment. In nine cases, ibuprofen treatment was begun with analgesic purposes which was not routine. No patient died during follow-up. Median duration of hospital stay was six days (4-14 days). During monitoring all cases had troponin levels return to normal in median four days (2-12 days). During follow-up, cardiac functions normalized in all cases within four months. Follow-up ECHO found mild MY in one case, with mild LV dilatation continuing in one case (Table 1). Recurrent attack of myopericarditis was not observed in any patient during the follow-up period. All cases were banned from activities requiring effort for one year.

## DISCUSSION

Myopericarditis is a pericarditic syndrome accompanied by elevated cardiac enzymes with a degree of myocardial involvement. Pericarditic typical chest pain, pericardial rubbing sound, ECG changes (new widespread ST segment elevation or PR segment collapse) and pericardial effusion are included among classic diagnostic criteria for acute pericarditis (7,8). Acute pericarditis diagnosis is made in

the presence of at least two of these criteria. The presence of myopericarditis is diagnosed with high cardiac biomarkers (creatine kinase-MB fraction or troponin I or T), generally left ventricular systolic dysfunction on ECHO or cardiac magnetic resonance (CMR) imaging, and the presence of myocardial inflammation on CMR imaging (9-11).

Just as myopericarditis may be clinically asymptomatic, it may have symptoms such as chest pain, fever, myalgia, abdominal pain, diarrhea, fatigue, reduced capacity for exercise, shortness of breath and palpitations (4,12). The best classic examination finding is the pericardial rubbing sound heard at the left sternal edge. All of our patients had myopericarditis diagnosis made after history, physical examination, elevated cardiac biomarkers and ECG and ECHO assessment at time of attendance. For 73.3% of cases, the most common complaint during attendance was sudden-onset chest pain. Other complaints at attendance were palpitations, respiratory distress, abdominal pain and vomiting. Myopericarditis is a clinical situation commonly observed in male children in the adolescent age group (13,14). However, diagnosis may be missed due to nonspecific and mild symptoms in children, especially under the age of five (6). In our study, 73.3% of patients were in the adolescent age group and 66.6% were male.

More than 80% of myopericarditis cases are idiopathic (15). The most common identifiable, infectious cause is viral infections (5,15). Cardiotropic viruses have direct cytolytic or cytotoxic effect and may cause inflammation in the pericardia and myocardium. The viruses most frequently encountered in myocarditis etiology are coxsackie viruses (especially B), adenovirus, cytomegalovirus, echovirus, influenza virus, Epstein Barr virus, human herpes virus 6 (HHV6), hepatitis C virus, and parvovirus B19 (4,5). A study by Aliva et al. (16) presented a rare clinical case of myopericarditis as a cardiac sequel to chicken pox. Jin et al. (17) assessed another myopericarditis case caused by Salmonella typhimurium in an article in 2020. A study investigating 18 myopericarditis patients identified positivity for EBV in one patient, rhinovirus in five patients, adenovirus in three patients and parainfluenza virus in one patient (13). In our study, assessment about etiology of patients measured high antibody titers for adenovirus in one case, echovirus in one case and Epstein-Barr virus in one case. Two cases with myopericarditis diagnosis during the COVID-19 pandemic were negative on COVID-19 swab tests. Of cases, 80% were assessed as idiopathic.

Elevated cardiac enzymes show myocardial tissue damage. Troponin elevation isolated with normal myoglobin and CK-MB may reflect even the mildest myocardial injury. The increase in troponin is associated with the degree of myocardial inflammatory involvement; however, it is not accepted as a marker of negative prognosis (11). In all patients, troponin values at time of diagnosis were at least 1.5 times elevated; however, there was no correlation between troponin values and clinic for patients.

N-terminal-ProBNP is an important biomarker showing cardiovascular stress. It is released into circulation from the synthesizing myocytes linked to the intensity of volume or pressure load in the ventricles and atria. As a result, serum levels increase in myocarditis and dilated cardiomyopathies caused by heart failure (18). A 2017 study by Butts et al. observed a significant correlation between the intensity of ventricular dysfunction degree and high BNP values (19). Another study similarly showed that as left ventricular systolic dysfunction increased, NT-proBNP levels increased (20). In this study, a total of 7 (46.6%) of patients had NT-proBNP levels >100 pg/mL. The first three cases had much higher NT-proBNP levels compared to the other four cases. Our case numbers are insufficient, so we cannot say whether the elevation in NT-proBNP levels is as high as the effect rate on heart functions. Additionally, though there was no correlation found between the troponin values in these three cases with the clinic, the duration for the troponin values to return to normal was longer than the other cases.

The typical ECG finding in myopericarditis of ST segment elevation was the most frequently identified pathology observed in 90% of cases. Additionally, collapse in the PR interval, and T wave inversion before ST segment normalization may be observed. In more than 60% of patients, generally ventricular-derived arrhythmia is identified (11). Electrocardiographics taken in our cases identified common ST elevation in chest derivations for 80% of cases, with sinus tachycardia in 40%. A variety of traits in myopericarditis may mimic acute coronary syndrome with ST segment elevation. In this situation, coronary angiography is beneficial in terms of diagnosis or exclusion of coronary artery disease, while MRI is promising as an effective and noninvasive diagnostic tool. On cardiac MR, ischemic contrasting always involves the subendocardium, while contrarily myocarditis generally involves the left ventricular wall and/or one quarter of the epicardia in the interventricular septum or central wall area (21,22). Additionally, it is reported that alternative imaging techniques like stress ECHO or nuclear stress perfusion screening can be used in order to exclude ischemic heart disease non-invasively (23). Among our cases, coronary angiography was performed in a 17-year old male patient due to ST elevation in inferior derivations and high troponin levels after one week; however, no pathology was identified. Due to technical and infrastructure inadequacies, none of our cases had cardiac MRI or nuclear stress perfusion screening performed.

Pericardial effusion may occur in myopericarditis (11). Echocardiography is the primary method to detect the presence of pericardial effusion due to high degree of specificity and sensitivity. Additionally, increased sheen of the pericardia linked to fibrin accumulation in inflamed pericardial layers is a non-specific ECHO finding. Additionally, ECHO is a valuable way to identify reduced ventricular function, even subclinical (24). Echocardiography observed EF <50% in three cases, and

mild or more intense MY in four cases. Pericardial effusion was not observed in any case.

Endomyocardial biopsy (EMB) has limited clinical benefit for myopericarditis with widespread pericardial involvement. Biopsy has 1/250 risk of perforation and 1/1000 risk of death even in experienced hands (25). Considering the limited benefit in terms of risks and therapy, it was recommended to limit the use of EMB to patients with left ventricular functions and symptoms which do not respond to traditional medical treatments and with significant myocardial involvement (23). The EMB procedure was not performed on any of our cases.

Controlled clinical studies about acute pericarditis or myopericarditis treatment are insufficient (7,8). Additionally, if myocardial failure is not severe, treatment for myopericarditis is similar to acute pericarditis and empirical anti-inflammatory treatments (aspirin, ibuprofen, indomethacin) are generally used to control chest pain (26). Ibuprofen may be chosen due to rare side effects, positive effect on coronary artery perfusion and broad dose interval (27). However, nonsteroidal antiinflammatory drug (NSAID) use in myopericarditis should be assessed according to degree of myocardial involvement because NSAIDs were not effective in animal models of myocarditis and were shown to worsen the myocarditis process and increase mortality (28,29). In our patients, we did not administer routine anti-inflammatory treatment, but began ibuprofen treatment in only nine patients to benefit from analgesic effect.

Intravenous immunoglobulin treatment is used for myopericarditis (30). Intravenous immunoglobulin has antiviral and immunomodulatory effect and this is thought to be beneficial for treatment of viral myopericardial diseases. Additionally, a review by Robinson et al. concluded that data obtained from strong methodologic studies were insufficient to recommend routine IVIG treatment for myopericarditis patients (31). In this study, IVIG treatment was only administered to three patients with heart failure.

Recommendations about rest after myopericarditis are based on increased death rates in rats with intensive exercise after Coxsackie infection as a result of increased viral replication in the heart in animal studies (32). Additionally, more ectopy was shown in myopericarditis patients even while resting and it is stated that exercise may worsen these arrhythmia (4). As a result, during the myopericarditis healing stage and for four to six weeks afterward, it is recommended to avoid high intensity effort (27).

All cases were monitored in intensive care after first attendance and taken for bed rest. The duration of hospitalization was median six days for patients (4-14 days). In the literature patients are recommended to be followed with ECG, ECHO, cardiac enzymes and exercise test in the 1st month, 6th month and 1st year (4). During monitoring, troponin levels in all cases returned to normal

in median 4 days (2-12 days). In line with literature recommendations, ECHO performed during follow-up of patients observed that all cardiac functions normalized within four months. One case continued to have mild MY, while one case had mild left ventricle dilatation.

## CONCLUSION

In conclusion, patients attending with complaints like chest pain and palpitations should have myopericarditis considered for differential diagnosis. Electrocardiography, ECHO, troponin and NT-proBNP levels are very helpful for monitoring and treatment of these patients. Acute myopericarditis has a broad clinical spectrum that may result in asymptomatic subclinical myocardial dysfunction to severe heart failure or sudden death. Diagnosis requires high clinical suspicion as signs and symptoms mimic may other diseases in the pediatric age group.

When the general literature is examined, treatment of myocarditis still remains a supportive treatment. Though most patients are observed to have spontaneous amelioration of cardiac functions and symptoms, it is still a significant cause of morbidity and mortality.

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