Successful treatment of severe cardiomyopathy with NTBC in a child with tyrosinaemia type I

N. André1,2*, B. Roquelaure1, V. Jubin1 and C. Ovaert3

1Multidisciplinary Pediatric Department, 2Pediatric Oncology Department, 3Pediatric Cardiology Department, Children’s Hospital of ‘La Timone’, Marseille, France

*Correspondence: Multidisciplinary Pediatric Department, Children’s Hospital of ‘La Timone’ Boulevard Jean Moulin, 13885 Marseille Cedex 5, France.
E-mail: nicolas.andre@mail.ap-hm.fr

Summary: We report the case of a child who developed severe obstructive hypertrophic cardiomyopathy revealing hereditary tyrosinaemia type I, who was successfully treated with NTBC. The mechanisms underlying the association are discussed.

Hereditary tyrosinaemia type I, the most common of the diseases caused by defects in tyrosine metabolism, is secondary to a mutation in the gene for fumarylacetoacetate hydrolase, the last enzyme in the tyrosine catabolic pathway (Holme and Lindstedt 1998).

The main clinical consequences of this defect include hepatic involvement, with a high risk for liver cancer, and renal tubular dysfunction. Cardiomyopathy has also been described in patients with hereditary tyrosinaemia type I (Edwards et al 1987; Mohan et al 1999). It has also been suggested that cardiomyopathy, usually subclinical, is a frequent finding (Lindblad et al 1987). The recent development of a pharmacological treatment with a peroral inhibitor of the tyrosine catabolic pathway, 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione (NTBC), offers a new and promising tool for the treatment of patients with hereditary tyrosinaemia type I.

We report the case of a child who developed severe obstructive hypertrophic cardiomyopathy revealing hereditary tyrosinaemia type I, who was successfully treated with NTBC.

A 5-week-old boy was admitted to the hospital with diffuse bruising, oedema and systolic heart murmur. Past medical history and family history were unremarkable. The diagnosis of hereditary tyrosinaemia type I was suspected because of the presence of hepatic dysfunction (perturbed coagulation studies) in the absence of overt liver disease. Diagnosis was confirmed by the presence of succinyl acetone in urine (360 μmol/L) and hypertyrosinaemia (957 μmol/L).

Echocardiography showed marked hypertrophy preferentially affecting the interventricular septum (IVS) (Figure 1A) with significant obstruction of the left ventricular outflow tract (LVOT) (Figure 1B). The child was transferred to the
Paediatric intensive-care unit, where multiple blood and crystalloid transfusions and also beta-blockers were administered. NTBC treatment was rapidly initiated, 2 days later, at a dose of 2 mg/kg per day. Haemodynamics gradually improved. Repeated echocardiography performed 4 and 14 days after initiation of the treatment showed persistent hypertrophy but disappearance of the intraventricular obstruction (Figure 1C). Beta-blockers were continued.

**Figure 1** (A) Two-dimensional echocardiography on admission, showing marked hypertrophy of the interventricular septum (IVS). RV = right ventricle, LV = left ventricle, LA = left atrium. (B) Doppler measurement on admission, showing increased velocity (2.9 m/s) in the left ventricular outflow tract, caused by obstructive hypertrophy of the septum. (C) M-Mode echocardiography 2 weeks after admission, showing the persistent hypertrophy of the interventricular septum (IVS). PW = posterior wall. (D) M-Mode echocardiography 3 months after starting NTBC treatment, showing nearly normal IVS dimensions. (E) Evolution of cardiac dimensions, expressed in mm and in z-scores, urine succinylacetone concentrations and plasma tyrosine concentrations with time. IVSd = diastolic diameter of interventricular septum; PWd = diastolic diameter of posterior wall; uSCA = urine succinylacetone level, Tyr = plasma tyrosine level.