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Case Report

Takotsubo cardiomyopathy-like phenotype in a boy

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Abstract. Takotsubo cardiomyopathy is characterized by the acute onset of a reversible left ventricular wall motion abnormality that extends beyond a single coronary artery's distribution, following a period of emotional or physical stress. We present a 4 yr 11 mo old boy who was admitted to the pediatric intensive care unit a few days following tonsillectomy and adenoidectomy. The patient presented with mild cyanosis, shortness of breath and decreased levels of consciousness. Initial investigations revealed significant hypokinesia and dilatation of the mid and apical segments of the left ventricle along with preserved function of the basal segment. The patient was given inotropes and diuretics for hemodynamic management. The patient made a complete recovery with normalization of cardiac function within 3-4 wk. Upon follow up, the patient had normal sinus rhythm, improved ejection fraction and no ventricular wall motion abnormalities. The authors believe the myocarditis, rhabdomyolysis, and sepsis following tonsillectomy and adenoidectomy to be the stressors in this case. The rarity of cases that phenotypically mimic classical Takotsubo cardiomyopathy in children makes this case of special interest to pediatricians and cardiologists.

Keywords: Takotsubo cardiomyopathy, broken heart syndrome, transient left apical ballooning, stress cardiomyopathy, myocardial stunning

1. Introduction

Takotsubo cardiomyopathy (TC), also known as broken heart syndrome, is characterized by the acute onset of a reversible hypokinesis or akinesis of the apical and mid left ventricular (LV) segments accompanied with basal hyperkinesis. Patients with TC have transient LV apical ballooning and often present with symptoms similar to that of acute myocardial infarction (MI). However, the return to normal biventricular function and the absence of any coronary obstructions are characteristic features that differentiate TC from MI [1]. Sato et al. [2] was the first to describe this pathology in a case series of five patients in 1991. This condition's name is derived from the traditional Japanese pot ("*tsubo*") used for catching octopus ("*tako*"). These pots have a narrow neck and a round bottom, which strikingly resemble the contours of the LV during systole in TC.

Although the exact etiology and pathophysiology of TC remains unknown, literature has reported its incidence to be highest in adults and postmenopausal women following emotional or physical stress [3]. Electrocardiography, echocardiography, cardiac catheterization and laboratory findings are vital diagnostic tools currently used by physicians to appropriately diagnose and treat TC in a timely manner. With technological advancements, nuclear imaging, tissue Doppler and magnetic resonance imaging are also increasingly being used to

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assess cardiac anatomy and function in patients with suspected TC [4]. The rarity of the TC phenotype in children and the lack of an obvious stressor makes our case of special interest to pediatricians and cardiologists.

2. Case report

We present a 4 yr 11 mo old boy who was admitted to the pediatric intensive care unit at McMaster University a few days following his tonsillectomy and adenoidectomy. He had symptoms of high fever, lethargy and mild cough. No chest pain was reported and cardiac auscultation was normal. Upon arrival to the hospital, he showed signs of acute respiratory insufficiency, and tracheal intubation was required. He progressed with signs of shock and presented with two episodes of bradycardia requiring resuscitation and use of inotropes. Nasopharyngeal secretions were positive for Influenza B and blood culture was positive for *Streptococcus viridans*.

An investigatory echocardiography showed no pericardial effusion; however, tissue Doppler revealed significant LV dysfunction. Mid to apical portions of the LV were noted to be hypokinetic and dilated; however the basal portion of the LV had preserved function. Furthermore, no atrial septal defects, ventricular septal defects, patent ductus arteriosus or outflow tract obstructions were seen which could have accounted for the mild cyanosis at presentation. No obvious intracardiac vegetation or clots were noted. The patient had a poor ejection fraction (EF) of 40% by Simpson's rule. An electrocardiogram (ECG) showed significantly low voltages and abnormal ventricular repolarization, indicative of non-specific myocardial injury. The patient's condition was suspected to be related to a paternal family history of dilated cardiomyopathy. However, the patient's grandfather was previously tested to be negative for the myosin heavy chain 7 genes, which is transferred in an autosomal dominant manner. Thus, a genetic cause was not suspected, but could not be entirely ruled out due to the gene's variable penetrance. Myositis was suspected based on the finding of elevated creatine kinase levels of 62,225 U/L (normal < 225 U/L). Troponins were mildly increased at 0.25 ug/L (normal < 0.04 ug/L). A diagnosis of myocarditis was suspected based on the patient's high fever, lethargy, documented viral infection, imposed sepsis, elevated CK and mildly elevated troponin levels, and the patient was administered inotropes and diuretics for hemodynamic management [Figs 1-3].

A follow up echocardiography after 3 wk showed resolution of previously identified LV dysfunction. All chamber sizes were noted to be normal. Follow up tissue Doppler also confirmed synchronized LV wall motion. The patient had an improved EF of 63% by Simpson's rule. Follow up ECG had normal sinus rhythm and biventricular function. The patient is now 5 yr 1 mo old, with no symptoms of fatigue or shortness of breath and remains in good cardiac status [Figs 4-6].

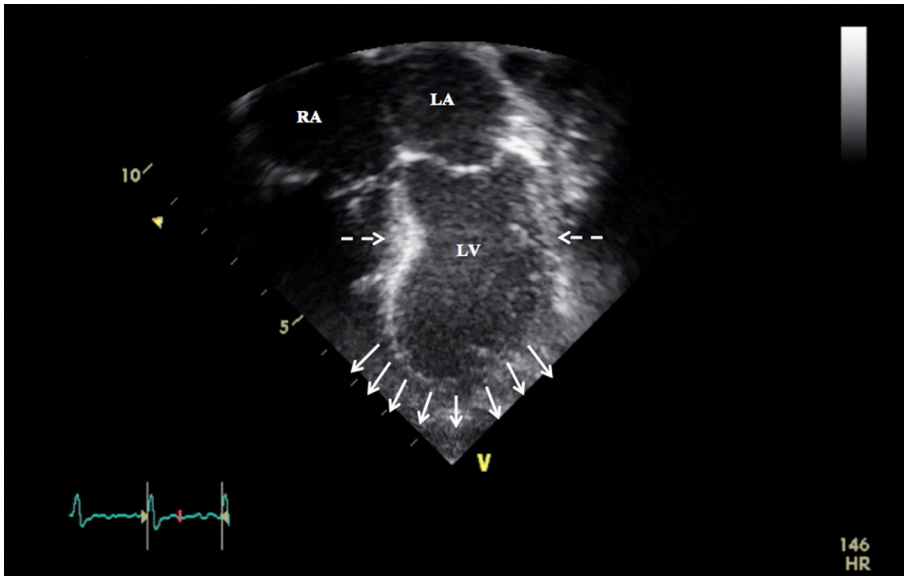

Fig. 1. Four chamber echocardiographic view during systole. The dashed arrows point at the narrowing in the mid and basal segments of the left ventricle. The solid arrows represent left ventricular apical ballooning.

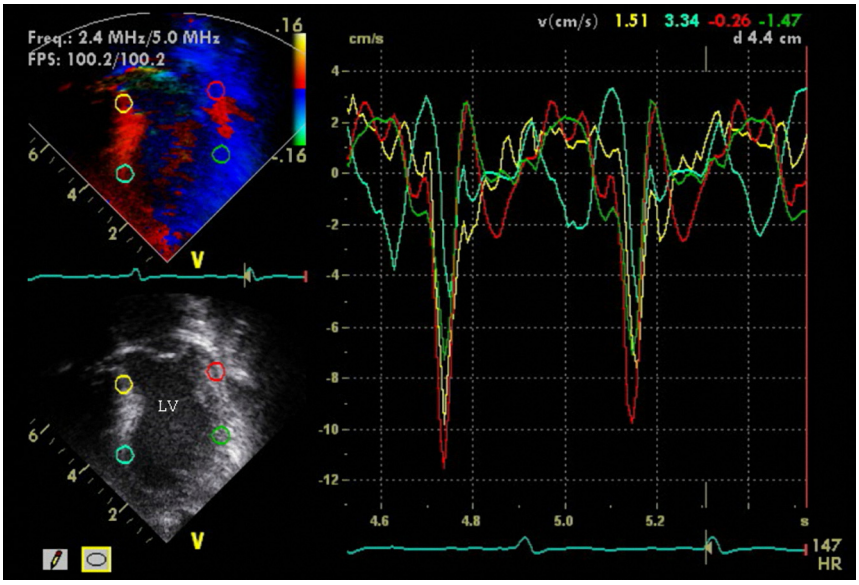

Fig. 2. Tissue Doppler Imaging showing apical wall motion to be both significantly dyskinetic and hypokinetic with respect to the mid and basal segment of the left ventricle.

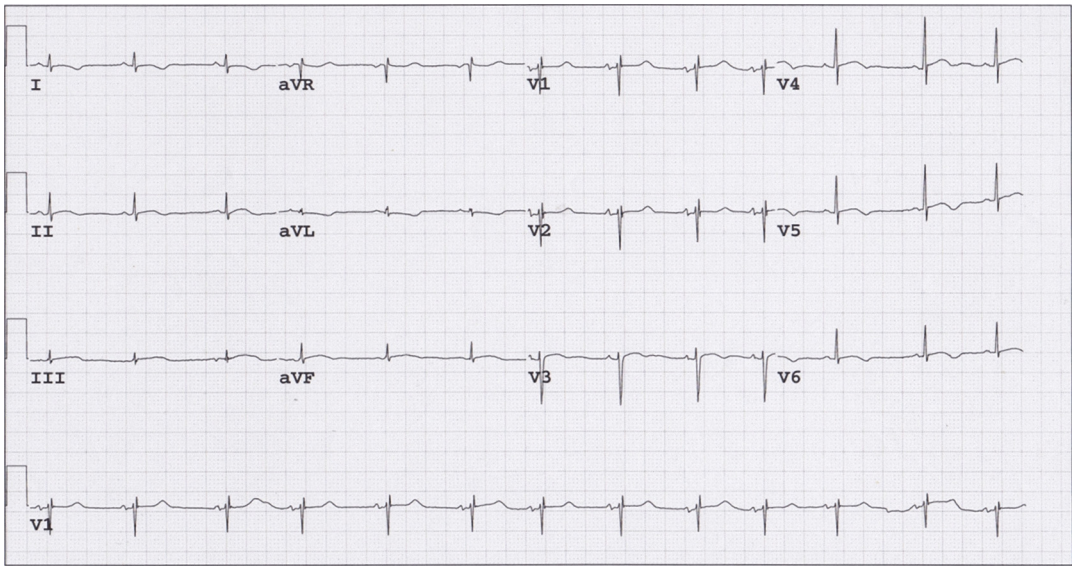

Fig. 3. ECG of patient at presentation showing T-wave inversion in lateral leads and borderline prolonged QTc interval.

3. Discussion

The Mayo Clinic has proposed the following criteria to be present for diagnosing TC [5]: (a) Transient hypokinesis, akinesis, or dyskinesis in the LV mid-segments with or without apical involvement; regional wall motion abnormalities extending beyond a single epicardial vascular distribution; the presence of a stress trigger. (b) The absence of obstructive coronary disease or angiographic evidence of acute plaque rupture. (c) New electrocardiographic abnormalities (ST-segment elevation and/or T-wave inversion) or mild elevation of cardiac troponin levels in the serum. (d) The absence of pheochromocytoma or myocarditis.

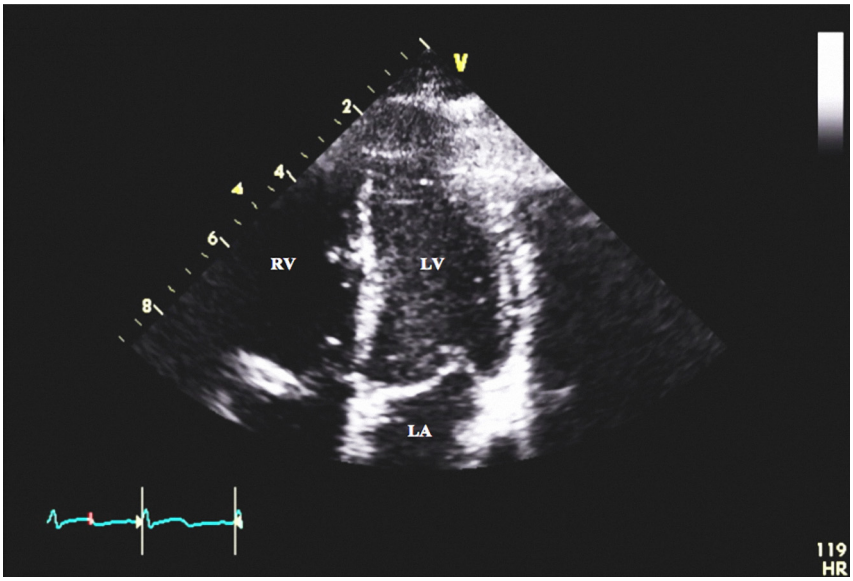

Fig. 4. Four chamber echocardiographic view during systole shows the left ventricle has a normal contour and the earlier apical ballooning has improved.

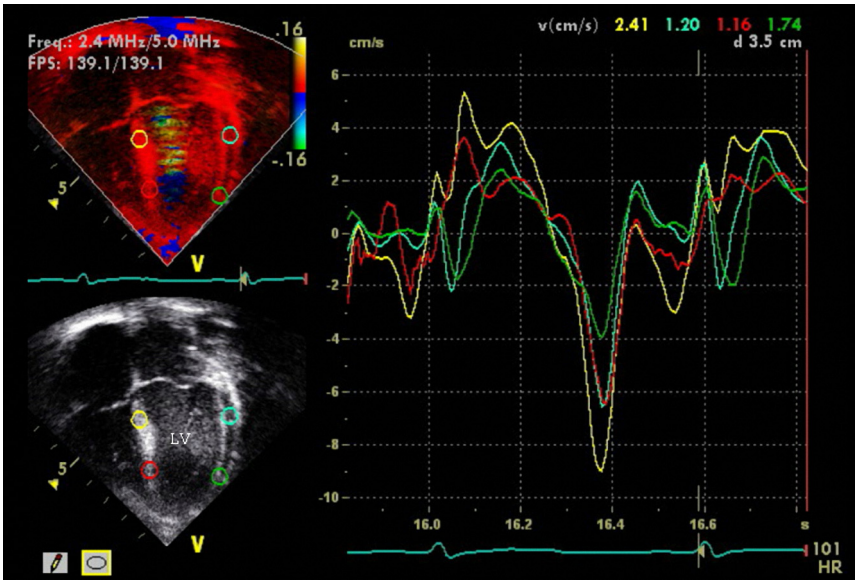

Fig. 5. Tissue Doppler imaging showing improvement in dyskinesia and improving synchronization of left ventricular wall motion.

The most widely accepted hypotheses for the cause of TC include adrenoreceptor hyperactivity [6] or surge in catecholamine levels resulting in paradoxical LV wall dysfunction following a period of emotional or physical stress [7]. Thus, TC is sometimes also referred as stress cardiomyopathy. Furthermore, estrogen has been shown to play a key role in attenuating the stress-induced hypothalamic-adrenal sympathetic outflow. Estrogen levels influence the beta 1: beta 2 adrenergic receptor ratio by favoring beta 2-adrenergic receptor inhibitory regulatory G protein signaling. This effect protects the myocardium from surges in catecholamine levels, especially in stressful situations. As such, a plausible explanation for the increased

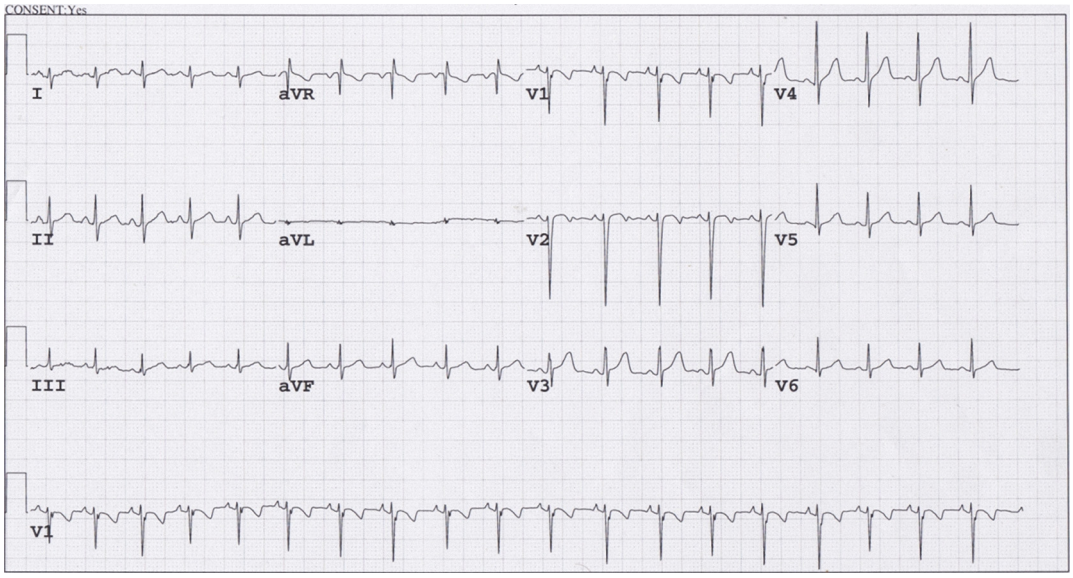

Fig. 6. Follow-up electrocardiogram of patient showing sinus rhythm and normal for age.

occurrence of TC in postmenopausal women might be a reduction in circulating estrogen levels [7, 8].

Ventricular dysfunction is generally caused by lesions in coronary arteries and the resulting ischemia of the myocardium. Although coronary artery disease is extremely rare in young children [9], it must be noted that ischemic cardiomyopathy may be observed in this age group as well due to conditions such as coronary artery vasospasms and type 2 myocardial infarctions. Moreover, transient mid and apical LV wall motion abnormalities that extend beyond a single coronary vascular bed, as seen in our case, could be indicative of TC. The unique segmental dysfunction in TC has been attributed to the difference in density and distribution of adrenoreceptors throughout the heart [10].

Although myocarditis was suspected, a retrospective analysis of echocardiograms, ECG and tissue Doppler data is highly suggestive of a TC-like manifestation. Despite this discrepancy with the Mayo Clinic's criteria for diagnosing TC, the clinical features of our case, combined with the lack of magnetic resonance imaging and microscopic evidence of myocarditis, is indicative of a phenotype similar to TC. Further, previous authors have proposed the association of TC with viral myocarditis [11]. While hypoxia, fever, pain, sepsis, hemodynamic instability, tracheal intubation, cardiac resuscitation and the use of inotropic agents could have triggered the onset of a catecholamine surge following sympathetic activation, the authors believe that the observed LV myocardial dysfunction and respiratory failure was most likely an acute and transient response to myocarditis, rhabdomyolysis, and sepsis following tonsillectomy and adenoidectomy.

Determining the exact etiology of cardiomyopathies with clinical, laboratory, electrocardiographic, echocardiographic and even angiographic data can be challenging. Further investigations using cardiac magnetic resonance and gadolinium enhancements can be useful tools for making timely and accurate diagnoses of TC.

In conclusion, our case demonstrates that TC-like phenotypes should be included in the differential diagnoses of patients, irrespective of their age, presenting with LV apical dysfunction, reduced EF and symptoms similar to an MI, following a stressful situation. Takotsubo-shaped ventricular dysfunction may be present in the setting of different clinical conditions associated with catecholamine excess, and are not limited to the typical psychological or emotional stressors in post-menopausal women, which have been described as the mainstay of TC.

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