Myopericarditis in Children: Elevated Troponin I Level Does Not Predict Outcome

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Abstract Myopericarditis is primarily a pericarditic syndrome with some degree of myocardial involvement, as evident by elevated cardiac enzymes. Differentiating myopericarditis from acute coronary syndromes can be challenging and may require coronary angiography or perfusion studies. Data on myopericarditis and its outcome for children are scarce. This study delineates the demographics, clinical presentation, and outcomes of myopericarditis for children and evaluates the prognostic value of elevated troponin I. The authors retrospectively reviewed 880 patients younger than 18 years of age who were admitted with diagnoses of chest pain, myocarditis, or pericarditis between 2000 and 2010 at their institution. Myopericarditis was defined as a clinical presentation of pericarditis in the presence of elevated levels of cardiac enzymes. Medical records were reviewed to abstract the demographic data, clinical presentation, evaluation, treatment, and follow-up outcomes. A total of 12 patients (1.4%) with myopericarditis were identified. All the patients were male, 8 (67%) of whom were Caucasian, and their median age was 16 years (range, 11–17 years). Two of the patients (17%) had recently used illicit drugs, and two (17%) had recently smoked cigarettes. At presentation, symptoms included chest pain in 12 patients (100%, 12/12), upper respiratory symptoms in 3 patients (25%, 3/12), and shortness of breath in 3 patients (25%, 3/12). No cardiac murmur or gallop was noted in any patient. Electrocardiographic (ECG) changes included diffuse ST-T changes (5 patients), localized ST-T changes (6 patients), and no ST-T changes (1 patient). All the patients had elevated levels of cardiac enzymes, with a median Troponin I level of 21.4 ng/ml (range, 5.0–134.4 ng/ml) and a median CK-MB level of 50.2 ng/ml (range, 7–135 ng/ml). Echocardiography showed normal left ventricular systolic function in all the patients (median ejection fraction, 61%; range, 56–69%). None had pericardial effusion during the first echocardiographic evaluation. Coronary angiography showed normal coronary arteries in all nine subjects for whom it was performed. Treatment of myopericarditis consisted of ibuprofen, acetaminophen, and/or aspirin. During a median follow-up period of 2 months (range, 2 weeks to 3 years), all the patients were asymptomatic with echocardiography showing normal left ventricular size and function. Myopericarditis was exclusively seen in male adolescents. Despite markedly elevated levels of cardiac enzymes, the clinical evolution of myopericarditis seems benign without any myocardial dysfunction. The inflammatory involvement of the myocardium appears to be self-limited without short-term, overt sequelae. An elevated troponin I level in myopericarditis, unlike acute coronary syndromes, does not seem to carry an adverse prognosis. Further studies are needed to evaluate the long-term prognosis for such patients.

Keywords Children · Myopericarditis · Troponin

Myopericarditis is primarily a “pericarditic syndrome” in which acute pericarditis often is accompanied by some degree of myocarditis, as evident by elevated cardiac enzymes [9]. Pericarditis typically is diagnosed by clinical features such as typical chest pain and pericardial friction rub as well as electrocardiographic changes characterized by diffuse ST segment changes.
In the setting of chest pain, elevated cardiac enzymes can be seen in acute coronary syndrome, myocarditis, and myopericarditis. Therefore, patients presenting with chest pain and found to have elevated cardiac enzymes typically are further evaluated by serial measurement of myocardial injury enzymes, an echocardiogram, a coronary angiogram, and/or myocardial perfusion scintigraphy.

Myopericarditis, either spontaneous or after viral infection, has been reported in adults and in a few case reports in pediatrics. Imazio et al. [8] reported myopericarditis in 15% of 274 adults with symptoms of pericarditis. Serum troponin I level was related to the degree of myocardial inflammation but had no prognostic implication in adults. Brandt et al. [1] found that the temporal release pattern of troponin I was similar in myopericarditis and acute coronary syndromes. The data on the incidence, clinical profiles, natural history, and outcomes of myopericarditis in children are scarce. Also, data on the prognostic utility of the serum troponin I level in myopericarditis found in children are lacking. This study aimed to address these knowledge gaps.

Materials and Methods

This retrospective chart review of eligible subjects was conducted in a single tertiary children’s hospital. The study was approved by the institutional review board as was a waiver of parental consent or patient assent. We identified eligible subjects using Data Management Services of our institute, with the International Classification of Diseases (ICD) codes for chest pain, pericarditis, and/or myocarditis used as criteria to select children 18 years of age or younger who presented between 1 October 2000 and 31 October 2010. A comprehensive chart review of all the patients who met the criteria for myopericarditis then was performed.

Myopericarditis was defined as a condition presenting with chest pain or pericardial friction rub, electrocardiographic findings of pericarditis (ST-T changes), elevated cardiac enzymes such as troponin I and CK-MB, and normal left ventricular global systolic function. Patients with congenital heart disease, acute chest trauma, myocarditis, and known causes of pericardial effusion were excluded from the study.

Data collection included demographic characteristics, outcomes, and electrocardiogram reports. Echocardiograms were reviewed, and the results of cardiac catheterization or other perfusion studies when available were recorded. Electrocardiographic findings were classified into diffuse and localized ST-T changes. Changes in ST were considered significant if ST segment elevation/depression exceeded 1 mm in a limb lead or 2 mm in a precordial lead.

At our center, all patients presenting with chest pain suspected to be of cardiac etiology undergo electrocardiogram testing. If found to have an abnormal electrocardiogram, they undergo cardiac enzymes measurement.

Statistical Analysis

Statistical analyses were conducted using SPSS software for PC, version 17 (SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation or as median or number and percentage where appropriate. Significance was determined by a p value less than 0.05.

Results

The study reviewed 880 charts of patients 18 years old or younger who presented with chest pain and/or myocarditis or pericarditis between 1 October 2000 and 31 October 2010 at our institution. Serum troponin I levels were available for 36 patients and found to be elevated in 19 patients. Of the 19 patients with high troponin, 3 had a diagnosis of myocarditis and showed abnormal left ventricular function on an echocardiogram, 1 had cardiac contusion due to chest trauma from a car accident, 1 had a myocardial infarction after coil occlusion of a coronary artery fistula, 1 had systemic lupus erythematosus causing large pericardial effusion, and 1 had recurrent pericarditis. A total of 12 patients (1.4%) fulfilled our criteria for acute myopericarditis (Fig. 1).

Demographics (Table 1)

The median age at diagnosis was 16 years (range, 11–17 years). All 12 patients were male (100%). These 12 patients consisted of 4 African Americans (33%) and 8 Caucasians (67%). The median body mass index (BMI) was 25.6 kg/m² (range, 17.9–44.1 kg/m²). Four patients were overweight (85–95th percentile), and 4 patients were obese (>95th percentile). Urine drug screens were performed for eight patients, two of whom had evidence of illicit drug use. Cigarette smoking was noted for two patients. In terms of other significant medical history, three patients had asthma, one patient had attention deficit hyperactivity disorder (ADHD), and two patients had both ADHD and bipolar disorder.

Clinical Features

In addition to chest pain, symptoms at initial presentation were suggestive of upper respiratory infection in three patients (25%), shortness of breath in three patients (25%), and emesis in two patients (17%). At physical examination, vitals were normal, with mean blood pressures of
120 ± 13 mmHg (systolic) and 68 ± 9 mmHg (diastolic). The mean heart rate was 84 ± 16 bpm. Cardiovascular examination results were benign in all cases, with normal first and second heart sounds and no appreciable third or fourth heart sounds, murmurs, gallops, or pericardial friction rubs. All the subjects were assessed as having good peripheral perfusion.

Electro- and Echocardiography

Electrocardiography showed diffuse ST-T changes in six patients (50%), localized ST-T changes in five patients (42%), and no ST-T changes in one patient (8%). Echocardiography results were normal for all 12 patients, with a median ejection fraction of 61% (range, 56–69%). No patient had pericardial effusion. In all cases, the coronary arteries were normal in origin.

Cardiac Enzymes

Troponin I (normal reference, <0.4 ng/ml) was obtained from 12 patients and CK-MB (normal reference, <10 ng/ml) from 10 patients (Fig. 2). The median peak value of troponin I was 21.4 (range, 5.0–134.4), and that of CK-MB was 50.2 (range, 7–135). The troponin I level was followed serially in seven patients during their hospital stay (Fig. 3). The troponin I level gradually decreased in the following 2 or 3 days. At the time of discharge, the troponin I levels were in the normal range in one patient and remained elevated in six patients.

Coronary Angiography

To exclude the possibility of acute coronary syndrome, coronary angiography was performed for nine patients. All nine patients had normal origin of coronary arteries without evidence of focal stenosis or aneurysm.

Hospital Stay and Follow-up Data

The median hospital stay was 3 days (range, 1–5 days). None of the patients required inotropic or ventilatory support.
Support. Symptoms resolved before discharge in all cases. Follow-up data were available for 9 (75%) of the 12 patients. The median follow-up period was 2 months (range, 2 weeks–3 years). An evaluation for viral etiology of myopericarditis showed that one patient had high immunoglobulin M and G for Epstein-Barr virus and another had elevated antibody titer of Coxsakie type 9 virus. Treatment consisted of aspirin, ibuprofen, and acetoaminophen.

From the cardiovascular standpoint, all the patients were asymptomatic at their follow-up visit. For all the patients, repeat echocardiography showed normal left ventricular size and function with no pericardial effusion. Repeat cardiac enzymes were normal in one patient at the follow-up visit. Nine of the patients underwent a follow-up electrocardiogram, and four showed inverted T waves. Two of these patients underwent exercise stress testing, which yielded normal results.

Discussion

To our knowledge, this is the first study to describe clinical profiles and outcomes of myopericarditis in children. The
prognostic value of elevated troponin I also was explored. Our results demonstrate that myopericarditis was exclusively seen in male adolescents. Despite markedly elevated myocardial cardiac enzymes, the clinical evolution of myopericarditis seems benign without any left ventricular systolic dysfunction or clinical sequelae.

The incidence of myopericarditis in children has not been reported previously. Imazio et al. [7] reported a series of 274 adult patients with acute pericarditis whose incidence of myopericarditis was 14.6% (40/274). At presentation, myopericarditis was associated with arrhythmia, male gender, age younger than 40 years, ST elevation on electrocardiogram, and a recent febrile syndrome. Our study investigating the pediatric population showed a lower incidence (1.4%) of myopericarditis. It was seen exclusively in male adolescents, two thirds of whom were obese or overweight. This association may be incidental, reflecting our population but bears further investigation. None of our patients presented with documented arrhythmia.

Viral infections appear to be the most common causes of myopericarditis in developed countries [9]. In scattered cases of myopericarditis in children, Chlamydophila pneumoniae [12], Campylobacter jejuni [6], group A streptococcus [5], and central European tick-borne encephalitis [3] have been reported associations. In addition, Thanjan et al. [13] reported a 17-year-old boy who experienced myopericarditis after vaccination (booster DTaP administered simultaneously with hepatitis A and meningococcal vaccines). In our study, Epstein-Barr virus and Coxsackie virus type 2, potential etiologic agents of myopericarditis, were identified by serology in two cases.

Elevations of cardiac enzymes such as CK-MB and troponin I may reflect the extent of myocardial inflammatory involvement [1]. Peak troponin T is suggested to predict infarct size and to be a prognostic indicator in adults with acute myocardial infarction [4]. The troponin I increase does not seem to carry an adverse prognosis in adult myopericarditis [7, 8].

Our results are consistent with the adult studies. All 12 patients had elevated cardiac enzymes and no evidence of myocardial dysfunction on echocardiography or cardiac sequelae in the short term. In children, an elevated troponin I in myopericarditis does not appear to be a negative prognostic marker in the short term.

In the setting of chest pain and elevated cardiac enzymes, acute coronary syndrome is a grave concern despite its very low incidence in the general pediatric population. Myopericarditis can mimick acute myocardial infarction [2, 10, 11]. However, Thanjan et al. [13] suggested that a noninvasive test such as cardiac magnetic resonance imaging (MRI) to rule out ischemic heart disease can be an alternative to cardiac catheterization in cases with high suspicion of myopericarditis and low risk for coronary artery disease. Cardiac MRI and indium-111 antimony antibody scintigraphy can be useful for distinguishing between myocarditis and an acute myocardial infarction [9].

In our study, nine patients (75%) underwent coronary angiography. There was no evidence of acute coronary syndrome in any patient. The decision to perform the coronary angiography was made by the individual pediatric cardiologists. The three patients who did not undergo cardiac angiography were the most recent in our cohort. A conservative approach was selected because these patients had a likely diagnosis of myopericarditis based on their clinical presentation but no identifiable risk factors for coronary artery disease.

Because no patients had abnormal findings of coronary angiography, it is difficult to draw any conclusions on the indications for cardiac angiography from our data. Cardiac catheterization may be unnecessary for patients with a typical presentation of myopericarditis and low risk for coronary artery disease.

Study Limitations

This retrospective study had all the limitations associated with such studies. Although this was the largest series of this entity in pediatric patients, our sample size was relatively small. The series could have had a selection bias because only those patients admitted to the hospital who had troponin I level measured were included in the study. However, at our hospital, electrocardiography (ECG) is performed for any adolescent presenting with chest pain, and if the ECG is abnormal, troponin I level is measured, and the child is admitted. The evaluation for potential etiologies of myopericarditis varied and may have affected the prognosis. Nonetheless, this is the first study to explore the natural history and outcomes of myopericarditis in a hospitalized cohort of children.

Conclusion

In this investigation of spontaneous or viral myopericarditis in children, we found that the entity is relatively uncommon, with an incidence of 1.5% among admitted children with chest pain. Seen exclusively in male adolescents, myopericarditis is associated with a benign course and a lack of short-term sequelae. Although troponin I levels may be markedly elevated at presentation, they do not appear to be associated with adverse outcomes. Further investigation is needed to evaluate the long-term prognosis for children with myopericarditis.
References