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Cytomegalovirus myocarditis with rapid response to intravenous immunoglobulin therapy

İntravenöz immünoglobulin tedavisine hızlı yanıt veren Sitomegalovirüs miyokarditi

Mehmet Türe [1], Hasan Balık [1], Meki Bilici [1], Alper Akın [1], Savaş Mert Darakci [2], Sercan Yücel Yanmaz [2]

[1] Dicle University Hospital, Department of Pediatric Cardiology, Diyarbakır, Turkey
[2] Dicle University Hospital, Department of Pediatric, Diyarbakır, Turkey

ORCID ID of the authors
MT: 0000-0002-8167-4714
HB: 0000-0002-3373-1585
MB: 0000-0001-8316-7102
AA: 0000-0003-1587-9559
SMD: 0000-0001-7788-9248
SYY: 0000-0002-2930-2817

Abstract

Myocarditis is an inflammatory disease of the heart muscle. Most cases are caused by viral agents such as enteroviruses and adenoviruses. Cytomegalovirus is one of the more rare causes of viral myocarditis. In this article, case is reported of viral myocarditis diagnosed due to Cytomegalovirus infection and which then responded very rapidly to intravenous immunoglobulin treatment. This case report can be considered to contribute to literature as there are not enough data about intravenous immunoglobulin treatment results in Cytomegalovirus myocarditis.

Keywords: Cytomegalovirus, Myocarditis, Intravenous immunoglobulin therapy

Öz

Miyokardit; kalp kasının enflamatuar bir hastalığıdır. Olguların çoğunda etken enterovirüsler ve adenovirüsler gibi viral ajanlardır. Sitomegalovirüs viral miyokarditin daha nadir görülen nedenlerinden biridir. Bu makalede Sitomegalovirüs enfeksiyonuna bağlı viral miyokardit tanısı konulan ve intravenöz immunglobulin tedavisine çok hızlı yanıt veren bir olgu sunuldu. Sitomegalovirüs miyokarditinde intravenöz immunglobulin tedavisi sonuçları ile ilgili yeterli veri olmaması nedeniyle bu olgu sunumunun literatüre katkıda bulunacağını düşünüyoruz.

Anahtar kelimeler: Sitomegalovirüs, Miyokardit, İntravenöz immunglobulin tedavisi

Introduction

Myocarditis is a disease progressing with inflammatory cell infiltration of the myocardium, caused primarily by viral infections. Cytomegalovirus (CMV), which is a member of the herpes virus family, is one of the more uncommon agents of myocarditis [1]. Cardiac complications associated with CMV infection are rarely seen and only a few cases have been reported. Primary cardiac involvement is pericarditis and/or myocarditis [2]. The first stage of treatment in myocarditis is supportive treatment. Although studies have reported positive effects of intravenous immunoglobulin (IVIG) treatment in acute viral myocarditis, the use of immunosuppressive agents remains controversial. Antiviral treatment has been used in some cases of viral myocarditis associated with CMV infection. However, there have been insufficient studies related to IVIG treatment efficacy in these patients [3]. We aimed to present a successful treatment of CMV myocarditis with IVIG therapy.

Corresponding author / Sorumlu yazar:
Mehmet Türe
Address / Adres: Dicle Üniversite Hastanesi, Çocuk Kardiyoloji Bölümü, Diyarbakır, Türkiye
e-Mail: drture21@gmail.com

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Case presentation

A 3-month old male infant presented at our center because of discomfort and on determination of cardiomegaly, was referred to the Pediatric Cardiology Polyclinic. In the physical examination, the general status was fair, with agitation and discomfort. Body weight was 4.2 kg, body temperature 36.4°C, respiratory rate 46/min and arterial blood pressure 64/43 mmHg. In the cardiac examination, there was determined to be tachycardia (heart rate 154 bpm), heart sounds were normal and there was no murmur. Findings of the 12-derivation surface electrocardiograph were consistent with sinus tachycardia. On telegraphy, the cardiothoracic ratio was measured as 63%. On transthoracic echocardiography (ECO), the left ventricle was determined to be wider than normal, left ventricle diastole end diameter (LVEDd) was 27 mm (Z score 4.18), left ventricle systole end diameter (LVESd) was 20 mm (Z score 4.84), left ventricle ejection fraction (LVEF) was 50%, left ventricle shortening fraction (LVSF) was 24% and there was a mild level of mitral failure. CK-MB (Creatinine kinase myocardial isoenzyme) was determined as 8.8 ng/ml (normal: 0.6-6.3), troponin I 0.06 ng/ml (normal 0-0.04), C-reactive protein 0.02 mg/dl (normal: 0-0.5), and white blood cell as 9.8 K/uL. Liver and kidney function test results and thyroid functions were normal. There was no production in blood, urine or feces cultures. Tandem mass, and amino acid levels in the blood and urine, antinuclear antibodies (ANA) and anti-dsDNA and blood gas values were normal. Anti CMV IgM was determined as 45.1 % (normal <22%), anti CMV IgG 48.1 UA/ml (normal <14 UA/ml), CMV IgG avidity <0.3 UA/ml (low avidity), and CMV PCR 1.58x 102 cp/ml (positive). When these results were evaluated together with the ECO findings, viral myocarditis associated with active CMV infection was considered. Treatment of furosemide, captopril and low-dose digoxin was started. On the third day of hospitalization, as the discomfort of the patient increased and the ECO findings and clinical findings continued, IVIG of 1gr/kg/day (48 hours) was started. The changes in the ECO and laboratory findings from before and after the IVIG treatment are shown in Table 1. On the thirteenth day of hospitalization, the general status was good so the patient was discharged with digoxin, captopril and furosemide. At the first and sixth month follow-up examinations, the left ventricular systolic and diastolic functions on ECO were determined to be normal. The written consent was obtained from the parent of the patient presented in the study.

Table 1: Laboratory and ECO findings before and after IVIG treatment (Note: IVIG treatment was given on the 3rd day of hospitalization)

	At the time of diagnosis	1st Day	3rd Day	1st Week	1st Month	6th Month
LVEF (%)	50		51	65	71	69
LVSF (%)	24		25	34	39	37
LVEDd (mm)	27		28	24	25	25
LVESd (mm)	20.5		21	16	15	16
Troponin I (ng/ml)	0.06	0.05		0.04	0.01	0.02
CK-MB (ng/ml)	9.9	8.8		7.1	5	6

LVEF: left ventricle ejection fraction LVSF, left ventricle shortening fraction, LVEDd: left ventricle diastole end diameter, LVESd: left ventricle systole end diameter, CK-MB: Creatinine kinase myocardial isoenzyme

Discussion

It has been reported that the myocardial damage seen in myocarditis could be related to immunological mechanisms rather than the direct effect of viral infections. Therefore, there are studies supporting the use of IVIG, which is an immunomodulator, in the treatment of viral myocarditis in children [4]. IVIG treatment increases the plasma level of the anti-inflammatory mediator, IL-10, IL-1 receptor antagonist and tumor necrosis factor receptors. It also reduces the N-terminal pro-atrial natriuretic peptide level. The use of IVIG in viral myocarditis has been reported to decrease cardiac inflammation and pro-inflammatory cytokines [5]. Nevertheless, as the efficacy of IVIG in viral myocarditis patients has not been proven in studies, its use in the treatment of myocarditis remains controversial [6].

In a randomized study of 62 patients with dilated cardiomyopathy, no effect of IVIG treatment was seen on ventricular ejection fraction. This showed that there was no positive effect on cardiac functions and life expectancy [6]. However, there are also studies of patients with myocarditis showing that IVIG was effective in children by regulating left ventricular function and increasing survival [4]. High-dose IVIG treatment has been shown to correct newly-developed dilated cardiomyopathy and increase ejection fraction by 17 units [7]. Although the definitive diagnosis of myocarditis is made from endomyocardial biopsy, definitive diagnosis cannot be made in some patients despite the biopsy and when this procedure is applied in only a few selected patients because of the risk of biopsy, the treatment decision including IVIG is made based on the laboratory, ECO and clinical findings of the patient.

In the current study as viral myocarditis associated with CMV was supported by the clinical, laboratory and ECO findings and the left ventricle systolic functions were impaired, IVIG was started. Although there are publications related to antiviral treatment or the use of IVIG in CMV myocarditis [3,8], there are insufficient data of the results of IVG use in these patients. As a CMV myocarditis patient who improved following IVIG, although this has been rarely reported in literature, the echocardiographic and clinical recovery in this patient was considered to be associated with the IVIG treatment.

Conclusion

Although there are studies in literature that have shown the efficacy of IVIG in the treatment of viral myocarditis in children, as there are also studies showing no effect, the use of IVIG in treatment is still a matter of debate. However, as seen in the current patient, it is possible to achieve a rapid recovery in cardiac functions with this treatment. As there are insufficient studies related to the response to IVIG in CMV myocarditis, there is a need for the evaluation of many more patients to confirm the positive effects of IVIG treatment on cardiac functions.

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