Left Ventricular Noncompaction Suggests Myopathy

To the Editor:

We read with interest the article on left ventricular noncompaction (LVNC) in children by Pignatelli et al, who found that LVNC has a good prognosis and that LV systolic function may undulate between deterioration and recovery. The report raises several concerns: Thirteen of the 36 patients (36%) were suspected of having mitochondrial myopathy (MM), although only 5 underwent muscle biopsy. Muscle biopsy is an absolute requisite for diagnosing MM. Essential also are biochemical and genetic investigations, but abnormal biochemical investigations were reported only in a single patient. “Mitochondrial structural abnormalities with inclusion bodies” on electron-microscopy are non-specific and are found as well in other neuromuscular disorders (NMD). LVNC has been repeatedly reported in MM under the terms LV hypertrabeculation and isolated LV trabeculations. The underlying cause of LVNC is heterogeneous. Besides Barth syndrome and dystrobinopathy, LVNC is associated with myotonic dystrophy type-1, M. Pompe, cypher gene mutations, Becker muscular dystrophy, myoadenylate deaminase deficiency, and other rare genetic disorders. Coenzyme Q10, thiamine, riboflavin, and carnitine are not established therapy for MM. Uncritical administration of an obscure “metabolic cocktail” may have side effects, particularly in a disorder whose pathogenesis is not fully understood, and may be expensive. No data are presented on creatine-kinase, electromyography, nerve conduction studies, and imaging investigations, which may be abnormal in NMD. As LVNC has been reported to occur familially and is frequently associated with NMD, relatives of the 36 children should also have undergone neurologic investigation. In patients with LVNC but without NMD, muscle biopsy will be normal; therefore, endomyocardial biopsy remains a diagnostic option in these cases.

What was the indication for echocardiography in 3 asymptomatic and 1 dysmorphic patient(s)? Was it possible to calculate the ejection fraction in all patients, despite the heavily trabeculated ventricles? Restrictive filling-pattern is characterized by increased, not decreased, E/A ratio. In adults, LVNC is predominately located in the lateral and anterior wall and the apex, sparing the interventricular septum. Was this distribution also found in children? How do the authors explain undulation of the left ventricular function? Could this finding be due to effective cardiac therapy or interobserver-variability? Did the authors observe growth or regression of LVNC in any of the patients? In how many patients did cardiac magnetic resonance imaging confirm LVNC? Why was acetyl salicylic acid given? The statement that undulation of LV function is responsible for the occurrence of LVNC in adulthood is not substantiated by the data presented. Because NMD are found in 82% of adults with LVNC, children with LVNC also require thorough neurological investigation.

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Response

We appreciate the comments of Finsterer et al regarding our article, which raise several salient points.

1. Regarding the suggestion that skeletal muscle biopsy is “an absolute requisite for diagnosing mitochondrial myopathy,” there is some truth to this comment. However, unlike their adult patients, our patients are extremely small (9 children less than 1 week of age, 17 children less than 1 year of age) and ill, making biopsy clinically problematic, inaccurate, and dangerous. In their own recent report, the majority of adult patients did not undergo biopsy.

2. The etiology of left ventricular noncompaction (LVNC) is clearly heterogeneous. We have identified mutations in G4.5, α-dystrobin, and ZASP, and have shown metabolic and biochemical abnormalities in others. The metabolic cocktail of coenzyme Q10, riboflavin, carnitine, and thiamine has been used in large populations of children with mitochondrial dysfunction with good results in the United States, with low side-effect profile, cost, and clinical benefit.


4. Echocardiography was performed in the 3 asymptomatic patients because of disease in other organ systems and in 1 dysmorphic patient because of the high incidence of cardiac disease in these children.

5. We agree that it is difficult to accurately analyze ventricular volume of a “sponge-like” structure. Ichida et al reported evaluation of ventricular function using the Pombo method, but multiple artificial echo lines can be generated on the posterior wall by trabeculations, making the analysis unreliable. Use of shortening fraction may not be optimal because of wall motion abnormalities. In our experience, the biplane Simpson’s method produces less interobserver variation than the bullet method.

6. Several patients had a decrease in E/A ratio consistent with impaired left ventricular diastolic relaxation.

7. In our population, LVNC was predominantly located in the apex and lateral wall, as reported by Stöllberger et al. However, unlike in adults, the interventricular septum was involved in several patients, which has been previously reported.

8. We did not observe regression in LVNC. Some patients did progress from dilated to hypertrophic cardiomyopathy.

9. Only one patient had magnetic resonance imaging to delineate the cardiac diagnosis, as echocardiography is sufficiently sensitive for diagnosis of LVNC.
10. Acetyl-salicylic acid was used to minimized the risk of thrombosis.
11. Undulating phenotype clearly occurs in children. Left ventricular systolic function commonly improves and end-diastolic dimension commonly improves.

In summary, LVNC is relatively common in young children, has various etiologies, and in some children mitochondrial dysfunction and an undulating phenotype are noted. In addition, young children behave differently than adults.

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