

Cardiomyopathy and acquired long QT syndrome in propionic acidemia.

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Objectives

Propionic acidemia (PA) is an inborn error of metabolism caused by a deficiency of propionyl-CoA carboxylase. Cardiomyopathy (CMP) and QT prolongation are known to be potentially critical complications, but systematic analyses of cardiac phenotypes in PA patients are lacking.

Methods

18 patients diagnosed with PA were enrolled in a retrospective single center study (data from 1989-2017). Echocardiography parameters (left ventricular end-diastolic-diameter - LVEDD, systolic LV function - fractional shortening FS, mitral valve Doppler inflow patterns - E/A ratio) and 12-lead-electrocardiogram recordings (corrected QT interval QTc, according to Bazett's formula) were analyzed. Symptomatic patients were dichotomized to the group "neonatal onset" (symptoms within 28 days of life) and "late onset" (symptoms after 28 days). Besides descriptive analysis, correlations between cardiac function, LVEDD, QTc and clinical parameters (age at onset, beta-blocker or ACE-inhibitor therapy) were calculated.

Results

18 patients with PA were enrolled, 17 of them were symptomatic (n=1 asymptomatic) with a median age at diagnosis of 6.0 days. 15/17 (88%) were early onset and 2/17 (12%) late onset. CMP was diagnosed in 7/18 (39%) patients at a median age of 14.4 years; all of those were early onset patients. Mean QTc of all cases was 445 ms (+/- 18.11 SD); however individual range was up to 564 ms. Longer QTc is associated with higher LVEDD z-scores. Beta-blocker therapy leads to decreased QTc in all patients treated (n=4). However, decreased QTc intervals were observed also in untreated patients. ACE-I therapy did not improve FS. 11/18 (61%) individuals show pathological mitral valve inflow patterns (E/A ratio) demonstrating LV diastolic dysfunction.

Conclusions

We report a 39% CMP rate in our cohort, all of those early onset PA patients. Two thirds of those show signs of diastolic LV dysfunction. Mean QTc intervals are prolonged and directly correlated to higher LVEDD z-scores. Beta-blocker therapy may be considered effective for prolonged QTc in PA. In this cohort, ACE-I therapy did not lead to an improvement of systolic LV function. Prospective studies are warranted to further investigate cardiac phenotypes in PA. A multicenter approach is desirable due to limited case numbers per center for this rare disease.