CASE REPORT

# Ondansetron induced bradycardia complicated myocarditis in a child: A case report

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**ABSTRACT**

Acute viral myocarditis may have non-specific presentations that not only complicates the diagnosis but also may result in administration of medications that worsen the course of the disease. We present an 8-year-old boy with viral myocarditis in a boy that was complicated with oral ondansetron administration who was referred to our center with two episodes of syncope after an episode of nausea and weakness then administration of one dose oral ondansetron due to nausea and vomiting. He had Second type Mobitz AV block in electrocardiogram, leukocytosis and slight elevated troponin I in laboratory assessment. Serology evaluations were negative for viral infections. He was managed with Temporary Pacemaker (TPM) and corticosteroid and discharged in good condition. No sign of cardiac involvement was found in the Cardiovascular Magnetic Resonance Imaging (CMRI) in one week follow up. This case indicates the chance of worsened viral myocarditis by the administration of a single oral dose of ondansetron.

**Key Words:** *Ondansetron; Brady arrhythmia; Myocarditis, Pediatric*

## INTRODUCTION

Acute viral myocarditis is an inflammation of heart muscle and vessels mainly due to infectious causes [1]. The approximated incidence of viral myocarditis has been reported to range from 0.012% based on screening electrocardiogram in asymptomatic children to 0.5 in 10000 emergency department admitted children, while pot-mortem evaluations have shown that 15% to 0.6% of deceased children had myocarditis [2-5]. The most common infectious causes of viral myocarditis was the members of adenovirus and enterovirus family, but recently parvovirus B19 and human herpes virus 6 related myocarditis have become more prevalent. With the emergence of Coronavirus 2019 (COVID-19), myocarditis due to COVID-19 have been reported in as high as 5% of adult patients [6]. The exact prevalence of COVID-19 myocarditis in children has not yet reported but recent studies on critically ill children have showed a high prevalence of COVID-19 among children with myocarditis [7].

The typical course of acute viral myocarditis includes prodromal viral infection in more than 60% of the patients and fever in more than 50% of the patients [1]. Ventricular and atrial arrhythmias may present in 45% of cases, while syncope may occur in nearly 10% of cases [1]. Viral myocarditis might present with non-specific symptoms in children including nausea, vomiting, abdominal pain, fatigue and shortness of breath [1]. The Electrocardiogram (ECG) and echocardiographic findings of these patients may be inconclusive [8, 9]. Cardiovascular Magnetic Resonance Imaging (CMRI) imaging is the gold standard for evaluating ventricular volumes, ejection fraction and ventricular and atrial masses. CMR findings in viral myocarditis may identify signs of inflammation in myocardium [10].

Misdiagnosis of viral myocarditis due to non-specific signs and symptoms might result in the administration of medications that can aggravate the condition. Ondansetron is among the widely used medications in children that may have cardiac side effects including dose dependent prolongation of QT segment [11]. We report a case of healthy 8-year-old boy who presented with episodes of syncope due to viral myocarditis and oral administration of ondansetron.

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## CASE PRESENTATION

Patient was an 8-year old boy who referred to our medical center with the chief complaint of a sudden episode of loss of muscle tone and unconsciousness that lasted for 20 seconds. He regained consciousness after the episode. In the present medical history, he had a sudden nausea, vomiting, dizziness and pallor in the admission date, which was followed by fatigue and malaise. He was given an ondansetron 4 mg tablet. Then his confusion and dizziness was aggravated and the child went to sleep for two hours. He was stable after waking up but suddenly lost his consciousness for 20 seconds with fine tonic movements.

The patient was the second child of the family. He was born through Caesarean section at term and the birth weight was normal. His growth and development was normal. He had no positive past medical history except for atopic asthma. He had no history for fever, chills, cough, diarrhea or contact to sick patient. During the episode of unconsciousness, he did not have tonic colonic movements and upward gaze, or evidence of postictal phase. He was not any medication or exposed to new food or drug. The parents reported another episode of loss of consciousness similar to the previous episode during the ride to hospital. This second episode lasted for 40 seconds. His vital signs at time of admission were normal and the respiratory rate was 15/minute. The laboratory findings included ESR: 15 mm/hour, quantitative C-Reactive Protein (CRP) was negative, he had leukocytosis in Complete Blood Count (CBC) with White Blood Cell (WBC): 10700/µL with 76% Polymorph Nuclear (PMN), 13.4% lymphocyte and 10.1% mixed cells, which indicated low lymphocyte percentage and elevated mixed cells based on the normal range for age. His Polymerase Chain Reaction (PCR) test was negative for coronavirus 2019 (COVID-19). He also had negative serologic findings for COVID-19, and serologic test for both Immunoglobulin G (IgG) and IgM for toxoplasmosis, Epstein-Bar Virus (EBV), Cytomegalovirus (CMV), and varicella virus were negative. Laboratory findings also indicated slight elevated Troponin I (TPI). His ECG revealed Mobitz type 2 atrioventricular AV block with RBBB and intermittent superior axis and inferior axis suggestive for additional LAHB and LPHB (Figure 1 A and 1B). The patient was admitted with the primary diagnosis advanced symptomatic AV block in result of myocarditis.

He underwent echocardiography, which revealed EF of 55% without wall motion abnormality. High Resolution Computed Tomography (HRCT) revealed only a mild right side pleural effusion and mild splenomegaly (approximately 110 mm). A Temporary Pacemaker (TPM) was implanted from femoral right vein, classic myocarditis treatment was initiated with Methyl Prednisolone and the patient was transferred to Intensive Care Unit (ICU) for proper monitoring (Figure 1C). Next day, monitor shows sinus rhythm with acceptable heart rate but it still was RBBB with P-R interval about 220 ms and right axis deviation (RBBB+LPHB) and ST elevation in V2 and V3 (Figure 2A), in next 24 hours still we have sinus rhythm with acceptable heart rate but alters to LBBB and left axis deviation and ST elevation in pericardial leads (Figure 2B).

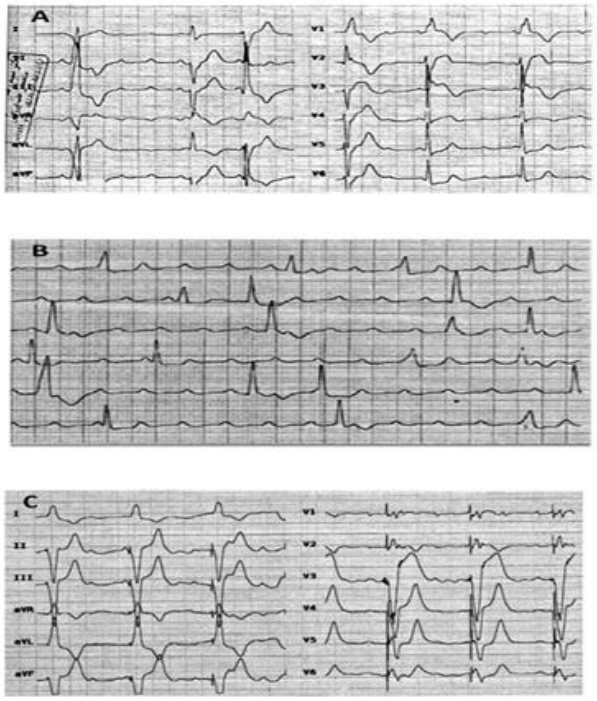


**Figure 1(A)** *ECG upon admission* ***(B)*** *long strip ECG upon admission* ***(C)*** *ECG after implanting TPM*

Next day patient had narrow QRS and LAHB with normal P-R interval and decreased ST elevation (Day 4). Next day LAHB disappeared and QRS duration and P-R intervals became shorter (Day 5) in next 3 days, ECG was normal rate and rhythm and independent from TPM, ST changes was completely resolved (Figure 2C).

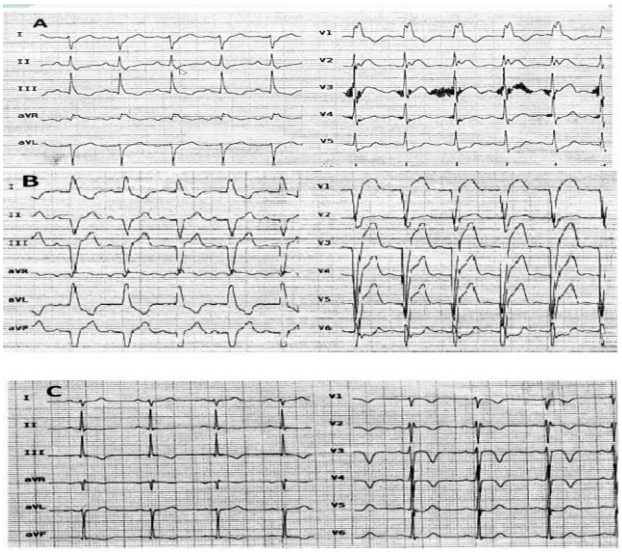


**Figure 2 (A)** *ECG upon day 2 of admission (NSR, RBBB and RAD, STE in V2-3);* **(B)** *ECG upon day 3 of admission (LBBB, LAD, STE in pericardial*

*leads); (C) ECG upon day 7 of admission (Narrow QRS, Normal axis, Resolved PR and ST changes)*

TPM was extracted at day 8 and Holter monitoring was performed for the patient, which showed no pathologic finding. During the monitoring, he had no syncope. He was discharged with good clinical condition. The patient underwent CMR during the first week after discharge, which was normal. The diagnosis was heart block caused by to viral myocarditis mainly due to COVID-19 and also Brady arrhythmia due to ondansetron use.

## DISCUSSION

The typical course of acute viral myocarditis includes prodromal viral infection in more than 60% of the patients and fever in more than 50% of the patients [1]. Ventricular and atrial arrhythmias may present in 45% of cases, while syncope may occur in nearly 10% of cases [1]. The incidence of sudden death has been reported to be 6% based on a study on young athletes in the United States [1, 12]. Other findings of myocarditis in children may include nausea, vomiting, or abdominal pain in 28% to 48%; fatigue in 25% to 70%, and shortness of breath in 35% to 69% of the cases [1]. ECG findings in these patients may indicate sinus tachycardia, atrioventricular conduction delays and non-specific ST-T wave changes [9]. Brady arrhythmias are rare findings in viral myocarditis [1]. The echocardiography findings might be non-specific and include changes in global left or right ventricular systolic dysfunction, Left Ventricular (LV) enlargement, wall edema, pericardial effusion, intra cardiac thrombus, or functional regurgitation of cardiac valves [8]. CMR findings in viral myocarditis may identify signs of inflammation in myocardium [10]. The CMR findings may include high signal intensity in T2-weighted images, signs of myocardial wall thickness due to edema evidenced by increased T1 and T2 timing, and hyperemia evidenced by rapid uptake [10]. In our case, echocardiography was not helpful in diagnosis of the case and the diagnosis was made based on the AV block in ECG, clinical and laboratory findings. CMR was not performed for the patient at the admission. Virology assessment is not always recommended for acute cases of myocarditis; however, in our case serological evaluation was performed but the findings were negative for common viral causes of myocarditis [1].

Acute viral myocarditis is a rapidly progressing condition in children and may result in hemodynamic compromise due to the borderline systolic function and development of arrhythmias [13]. Therefore, these patients should be closely monitored for arterial and ventricular arrhythmias [1]. These arrhythmias are related to poor outcome at early stages of viral myocarditis. There is no consensus of anti-arrhythmic medications for viral myocarditis in children. In case of brady arrhythmias temporary pace maker implantation is recommended [14]. In our case, patient was referred to ICU and TPM was inserted to manage Brady arrhythmia. Treatment of acute viral myocarditis is mainly related to the clinical judgment and may include the administration on Intravenous Immunoglobulin (IVIG) or corticosteroids. In our case, corticosteroid (Methyl Prednisolone) was administered to the patient due to the suspicion to COVID-19 infection.

Viral myocarditis is usually misdiagnosed due to its non-specific findings [15]. One of the differential diagnoses for viral endocarditis can be gastroenteritis in children. In our case, Ondensetron was administered to the child by parents for symptomatic management of nausea and vomiting. Ondansetron is a 5-hydroxytriptamine receptor antagonist that is widely used due to its antiemetic effects. Cardiac arrhythmia is possible at doses of 32 mg ondansetron administered intravenously [11, 16]. The most common cardiac arrhythmia attributed to ondansetron administration is prolonged QT segment; therefore, it is recommended that ondansetron should not be administered in patients with the history of congenital long QT syndrome [16]. ECG and serum electrolyte evaluation is recommended prior to ondansetron administration only in susceptible patients [16]. The incidence of cardiac side effects following oral administration of ondansetron has not been reported [16]. We believe that although oral ondansetron administration might not be able to cause fatal arrhythmias, but in our case, a single dose oral ondansetron resulted in the aggravation of bradycardia due to underlying viral myocarditis.

## CONCLUSION

Considering the increasing cases of COVID-19 infection in children and its cardiac involvement, physicians should be aware of the possible interaction of the widely used ondansetron in the symptomatic management of nausea and vomiting in children with suspicious viral, and especially COVID-19, infection with symptoms suggestive of cardiac involvement.

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