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Myocarditis associated with influenza infection in five children

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ABSTRACT

Background: Myocarditis is an inflammatory condition located mainly in the myocardium. It is caused by a variety of bacterial and viral infections. Influenza is one of the most common relevant viruses that cause myocarditis.

Objectives: We attempted to share our experiences about clinical and laboratory findings, cardiac evaluation, and treatment of children with influenza myocarditis.

Methods: This retrospective study was performed by the Department of Pediatric Infectious Diseases at the Faculty of Medicine, Hacettepe University in Turkey. The medical records of patients diagnosed with myocarditis associated with an influenza infection between January 2014 and January 2017 were systematically reviewed.

Results: Vaccination seems likely to be an important protection strategy for both influenza infections and complications.

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Introduction

Influenza occurs all over the world, with an annual global attack rate estimated at 5–10% in adults and 20–30% in children; unfortunately, annual epidemics are estimated to result in approximately 3–5 million cases of severe illness and approximately 250,000–500,000 deaths [1,2]. In addition to such moderate complications as sinusitis and otitis, myocarditis is one possible serious complications of influenza [3]. Myocarditis in children is one of the most important causes of acute cardiovascular death and requires early diagnosis and aggressive treatment to save the patient [4]. It is caused primarily by numerous infection agents, but it may also accompany autoimmune disease, hypersensitivity reactions, and toxins [5]. Influenza is one of the common relevant viruses caused by myocarditis, as well as Coxsackie B, adenovirus, echovirus, and cytomegalovirus. The actual incidence of influenza myocarditis in the general population is unknown because of the variable clinical presentation in a wide range—from asymptomatic electrocardiographic changes to fulminant heart failure with fatal arrhythmias

[6]. The prevalence of myocardial involvement in infections caused by influenza virus ranges from 0 to 11%, and the clinical appearance of influenza myocarditis is not common [7–9]. In the literature, few pediatric cases with influenza myocarditis were reported.

With this report, we attempted to share our experiences, which include a description of clinical findings, laboratory findings, and cardiac evaluation and treatment, with five children who had influenza myocarditis over three years.

Material and methods

This retrospective study was performed by the Department of Pediatric Infectious Diseases at the Faculty of Medicine, Hacettepe University in Turkey. The medical records of patients diagnosed with myocarditis associated with influenza infection between January 2014 and January 2017 were systematically reviewed. The diagnosis of acute myocarditis was confirmed according to criteria reported in “Guidelines for Diagnosis and Treatment of Myocarditis” as (1) a history of flu-like symptoms, (2) pathologic cardiac findings on physical examination, (3) abnormal electrocardiography (ECG), (4) abnormal ECHO findings, (5) elevated myocardial constitutive proteins, (6) changes in cardiac findings on physical examination within a few hours and myocardial constitutive pro-

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Table 1
Demographic and clinic data of patients.

Patient no.	Season	Age/sex	Virus type	Underlying disease	Clinic	Physical examination	Time ^b	Antibacterial drugs	Antiviral drug	Sonuç
Case 1	January 2014	9 years/F	Influenza A, influenza B	Metabolic disease, myocarditis history one year before	Cough, fever, myalgia, malasia,	Tachycardia	2 days	Yes	No	Recovered
Case 2	January 2017	4 year/M	Influenza B	Dilated cardiomyopathy	Cough, rhinorrhea	Lower extremity strength 3/5 Filiiform pulse, increased capillary refill time Hepatomegaly	20 days	Yes	Yes	Recovered
Case 3	January 2017	1 year/M	Influenza B, RSV A	Neurologic disease	Cough, fever, vomiting	Filiiform pulse, hypotension	5 days	Yes	Yes	Recovered
Case 4 ^a	January 2017	5 years/F	Influenza A, influenza B	No underlying disease	Cough, fever, vomiting, diarrhea	Dehydration Respiratory Depression Filiiform pulse increased capillary refill time	6 days	Yes	Yes	Dead
Case 5	January 2017	17 years/F	Influenza A, Parainfluenza 1, RSV A	Chronic granulomatous disease	Cough, fever, dyspnea	Hypotension Hypotension	3 days	Yes	Yes	Dead

^a Patient who had ECMO. IVIG: intravenous immunoglobulin.

^b Time to myocarditis findings from influenza findings.

teins, (7) exclusion of acute myocardial infarction, (8) abnormal histological findings on endomyocardial biopsy, and (9) detection of a virus [10]. Relevant information, such as demographics, clinical laboratory findings, and cardiac findings, were recorded on prepared forms. All laboratory tests had been performed in our local laboratory, and echocardiography (ECHO) was performed on all patients. Respiratory viruses were isolated from nasopharyngeal specimens, and the samples were analyzed by multiplex reverse transcription polymerase chain reaction (RT-PCR) to detect viral pathogens. We tested samples for 15 viruses (IFV A-B, PIV 1-2-3, hAD, RSV A, RSV B, CoV, EV, hRV, hBoV, CoV 229/NL63, and CoV OC43/HKU1). Nucleic acid isolation was performed with a GeneAll Ribospin vRD II Isolation Kit (Seoul, Korea). A real-time PCR method was carried out using a Seegene RV16 Detection Kit (Seoul, Korea). The study was approved by the Ethical Committee of the Hacettepe University (number: GO 17/88).

Results

Demographic, epidemiological, and clinical features

During the period between January 2014 and January 2017, 5 patients (3 female, 2 male) with a median age of 5 years were diagnosed with myocarditis associated with influenza infection among 241 patients with influenza infection. Only 1 patient had no underlying disease; the others had metabolic disease, dilated cardiomyopathy, neurologic disease, and chronic granulomatous disease, respectively. The most frequently reported presenting symptoms were fever and cough (100%); vomiting was seen in 2 (40%) of the patients, and only 1 patient had dyspnea. None of these patients were previously vaccinated with influenza. The demographic, epidemiological, and clinical features of these 5 patients are summarized in Table 1.

Laboratory

All 5 children had a positive RT-PCR test result from a nasopharyngeal swab sample that was subsequently confirmed as influenza at Hacettepe University Microbiology Laboratory. Two patients had both influenza A and B virus; 1 patient had only influenza B virus; 1 patient had RSV A and influenza B virus; and 1 patient had parainfluenza 1, RSV A, and the influenza A virus (Table 1).

Diagnosis

The first patient (Case 1) had elevated cardiac enzymes with pericardial effusion and mild valve deficiency. The second patient (Case 2), who also had dilated cardiomyopathy, had a decreased ejection fraction from 54% to 31%. Afterwards, he had the influenza infection, ejection fraction returned to 46% on ECHO. Global dyskinesia was detected on this patient's cardiac magnetic resonance imaging (see Supplementary Video S2 in the online version at DOI: 10.1016/j.jiph.2018.05.003). The third patient (Case 3) had a decrease in ejection fraction from 48% to 30%; after the influenza infection, this was 73% on ECHO. Mitral valve regurgitation also recovered. The fourth patient (Case 4) had fulminant myocarditis with sudden onset of cardiac symptoms. This rapidly progressed to severe hemodynamic deterioration with severe heart failure. This patient's ECG showed ST elevation and prolonged QRS. The patient's ECHO showed reduced systolic function (Fig. 1, see Supplementary Video S1 in the online version at DOI: 10.1016/j.jiph.2018.05.003). The last patient (Case 5) had subclinical myocarditis, as did the first patient, with elevated cardiac enzymes (Tables 1 and 2).

We were able to do a biopsy in only Case 1, who had fulminant myocarditis. However, it was reported that the biopsy material was not suitable for the examination of myocardial tissue. It is known

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