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Acute myocarditis associated with non-typhoidal *Salmonella* gastroenteritis

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Acute myocarditis is clinically rare in children, but poses a significant risk for morbidity and mortality. Children with myocarditis show a wide variety of clinical manifestations ranging from subclinical myocarditis to heart failure, hemodynamic compromise, arrhythmia, and even sudden death. *Salmonella* species are associated with clinical presentations including gastroenteritis, enteric fever, bacteremia, and extra-intestinal focal infections. Non-typhoidal *Salmonella* infections usually cause self-limiting gastroenteritis, but are rarely associated with myocarditis. In this report, we present a case of myocarditis associated with *Salmonella* serogroup B gastroenteritis in a previously healthy 15-year-old boy.

Key words: Child; Gastroenteritis; Magnetic Resonance Imaging; Myocarditis; Salmonella Infections

Introduction

Acute myocarditis is rare in children. It has an estimated annual incidence of 1 to 2 per 100,000 children¹⁻⁴. It is most commonly seen following a viral infection, and is rarely caused by bacteria in immunocompetent children. Affected children initially present with respiratory or gastrointestinal

symptoms, cardiovascular manifestations or shock. Approximately 50% of children with myocarditis have gastrointestinal symptoms such as vomiting or poor feeding⁵. Non-typhoidal *Salmonellae* (NTS) are an important cause of gastroenteritis (usually self-limiting) but are rarely associated with myocarditis. Here, we report a case of myocarditis associated with NTS gastroenteritis in a previously healthy 15-year-old boy. The case report was exempted from the requirement of informed consent by the Institutional Review Board (IRB No. KUMC 2019-07-052).

Case

A 15-year-old boy visited the emergency

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department with fever (up to 38.5°C). He presented with 1-day history of profuse watery, non-bloody diarrhea, peri-umbilical abdominal pain, and chest discomfort around the mid-sternum. He reported no significant past medical history or family history.

The initial vital signs were as follows: blood pressure, 112/64 mmHg; heart rate, 64 beats per minute; respiratory rates, 20 breaths per minute; temperature, 37.7°C; and oxygen saturation, 100% on room air. Cardiac examination was unremarkable, and lung sounds were clear. Abdominal examination showed mild epigastric tenderness without rebound one.

Initial laboratory evaluation showed a white

blood cell count of 10,850/ μ L with 79% segmented neutrophil without anemia or thrombocytopenia and a C-reactive protein concentration of 2.3 mg/dL. The serum electrolytes, glucose, creatinine, liver function tests and urinalysis were all within normal limits. We measured concentration of troponin I to assess myocardial injury related to his chest discomfort. The concentration was 107.8 ng/L (reference value, < 20.7 ng/L). Concentrations of the other myocardial enzymes were within normal limits: creatinine kinase (CK), 110 U/L (reference value, 58–348 U/L); CK-MB, 1.4 ng/mL (reference value: < 6.6 ng/mL); and B-type natriuretic peptide, 10 pg/mL (reference value: < 100 ng/mL).

Fig. 1. Initial electrocardiogram showing normal sinus rhythm with nonspecific ST segment changes (A). Follow-up electrocardiogram showing sinus rhythm with ST segment elevation in leads II, III, aVF, and V3-V6, suggestive of inferolateral myocardial injury (B).

The venous blood gas analysis was normal: pH, 7.38; PCO₂, 41.7 mmHg; and HCO₃, 24.9 mEq/L. There were no remarkable findings on the initial electrocardiogram (ECG) (Fig. 1A) and chest radiograph. After his blood, urine, and stool cultures were collected, intravenous ceftriaxone was administered empirically based on the suspicion of bacterial gastroenteritis associated with unknown myocardial injury.

As his chest discomfort worsened with dizziness, follow-up laboratory evaluation and ECG were performed. The concentrations of troponin I and CK-MB increased to 4,370.0 ng/L and 15.2 ng/mL, respectively. Unlike the initial ECG, follow-up ECG performed after 12 hours showed an ST-segment elevation up to 1.8 mm in leads II, III, aVF, and V3–V6 suggestive of inferolateral myocardial injury (Fig. 1B). Findings suggesting pericardial effusion or tamponade, such as electrical alternans and low-voltage QRS complex, were not observed. Initial bedside echocardiogram did not show structural or regional wall motion abnormalities. However, there was mildly reduced left ventricular (LV) systolic function with an ejection fraction of approximately 50%. Based on clinical and laboratory findings, the presumed diagnosis was myocarditis

associated with bacterial gastroenteritis.

The boy was transferred to the intensive care unit. Intravenous immunoglobulin was administered once (400 mg/kg). Dopamine and milrinone were infused intravenously to improve the LV systolic dysfunction and reduce the afterload. On day 4, we noted resolution of the chest discomfort and normal LV function on a follow-up echocardiogram. At this point, intravenous dopamine and milrinone were discontinued. The abnormal ECG findings were normalized and troponin I was decreased to 992.8 ng/L. On day 6, cardiac magnetic resonance imaging (MRI) findings showed sub-epicardial lesions suggestive of myocarditis (Fig. 2). *Salmonella* serogroup B was identified in the stool culture; blood and urine cultures yielded negative results. No viruses were found in polymerase chain reaction. In addition, no other possible causes (drugs, autoimmune or metabolic diseases) could be recognized. The final diagnosis was myocarditis associated with *Salmonella* serogroup B gastroenteritis based on the clinical, microbiologic, and imaging findings. He was discharged in a stable condition on day 9. After 1 month, he was in a good condition and had no abnormalities in cardiac enzymes, ECG, and echocardiogram.

Fig. 2. Cardiac magnetic resonance images in long axis (A) and mid-short axis (B) planes showing late gadolinium enhancement in the sub-epicardium at the anterolateral and inferolateral left ventricle walls, suggestive of myocardial fibrosis-associated with myocarditis (arrows).

Discussion

The adolescent who presented with chest discomfort, fever, diarrhea, and abdominal pain was diagnosed with acute myocarditis associated with *Salmonella* serogroup B gastroenteritis. No complications developed due to early diagnosis and prompt management. The early diagnosis was possible thanks to the focus on aggravating chest discomfort and laboratory evidence of myocardial injury, and subsequent repetition of cardiac enzymes and ECG. Park et al.⁶⁾ first reported a case of a previously healthy 5-year-old Korean boy who had myocarditis associated with *Salmonella* gastroenteritis, complicated by complete atrioventricular block requiring permanent pacemaker insertion. This patient had a 3-day history of fever, abdominal pain, and vomiting. The most important therapeutic issue of myocarditis is prompt and appropriate diagnosis prior to clinical deterioration. Fortunately, our patient came to the emergency department early and was diagnosed promptly, allowing appropriate treatment to be carried out. Our experience suggests that myocarditis should be included in differential diagnosis when gastroenteritis patients present with cardiac manifestations.

Among diverse causes of myocarditis, viral infection is most common in children, whereas bacterial infections are comparatively rare^{7,8)}. Physical examination may show respiratory findings ranging from tachypnea, retraction, and rales to direct evidence of cardiac dysfunction, abnormal heart sounds, and murmurs⁷⁾. ECG findings are usually abnormal but nonspecific; for example, sinus tachycardia with nonspecific ST segment changes and T wave abnormalities. Cardiac enzymes, particularly troponins I and T, are commonly used to screen myocarditis. Although elevated concentrations of the enzymes reflect myocardial damage, troponins have a 34% sensitivity and 89% specificity for the diagnosis of myocarditis⁹⁾. Thus, the abnormalities should be interpreted cautiously along with other clinical and echocardiographic findings⁷⁾. Cardiac MRI can be

a noninvasive and valuable diagnostic tool to identify the location and extent of myocarditis, allowing the safe and efficient performance of endomyocardial biopsies¹⁰⁾. However, because of frequent delays in arranging the test, it is difficult to perform cardiac MRI in emergency settings, and it may not accurately reflect the initial severity.

Salmonella species are gram-negative bacilli responsible for significant morbidity and mortality. Both typhoidal *Salmonellae* and NTS can cause extra-intestinal manifestations. However, among the manifestations, myocarditis is uncommon¹¹⁾. Though antibiotic therapy is not recommended for NTS gastroenteritis, it is warranted in certain patients at high risk for infection¹²⁾. Recent systematic review on cases of NTS myocarditis shows predominant occurrence in young adults and association with poor outcome¹³⁾. Although *Salmonella* or other bacteria are rare causes, the possibility of myocarditis should be considered in any gastroenteritis patients presenting with cardiac manifestations. This is especially important considering known complications of myocarditis, such as dilated cardiomyopathy and sudden death.

It is worth mentioning 2 caveats in the diagnosis of the present case. First, endomyocardial biopsy is considered the gold standard for diagnosis, but the biopsy has limitations because of its invasiveness and low sensitivity due to patchiness of lesions¹⁴⁾. When the biopsy is not possible, cardiac MRI is increasingly used to diagnose the entity¹⁵⁾. In our patient, a sufficient diagnosis could be made based on the combination of clinical, laboratory, echocardiogram, and cardiac MRI findings. Second, according to somatic (O) and flagella (H) antigens, more than 2,500 *Salmonella* serotypes were identified¹⁶⁾. Although *Salmonella* serotyping is essential for specific diagnosis, treatment, and epidemiologic surveillance, it is time-consuming and expensive to perform. In our center, serotyping with only O antigen-specific and Vi-specific antibodies are performed. Thus, it was unable to serotype *Salmonella* species.

To summarize, children with myocarditis can

present with gastrointestinal manifestations. Particularly for children presenting with diarrhea, NTS may be considered as a microbiological diagnosis.

Conflicts of interest

No potential conflicts of interest relevant to this article were reported.

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