Original Contribution

Pediatric myocarditis: presenting clinical characteristics

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Abstract

Objective: The objective of the study was to characterize the clinical profiles of pediatric patients with acute myocarditis and dilated cardiomyopathy (DCM) before diagnosis.

Methods: A retrospective cross-sectional study was conducted to identify patients with myocarditis and DCM who presented over a 10-year span at 2 tertiary care pediatric hospitals. Patients were identified based on the International Classification of Diseases, Ninth Revision, diagnostic codes.

Results: A total of 693 charts were reviewed. Sixty-two patients were enrolled in the study. Twenty-four (39%) patients had a final diagnosis of myocarditis, and 38 (61%) had DCM. Of the 62 patients initially evaluated, 10 were diagnosed with myocarditis or DCM immediately, leaving 52 patients who required subsequent evaluation before a diagnosis was determined. Study patients had a mean age of 3.5 years, 47% were male, and 53% were female. Common primary complaints were shortness of breath, vomiting, poor feeding, upper respiratory infection (URI), and fever. Common examination findings were tachypnea, hepatomegaly, respiratory distress, fever, and abnormal lung examination result. Sixty-three percent had cardiomegaly on chest x-ray, and all had an abnormal electrocardiogram results.

Conclusions: These data suggest children with acute myocarditis and DCM most commonly present with difficulty breathing. Myocarditis and DCM may mimic other respiratory or viral illnesses, but hepatomegaly or the finding of cardiomegaly and an abnormal electrocardiogram result may help distinguish these diagnoses from other more common pediatric illnesses.

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1. Background

Myocarditis, the inflammation of the muscular walls of the heart, remains a diagnostic challenge in the clinical setting because of the variability of presentations in the pediatric population. It is nonetheless an important
diagnosis, as it is the most common etiology of heart failure in previously healthy pediatric patients [1]. The initial diagnosis of myocarditis is highly dependent upon clinical suspicion because diagnosis based on endomyocardial biopsy has many inherent risks and is therefore not performed routinely. Unless a high index of suspicion is maintained, acute myocarditis may easily be missed; and the diagnosis may only be obvious in cases when fulminant disease is present.

Patients often present with prodromal symptoms that are not recognized to be associated with myocarditis initially. In a study of 90 patients younger than 16 years who died suddenly and unexpectedly, myocarditis was initially. In a study of 90 patients younger than 16 years are not recognized to be associated with myocarditis. Patients with myocarditis were included in the study. Patients with DCM secondary to other causes such as cardiotoxic drugs, inborn errors of metabolism, malformation syndromes, neuromuscular disorders, or other familial syndromes were excluded. In all cases, the final diagnosis was based upon expert opinion of a pediatric cardiologist.

A standardized data collection form was used to abstract data from hospital medical records. Data were abstracted by 3 investigators. Data collected included demographics, clinical history, physical examination, and results of laboratory evaluation.

The clinical history and physical examination data were obtained from the first documented encounter at our institutions’ EDs. If patients were transferred to our facilities from an outside institution and did not have an ED evaluation, the historical and clinical data were collected from intensive care unit records or the referring hospital’s initial medical evaluation.

The presence or absence of the following clinical features was collected: fever, diaphoresis, lethargy, fatigue, change in exercise tolerance, syncope, seizures, difficulty breathing, rapid breathing, cyanosis, wheezing, apnea, cough, rhinorrhea, chest pain, palpitations, poor feeding, vomiting, diarrhea, abdominal pain, and decreased urination. Physical examination findings collected included triage or initial vital signs and the presence or absence of the following: respiratory distress, evidence of upper respiratory tract infection, abnormal lung examination results (wheezing, retractions, rales, decreased air exchange), gallop, murmur, hepatomegaly, perfusion/pulses, and cyanosis. If no documentation existed regarding a specific sign, symptom, medications, or other aspects of the history, it was recorded as “not documented.”

Initial laboratory findings that were abstracted included complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), troponin, and creatinine kinase (CK). Microbiology results were also abstracted, such as blood cultures, tracheal aspirate, nasal swab cultures, urine cultures, endomyocardial biopsy results, and more specific viral testing. The findings of the initial chest x-ray (CXR), electrocardiogram (EKG), and echocardiogram were abstracted. The results of these tests were based on reported data in the medical record.

If patients had medical evaluations by a physician in the 14 days preceding final diagnosis of myocarditis or DCM, the diagnoses given at these encounters were abstracted.

SPSS for Windows version 14.0 (SPSS Inc, Chicago, IL) [6] was used for data analysis. Descriptive statistics were used to describe patient characteristics and frequencies of signs, symptoms, and diagnoses.

2. Materials and methods

A retrospective cross-sectional study was conducted to identify patients with myocarditis and DCM who presented over a 10-year span from January 1, 1994, to December 31, 2003, at 2 tertiary care pediatric centers with annual emergency department (ED) visits of 35 000 and 62 000. The institutional review boards of both participating hospitals approved the study.

Children up to 18 years old who were identified as having myocarditis or DCM based on the International Classification of Diseases, Ninth Revision, codes were eligible for the study. Only patients diagnosed with DCM secondary to acute myocarditis were included in the study. Children up to 18 years old who were identified as having myocarditis or DCM based on the International Classification of Diseases, Ninth Revision, codes were eligible for the study. Only patients diagnosed with DCM secondary to acute myocarditis were included in the study. Patients with DCM secondary to other causes such as cardiotoxic drugs, inborn errors of metabolism, malformation syndromes, neuromuscular disorders, or other familial syndromes were excluded. In all cases, the final diagnosis was based upon expert opinion of a pediatric cardiologist.

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3. Results

A total of 693 charts were reviewed at the 2 participating institutions. Six hundred twenty-eight patients were excluded because their heart disease was not myocarditis or DCM, their heart disease was secondary to another primary diagnosis (eg, muscular dystrophy, metabolic disorder), or their heart disease was caused by medications. Three patients were excluded secondary to incomplete medical records, resulting in 62 patients available for data analysis: 24 patients from one institution (AI duPont) and 38 patients from the second institution (Childrens Hospital Los Angeles). Twenty-four (38%) patients had a final diagnosis of myocarditis, and 38 (61%) had DCM.

As depicted on Table 1, study patients had a mean age of 3.5 years and a range from 6 days to 17 years. Forty-seven percent were male, and 53% were female. Regarding race, 29% were African American; 29%, Hispanic; 14%, white; 10%, Asian/Pacific Islander; 8%, other; and 10%, not documented. The mean duration of symptoms, before final diagnosis, was 7.6 days (SD ± 13 days). Thirty-nine percent of patients were diagnosed with myocarditis, and 61% were diagnosed with DCM. In total, 8 (13%) patients died; and 54 (87%) survived. As shown on Table 2, a documented viral pathogen was found in 20 (32%) of study patients, with parainfluenza being the most common pathogen found.

 Sixty-two patients were initially evaluated during this analysis. Ten patients were diagnosed with myocarditis or DCM at the first encounter at our respective institutions, resulting in 52 patients who required subsequent evaluations by a physician before a definitive diagnosis was determined. Of these 52 patients, 32 (52%) patients had 1 additional evaluation within 14 days of symptoms. Twenty-four (32%) patients had 2 or 3 evaluations (18 with 2 visits, and 2 with 3 visits) before myocarditis or DCM was diagnosed. Table 3 shows data regarding diagnoses for the 52 patients at their first evaluation by a physician. A respiratory tract infection was diagnosed in 13 (25%) patients, including pneumonia, bronchiolitis, and upper respiratory tract infection. Cardiac disease was diagnosed in 8 (15%) patients, including cardiomegaly, arrhythmia, myocardial infarction, and myocarditis. Four patients had combined diagnoses, with pneumonia cardiomegaly in 3 patients and congenital heart disease cardiomegaly in 1 patient. Other diagnoses were given to 21 (40%) patients, and data were missing or not available for 6 (12%) patients. All patients who were suspected of having cardiac disease at the first visit were either diagnosed in our EDs or referred to our ED the first day the diagnosis was suspected, and all were admitted to the hospital.

Table 4 lists the diagnoses of patients evaluated during the second visit to a physician. A respiratory tract infection was diagnosed in 5 (25%) patients, all of whom had pneumonia.

Table 1  Characteristics of study patients

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>No. of patients (n = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>29 (47%)</td>
</tr>
<tr>
<td>Female</td>
<td>33 (53%)</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>3.5 y (SD ± 5.0)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>18 (29%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>18 (29%)</td>
</tr>
<tr>
<td>White</td>
<td>9 (14%)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Not documented</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>Mean duration of symptoms (d)</td>
<td>7.6 d (SD ± 13.0)</td>
</tr>
<tr>
<td>Final diagnosis</td>
<td></td>
</tr>
<tr>
<td>Myocarditis</td>
<td>24 (39%)</td>
</tr>
<tr>
<td>DCM</td>
<td>38 (61%)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>8 (13%)</td>
</tr>
<tr>
<td>Survived</td>
<td>54 (87%)</td>
</tr>
</tbody>
</table>
Cardiac disease was diagnosed in 4 (20%) patients. Two patients had combined diagnoses, with pneumonia/DCM in 1 patient and pneumonia/cardiomegaly in 1 patient. Other diagnoses were given to 5 (25%) patients, and data were missing or not available for 4 (20%) patients.

Of the 52 patients who were seen for their first medical evaluation before a final diagnosis, 21 (40%) patients were seen by their primary care provider, 21 (40%) were evaluated in a general ED, 2 (4%) were cared for in a pediatric ED, and 8 (15%) were seen in other settings (clinics, neonatal units, etc). Of the 20 patients who were seen at a second medical evaluation (including 18 who had 2 evaluations and 2 patients who had 3 evaluations) before final diagnosis, 7 (35%) were cared for by their primary care provider, 7 (35%) were seen in a general ED, 2 were evaluated in a pediatric ED, and 4 (20%) were seen in other areas.

Many of the patients studied had frequent and overlapping signs and symptoms at the time they were diagnosed with myocarditis or DCM. For the 62 patients studied, Table 5 lists various common symptoms and clinical findings. At the time of presentation to our institutions, 43 (69%) patients had a history of shortness of breath, 30 (48%) had vomiting, 25 (40%) presented with poor feeding, 24 (39%) showed upper respiratory symptoms, 22 (36%) had fever, and 22 (36%) presented with lethargy. On physical examination, 37 (60%) patients had clinical evidence of tachypnea, 31 (50%) had hepatomegaly, 29 (47%) patients had respiratory distress, 22 (36%) patients presented with fever, and 21 (34%) patients had an abnormal lung examination result.

A normal heart rate for age [7] was found in 41 (66%) patients studied. Of the 20 patients with tachycardia, 9 (45%) were febrile and 11 (55%) were afebrile. In addition, 1 afebrile patient was bradycardic. Heart rates were based on a single measurement in triage or the first available vital signs at the time of encounter at our institution.

Table 6 shows laboratory data, abnormalities found on CXR, EKG abnormalities, and results of echocardiography. The mean white blood cell count of patients was 11 400 (SD ± 5.4; range, 4100-34 200). Only 13 patients had a troponin level checked; and of these, 7 (54%) had an elevated level. Twenty-two patients had a CK checked; and of these, 16 (73%) were elevated. Six patients had an elevated ESR, and 4 patients had an elevated CRP.

An abnormal EKG was documented in 59 of 59 (100%) patients, with no EKG on 3 patients. The most common abnormal EKG finding was sinus tachycardia, with the next most common EKG abnormality demon-
stratifying evidence of ventricular hypertrophy followed by ST-wave abnormality. An abnormal CXR was documented in 53 of 59 (90%) patients. In addition, 6 (10%) had a normal CXR and 3 patients had no CXR. The most common abnormal CXR finding was cardiomegaly in 37 (60%) patients, followed by pulmonary edema and pulmonary infiltrate. An abnormal echocardiogram was found in 60 of 61 (97%) patients. One patient had a normal echocardiogram, and 1 patient died in the ED and had no echocardiogram performed. The patient with a normal echocardiogram result was diagnosed with myocarditis by a cardiologist based on a clinical picture of respiratory distress, upper respiratory tract infection, positive viral culture, and cardiac arrhythmia consisting of premature atrial contractions. The patient who died and had no echocardiogram performed was diagnosed with a probable myocarditis because of evidence of heart failure on CXR and cardiac arrhythmia that progressed to cardiac arrest. The patient’s cardiac rhythm was obtained from a cardiorespiratory monitor tracing; and the patient initially had a narrow QRS complex with peaked T waves that changed to a widened QRS complex, resulting eventually in cardiac arrest.

A myocardial biopsy was performed in 6 patients, and findings consistent with myocarditis were found in 5; 1 patient had an insufficient sample.

4. Discussion

This study has identified prodromal symptoms and signs associated with myocarditis and DCM in a diverse pediatric population. Myocarditis and DCM may vary from mild to fulminant disease. In milder cases, diagnosis at initial presentation may be challenging. However, because of the potential for severe and fatal disease, it is important to identify myocarditis and DCM early, so that monitoring and supportive treatment can be timely.

Most patients in this study population presented with complaints of shortness of breath and were found to have tachypnea with associated respiratory distress and an abnormal lung examination result. This is consistent with a case series of 7 myocarditis patients who all presented with respiratory distress, including tachypnea and intercostal retractions. In this series of patients, initial diagnoses included asthma, pneumonia, congestive heart failure, rule-out sepsis, and shock [8]. Although all of the patients in the study progressed and developed worsening symptoms, they nonetheless all started out with respiratory symptoms, similar to most of the patients in our study population. In another case series of 4 patients, all presented with the acute onset of severe respiratory distress, leading to shock; and all were subsequently diagnosed with myocarditis [9]. Therefore, a cardiac etiology should be considered among the differential diagnoses in patients with mild respiratory symptoms, respiratory distress, or unexplained shock.

Although many clinicians believe resting tachycardia is a common finding in patients with myocarditis, this study found that 66% of patients had a normal heart rate for age. In addition, the heart rate did not appear to be related to fever. It is our speculation that sequential vital signs to measure trends in the heart rate may be more helpful in future studies. A single heart rate measurement, therefore, may not be a useful objective marker of myocarditis.

Most cases of myocarditis or DCM were not initially recognized by either a primary care provider or a general emergency medicine health care provider. Of the 62 patients initially analyzed, 52 (84%) required more than 1 visit to a physician within 14 days before the diagnosis of myocarditis or DCM was made. Overall, most patients were initially diagnosed with a respiratory illness.

Although myocarditis and DCM may mimic other respiratory or viral illnesses, findings on physical examination such as hepatomegaly should not be overlooked; and the finding of cardiomegaly on CXR should help distinguish these diagnoses from other more common pediatric respiratory illnesses. In addition, although not apparent in our study, several case reports have included seizures as the inciting event, along with other cardiac signs and symptoms that led to the diagnosis of myocarditis [10,11]. Therefore, this variability in signs and symptoms, especially when they are associated with cardiac or radiographic findings, should alert the clinician to assess for myocarditis or DCM.

Our study is similar to a previously published study by Freedman et al, who examined signs and symptoms along with CXR and EKG findings in patients with myocarditis. Although the 2 studies were similar with regard to the predominance of respiratory and gastrointestinal symptoms, our study had a higher percentage of patients with respiratory complaints. In addition, our study demonstrated that 50% of patients at the time of diagnosis had hepatomegaly vs 36% in the study of Freedman et al. Regarding CXR evaluation, our study demonstrated that 60% of patients had evidence of cardiomegaly (vs 55%); and 95% of patients with myocarditis in our study had an abnormal EKG (vs 93%) [3].

Although the results of our studies differ to a small degree regarding clinical signs and symptoms (respiratory and gastrointestinal), such symptoms along with CXR and EKG findings ultimately led to the same cardiac diagnosis in both studies.

As demonstrated in our study, several laboratory tests were obtained in a relatively small proportion of patients. It has been postulated that troponin levels may provide the best evidence of myocyte injury in patients with myocarditis [12]. Our study, however, demonstrated that only 7 of 13 patients tested had a positive result. This small sample size does not allow us to draw the conclusion that this should be a mandatory laboratory test in the
evaluation of patients with suspected myocarditis or DCM until further large-scale studies are completed that may conclusively determine its utility. In addition, of 22 patients who had CK levels drawn, 73% had an elevated level. Although this is a relatively high percentage (based on a small sample size), this is a nonspecific marker of muscle breakdown and is not predictive or diagnostic of myocarditis or DCM.

This study has several limitations. It is a retrospective chart review that is limited by the available data in the medical record. Particularly, in patients who had prior medical evaluations, details of the clinical history and physical examination at that time were not available. In addition, most diagnoses of myocarditis and DCM were based on expert opinion of a cardiologist and not biopsy-proven disease, a reality in clinical practice. Long-term follow-up of patients who survived was not analyzed.

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References