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Brief Report

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Corresponding author: D. Mattia;
Email: djmattia14@gmail.com

Prinzmetal angina in a child with actin gene ACTC1 mutation

Donald Mattia, Chelsea Matney, Steven Zangwill, Bethany Wisotzkey, Edward Rhee and Christopher Knoll

Phoenix Children's Center for Heart Care, Phoenix, AZ, USA

Abstract

Prinzmetal angina is a rare cause of intermittent chest pain in paediatrics. Here, we report the case of a 2-year-old female who presented with episodic chest pain, malaise, diaphoresis, fatigue, and poor perfusion on exam. During her hospitalisation, these episodes were associated with significant low cardiac output as evidenced by lactic acidosis and low mixed venous oxygen saturations. Her workup revealed an actin alpha cardiac muscle 1 (ACTC1) gene mutation and associated left ventricular non-compaction with decreased systolic function. She was started on oral heart failure medications as well as a calcium channel blocker but continued to have episodes which were found to promptly resolve with nitroglycerine. She was ultimately listed for cardiac transplant given her perceived risk of sudden death.

Brief report

A 2-year-old female with a previous history of a multiple small ventricular septal defects was admitted with concern for episodic hypersomnolence and near-syncopal events. At baseline, the parents reported the child to be active and playful; however, during repeat episodes, she would acutely cease her activities, appear pale, diaphoretic, and rest her head in her caretaker's lap. These symptoms would typically last between 5 and 10 minutes before resolving without intervention. Episodes had started 2 months prior and increased in frequency to nearly daily occurrences just prior to admission. Of note, there was no known family history of cardiovascular disease. Initial evaluation included age-appropriate vital signs at rest, and basic laboratory evaluation was only notable for an elevated troponin of 295 ng/L (normal < 45 ng/L) and an elevated pro-B-type natriuretic peptide of 2569 pg/ml (normal < 300 pg/ml).[1] Electrocardiogram analysis at the patient's baseline revealed sinus rhythm without other abnormalities. An echocardiogram showed the previously described ventricular septal defects in addition to a dilated left ventricle with evidence of non-compaction and an ejection fraction of about 30%. She was admitted to the cardiac ICU and started on milrinone for presumed decompensated systolic heart failure. During her first night of admission, she developed transient ST segment changes (Fig. 1) with an increase in her lactate level that correlated temporally with her symptoms. Diagnostic catheterisation performed the following day showed normal intracardiac pressures with hyper-trabeculated left ventricular endocardium consistent with non-compaction. There was normal coronary artery anatomy without evidence of stenosis or obstruction (Fig. 2). Concurrently, a loop recorder was placed to assess for arrhythmias contributing to her symptomatology.

She was transitioned from milrinone to enalapril but had additional episodes consisting of concurrent ST changes, elevated troponin, and increased lactate levels (Fig. 2). The genetics team was consulted; a cardiomyopathy genetic panel was significant for a de novo likely pathogenic variant in the actin alpha cardiac muscle 1 (ACTC1) gene. This mutation of the actin alpha subunit leads to myofibrillar disarray and degradation of intercalated discs in cardiomyocytes which clinically has been linked to dilated, hypertrophic, and non-compaction cardiomyopathies.[2]

While this finding clarifies her ventricular non-compaction, it did not explain her acute coronary syndrome episodes. Intravenous nitroglycerine was started with a period of clinical stability and no episodes, which was subsequently transitioned to a calcium channel blocker. Given her persistent systolic dysfunction, profound haemodynamically significant vasospastic episodes, and her uncertain risk of sudden cardiac death, she was evaluated by the transplant team and listed status 1B for heart transplant. Our patient was able to discharge home; however, she had another ischaemic event 5 days after discharge prompting re-admission. During one of these acute episodes, she was promptly given 100 mcg of sublingual nitroglycerine with resolution of her symptoms within 2 minutes and normalisation of her ST segment depression shortly after. With ongoing episodes of ischaemic ST segment changes with concurrent low cardiac output, the presence of angiographically normal coronary

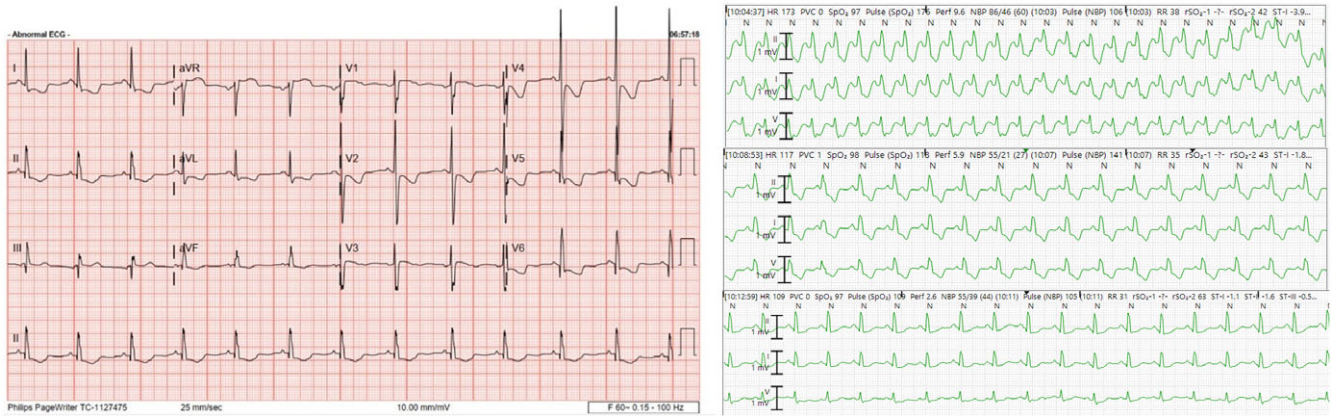

Figure 1. (Left) Twelve-lead electrocardiogram shortly after vasospastic episode began showing diffuse ST segment depression. (Right) Telemetry strips showing ST depression correlating to ischaemic symptoms (top), about 2 minutes later shortly after sublingual nitroglycerine was given (middle), and 2 minutes later showing normalisation of electrocardiogram (bottom).

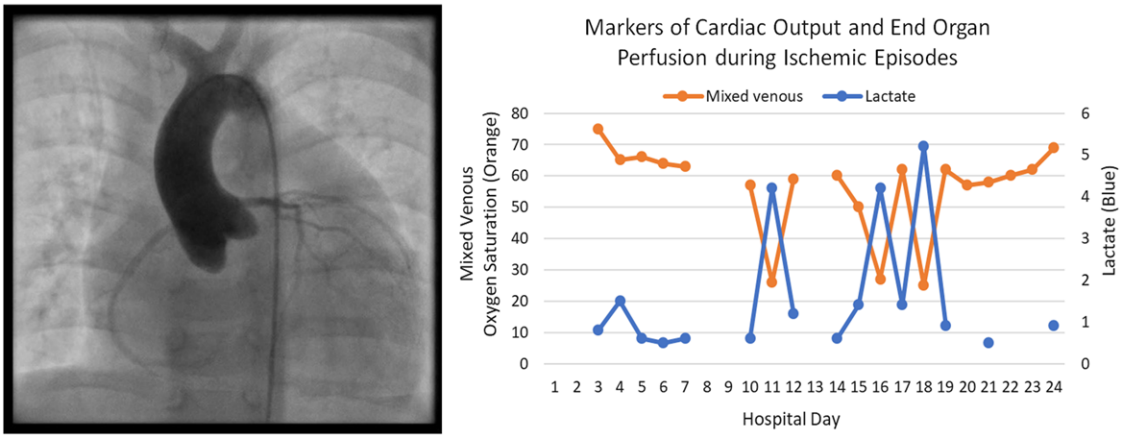

Figure 2. (Left) Cardiac catheterisation demonstrating normal coronary artery anatomy. (Right) Graph showing mixed venous oxygen saturation versus lactate levels over time. This demonstrates the acute, transient nature of the ischaemia which occurred intermittently during her admissions.

arteries, and prompt resolution with administration of nitroglycerine, the diagnosis of vasospastic angina was made. Shortly after she was listed 1A status by exception due to her perceived risk of sudden death.

Discussion

Symptom complex consistent with Prinzmetal angina is classically characterised by transient chest pain, ischaemic changes on electrocardiogram consisting of ST segment changes of ≥ 1 mm, and a prompt response to nitrates.[3] This diagnosis is made much more frequently in the adult population. The symptoms are believed to be related to transient coronary artery spasms without true anatomic obstruction. The exact mechanism of spasm is uncertain, but previous studies have hypothesised smooth muscle hypercontractility, endothelial dysfunction, low-grade inflammation, or potassium channel dysfunction as possible aetiologies.[4,5] This is a rarely reported phenomenon in the paediatric population with most published data existing in case reports and case series in the teenage population. Exact prevalence is difficult to determine as the diagnosis is difficult to make. A majority of reported cases involve adolescents who had similar presentations to adults.[6–9] Only a single reported case was associated with concurrent CHD (d-Transposition of the Great Arteries and coronary artery variant of left circumflex off the right coronary).[10] To our knowledge, this is the first paediatric report of Prinzmetal angina found in the setting of left ventricular non-compaction and heart failure at the time of presentation. The association between her congenital cardiac lesions, her underlying ACTC1 gene mutation, her propensity for vasospastic coronary episodes, and her underlying systolic cardiac dysfunction remains unclear. While Prinzmetal angina is rare in the paediatric population, it is important to include it in the differential diagnosis in children.

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Competing interests. None.

Ethical standards. The authors assert that all procedures contributing ot this work comply with ethical standards of relevant national guidelines on human procedures and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the phoenix Children's institutional review board as outlined below.

This case report was reviewed by the Institutional Review Board (IRB# 23-014) and was approved on 1/24/2023 as it met the criteria for a case report. The participant assented and parents consented to the submission of the case report to the journal.

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