# Pheochromocytoma presenting with QT prolongation and catecholamine-induced myocarditis in a child

**Kwannapas Saengsin[1], Saviga Sethasathien[1], Prapai Dejkhamron[2], Rekwan Sittiwangkul[1], Krit Makonkawkeyoon[1], Suchaya Silvilairat[1], Karn Wejaphikul[2], Yupada Pongprot[1]**

[1]Division of Cardiology, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand, [2]Division of Endocrine and Metabolism, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand

## ABSTRACT

**Pheochromocytomas are catecholamine-producing tumors derived from the adrenomedullary chromaffin cells. The presentation is a classic triad of episodic headaches, sweating, and tachycardia. Hypertensive crisis can occur due to profuse catecholamine excess. Unusual manifestations mimicking cardiogenic shock, arrhythmia, and myocarditis have been rarely reported in children. We present a case with uncommon manifestations of pheochromocytoma in a child, including the episodes of exercised-induced presyncope with QT prolongation, and subsequently cardiogenic shock due to fulminant myocarditis. He later developed hypertensive crisis. The adrenal mass on abdominal computed tomography with an increased chromogranin A level and elevated plasma normetanephrine, and the histological study confirmed the diagnosis of pheochromocytoma. Cardiac functions completely recovered after adrenalectomy. Genetic testing was positive for von Hippel-Lindau syndrome. We describe pheochromocytoma crisis presenting with prolonged QT and catecholamine-induced myocarditis. We discuss the clues to assist in the diagnosis of this condition and its appropriate treatment.**

**Keywords:** Catecholamine-induced myocarditis, child, pheochromocytoma, QT prolongation

## INTRODUCTION

Pheochromocytoma is a rare, catecholamine-producing tumor known as "the great mimic" due to a highly variable clinical presentation.[1] The presentation is a classic triad of episodic headaches, sweating, and tachycardia. Cardiovascular symptoms are common manifestations.[2] Clinical signs and symptoms vary from incidental findings to serious conditions, including palpitations, chest pain, diaphoresis, headaches, prolonged QT interval, hypertensive crisis, and acute heart failure.[2] Catecholamine-induced myocarditis and QT prolongation are rare clinical manifestations in pediatric patients with pheochromocytoma.[3]

Approximately 40% of pheochromocytomas are in the context of hereditary cancer syndromes such as Von Hipple-Lindau (VHL) syndrome, which predisposes affected patients to develop tumors in several organs e.g., retinal hemangioblastomas, clear cell renal cell carcinomas, etc.[4]

We report rare clinical presentation of pheochromocytoma in a child with catecholamine-induced myocarditis and a history of QT prolongation. Further investigation showed a missense VHL gene mutation.

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**Address for correspondence:** Dr. Yupada Pongprot, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.
E-mail: yupada@gmail.com

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## CLINICAL DETAILS

A 14-year-old boy had presented with two episodes of exercise-induced presyncope. He felt palpitations, headaches, diaphoresis, and excessive fatigue. He denied history of chest pain, seizures, trauma, or any history of drug use. He had no family history or personal history of syncope, cardiac arrest, or aborted sudden cardiac death. Physical examination was initially normal. Orthostatic hypotension was not documented. Investigations showed normal complete blood count, serum creatinine, electrolytes including potassium, and magnesium levels, thyroid function, and chest X-ray. An echocardiogram revealed normal function with left ventricular ejection fraction (LVEF) 56%. An electrocardiogram showed a corrected QT interval (QTc) prolongation of 500 ms with broad-based T wave and no ST-segment deviation [Figure 1]. Long QT syndrome was suspected. The exercise stress test (EST) was performed using the standard Bruce protocol on a treadmill. Total exercise time was 8.53 min. The patient's baseline rhythm and blood pressure (BP) were normal at the start of EST. As exercise intensity progressed, there was an appropriate heart rate response, demonstrated by sinus tachycardia at a peak rate of 160 bpm (126% predicted) and a target heart rate was 136 bpm. Metabolic equivalent achieved was 10.1. The QTc at baseline, during peak exercise, and the recovery phase were 435, 430, and 420 ms respectively. There were no premature ventricular contractions (PVCs), ventricular tachycardia, or QT prolongation during EST. Holter ECG monitoring for 24 h showed no QT prolongation and ventricular ectopic activity consisted of 11 beats (single PVCs).

Nine months later, he presented with palpitations, vomiting, and abdominal pain 6 h prior to arrival. His BP was 70/40 mmHg. He required intubation due to respiratory failure. Serum creatine kinase (CK) level was 1207 U/L (<190 U/L), CK-MB 56 U/L (<25 U/L), cardiac troponin T 1382.2 pg/mL (≤14 pg/mL), and pro-brain natriuretic (peptide pro BNP) 2750 pg/mL (<450 pg/dL). He was diagnosed with acute myocarditis with cardiogenic shock. Echocardiography showed 20% of LVEF. There was global left ventricular hypokinesia, no pericardial effusion or significant valvular regurgitation. Sinus tachycardia with heart rate of 180 bpm was observed. Hemodynamic supportive treatment with several intravenous inotropic drugs (dobutamine, dopamine, milrinone, and norepinephrine) and respiratory support were provided. His clinical condition improved within 2 days. The cardiac function returned to normal with LVEF of 64% under inotropic drugs. He was extubated on the 3rd day after admission, and all inotropic drugs were discontinued within 4 days. One month after discharge, his clinical situation improved, and echocardiography showed normal cardiac function.

Two months after discharge, he was re-admitted due to a hypertensive emergency (BP 214/161 mmHg) with palpitations. ECG showed sinus tachycardia without QT prolongation. The adrenal mass on abdominal computed tomography with an increased chromogranin A level (2486 [31–94] ng/mL) and elevated plasma normetanephrine (3134.99 pg/mL [0–163]) were consistent with pheochromocytoma [Figure 2]. He underwent adrenalectomy. His histological study confirmed the diagnosis. After surgery, he was asymptomatic and normotensive, and had normal urine catecholamines. Genetic testing showed a heterozygous missense variant mutation, NM_000551.2 (VHL):c.154G>A which was previously reported in VHL patients.[4]

Due to the nature of VHL syndrome for tumor predisposition, timely screening for lesions is cornerstone of management. Unfortunately, this patient refused further investigations and was lost to follow-up

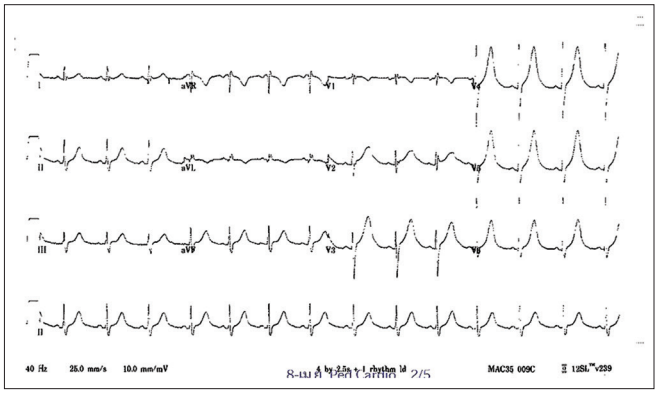

**Figure 1: An electrocardiogram showed QTc prolongation of 500 ms calculated by using Bazett formula with broad based T wave and no ST-segment deviation**

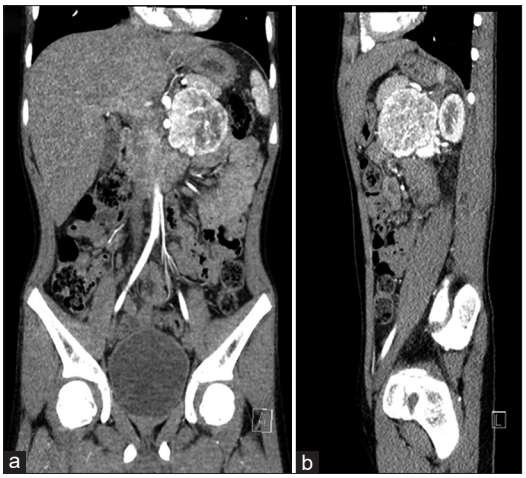


**Figure 2: Axial and coronal contrast-enhanced abdominal CT imaging. Axial. (a) And sagittal. (b) Contrast-enhanced CT images show heterogeneous arterial enhancing left adrenal mass (6.6 cm × 5.2 cm × 5.5 cm) above the left renal artery. Pheochromocytoma is first considered. CT: Computed tomography**

despite emphasizing the ongoing need to monitor this disease.

## DISCUSSION

The annual incidence of pheochromocytoma is approximately 0.8/100,000 person-years.[5] Our case demonstrated a rare presentation, including QT prolongation and fulminant catecholamine-induced myocarditis with cardiogenic shock.

Classic symptoms of catecholamine excess include headaches, diaphoresis, and palpitation in 30% of cases. Our case presented with typical symptoms but unfortunately was not diagnosed early. Intermittent QT prolongation is a rare clinical presentation. Prior literature reported that the variable effects on cardiac repolarization from increased catecholamine state may cause QT prolongation.[3]

Pheochromocytoma patients occasionally experience catecholamine-induced myocarditis. The high circulating levels of catecholamine and its oxidation products may cause direct myocardial injury.[6] Long-term increase of catecholamine causes the downregulation of beta-adrenergic receptors, which induce the suboptimal function of myofibers and decrease the number of contracting units.[7] Cardiogenic shock can develop from excessive norepinephrine inflicting myocardial damage and desensitizing blood vessels to adrenergic stimulation.[8] Protracted hypotension leading to the so-called adrenergic shock is rare. The high plasma epinephrine/norepinephrine ratio indicates that epinephrine-induced vasodilatation may be mainly responsible for hypotension.[9] The predominant norepinephrine secretion was also identified in our patient. Previous reports of catecholamine-induced myocardial injury or stunning have shown that cardiac dysfunction can quickly recover.[10] Our case recovered from catecholamine-induced myocarditis within 4 days.

The diagnosis is based on the symptoms, following the confirmation of catecholamine excess by biochemical testing, location of the tumor by imaging, and tissue pathology.[1] Cardiac dysfunction with rapid recovery is a clue of unusual myocarditis. Classic symptoms of catecholamine excess should be considered as warning signs. The catecholamine-induced cardiomyopathies are reversible with pharmacological and surgical tumor resection. Early recognition, careful intensive care, and pheochromocytoma tumor resection are crucial. Delayed diagnosis may lead to a bad prognostic outcome and death.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parents have given their consent for his images and other clinical information to be reported in the journal. The patient's parents understand that the patient's name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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