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When a Horse is a Zebra: The Importance in Maintaining a Broad Differential for Pediatric Cardiomyopathy

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Abstract

Pediatric heart failure is an uncommon but potentially life-threatening diagnosis. The differential diagnosis is broad and includes infection, structural abnormalities, arrhythmias, cardiomyopathies, toxidromes, and high output state. This case report highlights the importance of considering toxic ingestion when evaluating severe pediatric heart failure. This patient presented as a transfer to our institution for consideration of Extracorporeal Life Support (ECLS) initiation in the presence of poor ejection fraction and hypotension refractory to pressor management. Initial labs were significant for elevated cardiac markers and leukocytosis with decreased left ventricular systolic cardiac function demonstrated on echocardiogram. Prior to ECMO initiation, the patient's blood pressures improved and she self-extubated on hospital day two. After stabilization, further medical history was elicited from the patient and her family and she was noted to be taking guanfacine and dextroamphetamine-amphetamine at home. Consultation with Poison Control confirmed the suspicion that the association of patient's presenting vital sign and mental status abnormalities could be secondary to co-ingestion of the patient's home medications; further history revealed an intentional overdose of guanfacine and dextroamphetamine-amphetamine. The patient recovered on the pediatric floor after supportive management and was then transferred to an inpatient psychiatric facility for further care. She was discharged in good condition after 15 days with outpatient cardiology follow up. This patient's case reveals the importance of including toxidromes in the differential for pediatric heart failure and highlights how co-ingestions may lead to a misleading initial clinical picture.

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Introduction

Heart failure is a relatively uncommon occurrence in the pediatric population that requires careful attention to detail, evaluation, and management. When determining the etiology of a pediatric patient's heart failure, the differential is broad and includes congenital heart disease, cardiomyopathies, arrhythmias, ischemia, infection, and high output state [1]. Initial evaluation should include electrocardiogram, echocardiogram, chest radiography, and basic lab work including cardiac enzymes and markers [2]. While cardiac injury is often a result of infection, it is important to consider other inciting causes in cases in which the case progression does not follow a traditional course, regardless of presumed likelihood. As such, cardiac failure secondary to toxic ingestion should always be considered. Evaluation for ingestion includes thorough past medical history, detailed inquiry regarding access to medications, urine drug screen, and serum ingestion labs. Common toxic ingestions that lead to cardiomyopathy include chemotherapeutic medications, alcohol, cocaine, anti-retroviral agents, carbon monoxide, amphetamines, and heavy metal exposure [3]. The consideration of this etiology is often compounded by the fact that accurate diagnosis of this condition relies on the accuracy and cooperation of the patient. This case highlights a mixed ingestion leading to cardiac failure in a pediatric patient and the importance of an accurate and thorough history.

Case Presentation

The patient in this case is an 11-year-old female with history of Attention Deficit Hyperactivity Disorder (ADHD) controlled with guanfacine and extended release dextroamphetamine-amphetamine who presented to the Emergency Department (ED) with complaint of abrupt-onset, severe chest pain and shortness of breath. Prior to presentation, the patient reported she was in her usual state of health. Associated symptoms included dizziness, fatigue, and intermittent somnolence. In the ED, she was hypoxemic with oxygen saturation of 77% on room air, tachypneic, and hypertensive without tachycardia. She was placed on a non-rebreather which initially yielded

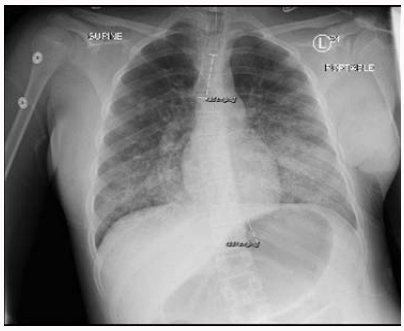

Figure 1: Initial CXR with bilateral hazy airspace opacities.

improvements in her oxygen saturation. Chest X-ray was obtained and showed hazy and patchy airspace opacity at the bilateral lung bases (Figure 1). Initial labs revealed elevated high sensitivity troponin I (695 ng/L, nl <18), elevated D-dimer (1.45 ug/mL), polycythemia (hemoglobin 19.7 g/dL, Hct 58%), leukocytosis (20.7 K/uL), normal coagulation factors, normal ferritin, normal CRP (<0.5 mg/dL), and normal BNP (55.1 pg/mL). In light of her overall clinical status and lab work, the patient was admitted to the Pediatric Intensive Care Unit (PICU). Poison Control was contacted on admission and did not, at that time, think her presentation was consistent with a toxidrome. Despite being on a non-rebreather, the patient developed worsening hypoxemia and required transition to high-flow nasal cannula. The patient continued to require increases in respiratory support with worsening hypoxemia and was ultimately intubated to better manage her respiratory status. Echocardiogram was obtained in response to her abnormal cardiac labs and demonstrated moderately decreased systolic function with ejection fraction of 36%. Repeat troponin increased to 1636 ng/L. At that time, she was started on milrinone and dobutamine infusions and transferred to a quaternary care center PICU for consideration of Extracorporeal Life Support (ECLS) given her severe degree of cardiac dysfunction (Figure 2). Following transfer, the patient remained hypotensive and hypoxemic despite multiple pressors, stress-dose hydrocortisone, and mechanical ventilation. While ECLS was initially considered, clinical improvement was noted following inotropic medication titration and ongoing volume resuscitation. Over the following day, the patient was weaned off pressor support and extubated on hospital day two. On day three, she no longer required respiratory support and left ventricular systolic ejection fraction had returned to normal on echocardiogram. Troponin (Figure 3) and pro-BNP gradually decreased throughout her hospitalization. After transfer to the floor, further chart review revealed that the patient was recently seen twice by her primary care provider for depression. Poison Control was contacted and it was discerned that a guanfacine ingestion combined with dextroamphetamine-amphetamine could explain her initial presentation. The patient initially denied any intentional ingestion or self-harm, but further questioning revealed an intentional attempt to take guanfacine and dextroamphetamine-amphetamine as an attempt to end her life. It was estimated she took about two weeks' worth of each medication, as no pills were found at home. Once medically stabilized, the patient required a ten-day psychiatric admission. During the hospital stay, she was started on fluoxetine for depression and methylphenidate in place of guanfacine and dextroamphetamine-amphetamine for ADHD. Since discharge, she has continued outpatient mental health follow up for ADHD and depression. The patient was seen in follow up by pediatric cardiology approximately one month after discharge from the inpatient pediatric cardiology service; at that time, her echocardiogram and EKG were both reassuringly normal (Figure 4). During that visit, the plan for six month follows up with repeat echocardiogram and EKG was made. If studies remain normal at her six month follow up, she will no longer need to follow with pediatric cardiology.

Discussion

Toxidromes of ADHD medications have been studied throughout the years and are well-documented in pediatric literature. While there is abundant data regarding individual toxicities, data surrounding overdoses of multiple ADHD medications have not been as thoroughly documented. Amphetamine toxicity has been described as a primarily sympathomimetic syndrome with some psychiatric symptoms [4]. The cardiac symptoms associated with amphetamine overdose include dysrhythmia, tachycardia, and hypertension [5]. Guanfacine overdose has been shown to lead to multiple cardiac adverse events, including cardiogenic pulmonary edema [6], hypotension and bradycardia [7], as well as the need for intubation and mechanical ventilation [8]. With our patient's mixed initial presentation of hypertension, bradycardia, severely depressed ejection fraction, and elevated cardiac markers, her symptoms and work up did not seem to be consistent with a known toxidrome, which led to a more dedicated pursuit of other causes for her presentation. The lab and imaging abnormalities of markedly elevated troponin, leukocytosis, and echocardiographic findings

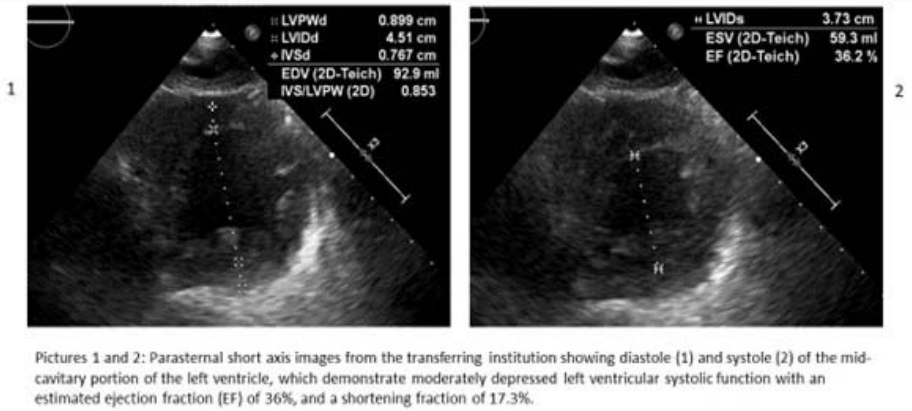

Figure 2: Echocardiogram revealing poor cardiac function.

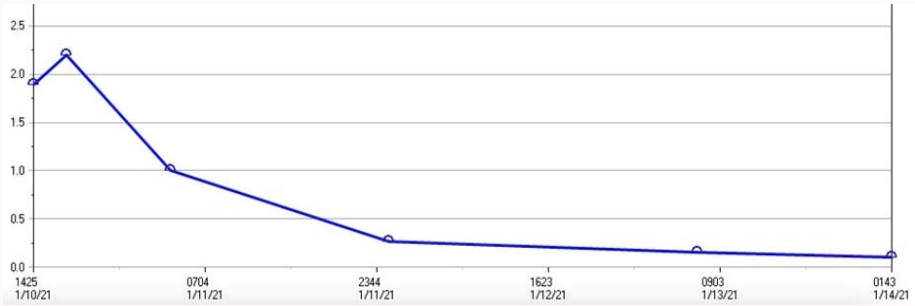

Figure 3: Graph of troponin levels during hospitalization.

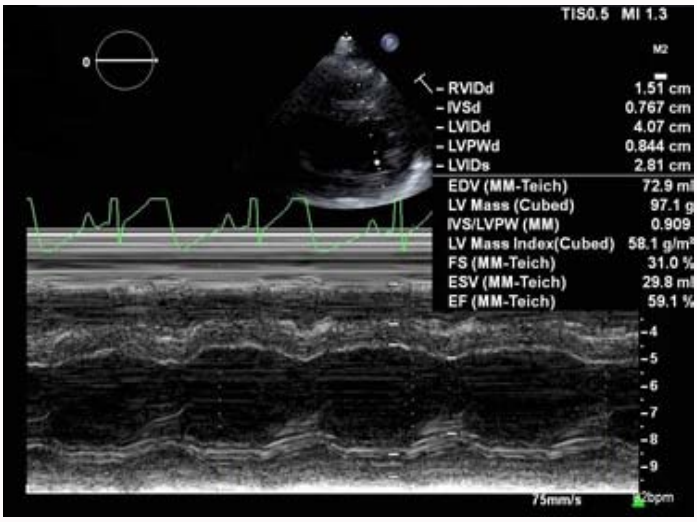

Figure 4: Parasternal short axis M Mode image of the mid-cavitary portion of the left ventricle on the day following transfer to our institution demonstrating normalization of left ventricular systolic function with an estimated Ejection Fraction (EF) of 59.1%, and a shortening fraction of 31.0%.

of decreased left ventricular systolic function for this patient were reflective of a severe myocarditis. This was supported by the patient's history of feeling fatigued, dizzy, and diaphoretic. There was initial concern for Multisystem Inflammatory Syndrome in Children (MIS-C) or other viral process. Her presentation was not thought to be consistent with an arrhythmia or infarction in the setting of normal EKG and absence of risk factors; such has family or personal history of cardiac pathology. While the patient presented critically ill, she was able to wean off vasopressor support in a relatively brief period and had return of normal cardiac function once her toxidrome resolved (a presentation inconsistent with infectious myocarditis or other causes of severe cardiac dysfunctions). With the patient's rapid improvement, our team decided to further investigate the possibility of toxic ingestion, as patients with infectious myocarditis usually do not improve so rapidly. Once a more detailed history of depression was elicited, combined with the patient's home medication list, we developed an increased suspicion for a toxidrome after intentional ingestion.

Conclusion

This case highlights the profound cardiac effects of combined guanfacine and dextroamphetamine-amphetamine toxidromes, which has not been well-documented in the current pediatric literature. Additionally, our case serves as an important reminder to maintain a broad differential diagnosis for pediatric heart failure, including intentional ingestion, especially in critically ill patients when a thorough history is not always available. Future studies may look into the benefits of hydrocortisone use in patients who are critically ill secondary to a toxidrome of this nature. While steroids were used in the setting of multiple pressor-resistant hypotension, the patient improved quickly after initiation of the steroids; however, it is difficult to know if our patient's rapid improvement was directly linked to the steroid administration or if it was a combination of an additional pressor, fluid resuscitation, and the natural course of the ingested medications. Overall, this case illustrates the potential life-threatening complications of combined ADHD medication overdoses as well as the importance of thorough history taking and differential diagnoses development.

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