Long QTc Syndrome and Propionic Acidemia

A 9-year-old boy diagnosed as Propionic acidemia at 2 months of age, complained of palpitations and near-syncope episodes related with exercise. His metabolic condition was well controlled on sodium benzoate, carnitine, protein-free diet and biotin treatment. A prolonged QTc interval was noted on ECG-Holter (***Fig.* 1**). Echocardiography showed no anomalies. He fulfilled criteria for diagnosis of Long QTc Syndrome (LQTS) [1], and treatment with propranolol was initiated with an observed decrease of the QTc interval to normal values. Acquired causes of LQTS were discarded, and genetic test was negative. At present he remains asymptomatic without cardiac events, and is under periodic follow-up.

Patients with propionic acidemia can develop cardiac complications such as dilated cardiomyopathy and sudden cardiac death, both dependent of the metabolic state [2]. Recent literature highlights the association of propionic acidemia and LQTS, two disorders that are potentially lethal separately [3-5]. This association increases the risk of life-threatening cardiac events in these patients. The QTc interval prolongation is observed up to 70% of patients with propionic acidemia during their follow-up [3]. It is independent of the metabolic state and tends to increase with age [3].

Various pathogenetic mechanisms have been proposed but not proved; *e.g.*, deficiency of carnitine, a direct toxic metabolic effect, an intracardiac depletion of essential substrates in the intermediary metabolism or the inhibition of the oxidative phosphorylation in mitochondria [3]. Recently the possibility of a genetic linkage has been proposed because of the genetic defect causing LQTS type 3 has been mapped to 3p-21 (*SCN5A* gene), and propionic acidemia encoding genes for the α subunit were found on chromosome 3q13.3-q2 [3].

Because of the increased risk of having LQTS and sudden cardiac death in children with propionic acidemia, a regular follow-up with a 12-lead ECG, echocardiography, Holter monitoring and exercise testing is warranted. When LQTS is diagnosed, therapy with beta-blockers along with lifestyle changes and avoidance of factors that prolong QTc interval must be initiated.

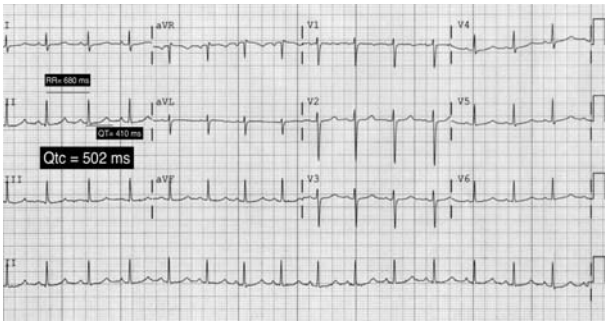

FIG. 1 *ECG showing prolonged QTc interval (Maximun 502 ms).*

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