Natural history of Barth syndrome: A national cohort study of 22 patients.


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This study describes the natural history of Barth syndrome (BTHS).

Methods: The medical records of all patients with BTHS living in France were identified in multiple sources and reviewed.

Results: We identified 16 BTHS pedigrees that included 22 patients. TAZ mutations were observed in 15 pedigrees. The estimated incidence for BTHS was 1.5 cases per million births (95%CI: 0.2–2.3). The median age at diagnosis was 3.1 weeks, and the median age at last follow-up was 4.75 years (range, 3–15 years). Eleven patients died at a median age of 5.1 months; 9 deaths were related to cardiomyopathy and 2 to sepsis. The 5-year survival rate was 51%, and no deaths were observed in patients ≥3 years. Fourteen patients presented with cardiomyopathy (dilated DCM and/or hypertrophic HCM), and cardiomyopathy was documented in 20 during follow-up. At diagnosis, the median LVEDD z-score was 4.5 (p 25: 1.9–7.5), the median LV-mass z-score was 3.5 (p 25: 1.7–p 75: 5.5), the median SF was 16% (p 25: 12.8–p 75: 25) and the median EF was 32.5% (p 25: 25.2–p 75: 43). At diagnosis, 6/11 patients had associated DCM and HCM (54.5%), 2 had DCM and 1 had HCM. In addition, 7 patients (32%) had prominent trabeculations of the LV, either on echocardiogram or on MRI, and were considered to have left ventricular noncompaction (LVNC). Left ventricular systolic function was very poor during the first year of life and tended to normalize over time. Nineteen patients had neutropenia. Metabolic investigations revealed inconstant moderate 3-methylglutaconic aciduria and plasma arginine levels that were reduced or in the low-normal range. Survival correlated with two prognostic factors: severe neutropenia at diagnosis (<0.5 G/L) and birth year. Specifically, the survival rate was 70% for patients born after 2000 and 20% for those born before 2000.

Conclusions: This survey found that BTHS outcome was affected by cardiac events and by a risk of infection that was related to neutropenia. Modern management of heart failure and prevention of infection in infancy may improve the survival of patients with BTHS.