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Coincidence of Long QT Syndrome and Propionic Acidemia

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Abstract. Propionic acidemia and long QT syndrome (LQTS) are rare disorders. In addition, both conditions are potentially lethal. The patient presented in this article was initially diagnosed with propionic acidemia. Incidentally, she was found to have LQTS on electrocardiogram and verified by stress test and epinephrine challenge. Although the patient was asymptomatic and arrhythmia free, we started her on atenolol. This is the first report of the association between LQTS and propionic acidemia.

Key words: Long QT syndrome — Propionic acidemia

Propionic acidemia and long QT syndrome (LQTS) are rare disorders that are potentially lethal. We report a patient with both diagnoses. Moreover, to our knowledge, this is the first publication reporting this association.

Case Report

The patient is a 7-year-old white female who was diagnosed in infancy with propionic acidemia. She had numerous hospitalizations for her inborn error of metabolism. However, she has faired well and now attends school with good performance. Recently, she was referred for a cardiology evaluation for a possible association between propionic acidemia and cardiomyopathy as reported in the literature [1]. From a cardiovascular standpoint, the patient had been asymptomatic. Cardiac physical examination and the echocardiogram were normal. Evidence of a myopathic process was not apparent on the echocardiogram. An electrocardiogram (ECG) was obtained that showed normal sinus rhythm and normal voltages. However, the QTc interval was borderline at 440 msec and the QTc dispersion was 46 msec, which was normal. The T peak-to-T end interval measured within normal limits at 40 msec (personal data, to be published). A previous ECG was not available for comparison. The patient was on a stable dose of carnitine, thiamine, as well as the dietary supplements Profree and Propomix. A focused interview with special attention to the arrhythmia was noncontributory. The biological mother's ECG was within normal limits. The biological father was alive but not available for an ECG. A treadmill stress test was performed by using a modified Balke protocol, which showed prolongation of the QTc from 427 msec at rest to 458 msec at peak exercise (heart rate, 150 beats per minute) to 448 msec at the sixth minute into the recovery. The patient was then scheduled for an epinephrine challenge. This was done in the electrophysiology laboratory according to a protocol previously published [5]. During the test, the QTc increased from 447 msec at baseline (Fig. 1) to 550 msec during the infusion at 0.1 μg/kg/min (Fig. 2). All measurements were done in lead II. Parallel measurements were conducted in lead V2. All electrolytes were normal during both tests. Thus, the diagnosis of LQTS was made. We suggested genetic testing but the patient's mother rejected our offer. The patient was subsequently started on atenolol.

Discussion

LQTS is a rare condition. Several genetic types of LQTS have been identified. The most common are LQTS types 1 and 2. The responsible genes are located on chromosomes 11 and 7, respectively [3, 7]. LQTS type 3 is the next in order of frequency, and the genetic defect has been mapped to 3p-21 [2]. Other types of LQTS with significantly less prevalence also exist. Propionic acidemia is caused by a deficiency in propionyl-CoA carboxylase and has a frequency of 1:100,000 in the United States. The genetic defect can involve either of the enzyme's α or β subunits. The encoding genes for the α and β subunits were found on chromosomes 13q32 and 3q13.3-q2, respectively [4]. To the best of our knowledge, LQTS has not been reported to be associated with propionic acidemia. A linkage between propionic acidemia and LQTS gene loci is conceivable but needs further investigation. Based on her response to the epinephrine challenge, our patient likely has LQTS type 1 or 2 [6]. However, other forms of LQTS with unknown genetic codes cannot be ruled out. The association between propionic acidemia and LQTS in our patient could be accidental or due to an unknown genetic association.

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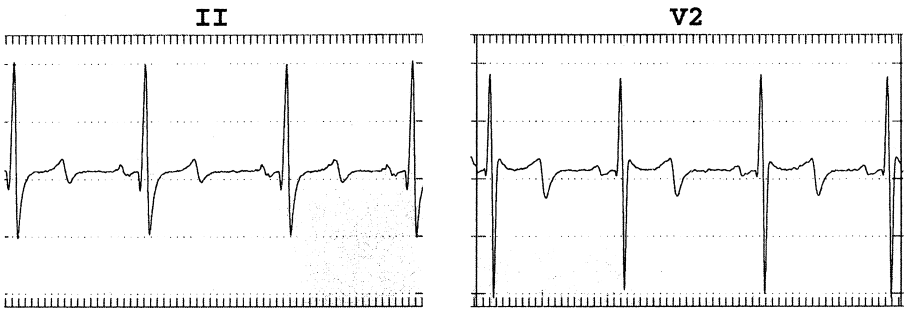

Fig. 1. Baseline QTc in leads II and V2 were 447 and 463 msec, respectively. Gridlines are 25 mm/sec.

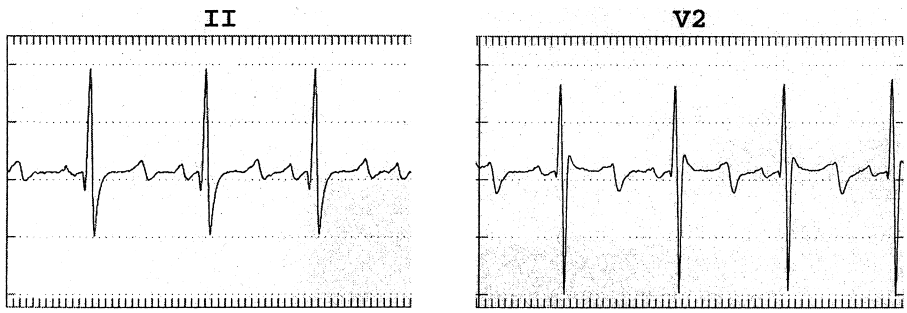

Fig. 2. During epinephrine infusion, the OTc interval in leads II and V2 to increased to 550 and 540 msec, respectively.

Conclusion

From a clinical standpoint, this case suggests that patients with propionic acidemia may have an increased risk of having LQTS and may require an evaluation that includes ECG with special attention to QTc interval.

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