Positive Newborn Screening for Multiple acyl-CoA Dehydrogenase Deficiency due to maternal riboflavin deficiency

Giorgia Oliveri1, Cristiano Rizzo1, Giulio Catesini1, Alessandra Ligouri1, Alessandra Di Pede2, Silvia Ottombrino3, Francesco Tagliaferri1, Francesca Romana Lepri2, Antonino Novelli3, Teresa Giovannelli4, Claudia Carducci4,5, Antonio Angeloni4,6 and Carlo Dionisi-Vici1

1 Division of Metabolism, Bambino Gesù Children’s Hospital, IRCCS, Rome, Italy; 2 Neonatal Intensive Care Unit, Bambino Gesù Pediatric Hospital, IRCCS, Rome, Italy; 3 Translational Cytogenetics Research Unit, Laboratory of Medical Genetics, Bambino Gesù Children Hospital, IRCCS, Rome, Italy; 4 4 Clinical Pathology Unit, AOU Policlinico Umberto I, Rome, Italy; 5 Department of Experimental Medicine, Sapienza University, Policlinico Umberto I, Rome, Italy

Background

Multiple acyl-CoA dehydrogenase deficiency (MADD) is detectable at NBS on the basis of multiple acylcarnitine (C4-C18) elevation, lactate, glutaric, ethylmalonic (EMA) and/or dicarboxylic acids in urine. Some cases respond to riboflavin (vitamin B2). We report on two asymptomatic unrelated newborns, referred to NBS for suspicion of MADD, concealing an underlying riboflavin defect due to maternal deficiency.

Patients & Methods

Patient I, 39w of gestational age, was referred for multiple acylcarnitine abnormalities (C4-C14) and EMA elevation at NBS. Patient II, 34w of gestational age, showed a mild increase of C4/EMA at NBS. In both patients, confirmatory testing showed plasmatic MADD-like acylcarnitine profile and positive urinary organic acids. Riboflavin supplementation 100 mg/d resulted in sudden normalization of metabolic abnormalities. Maternal acylcarnitine profiles were normal.

Conclusions

Similar to other vitamin deficiencies, maternal riboflavin levels may decrease under conditions of inadequate intake (dietary restrictions in food with high bioavailability, such as milk/dairy products, meat/fish) or high demand (third trimester pregnancy, breastfeeding, prematurity). The diffusion of NBS programs allowed to point-out non-hereditary conditions due to maternal nutritional deficiencies.

In case of NBS suggestive for MADD, especially if risk factors coexist, we recommend (Figure 1):

i. storing/measuring plasma levels of riboflavin in the newborn before starting riboflavin supplementation

ii. checking the maternal riboflavin status, to detect asymptomatic maternal deficiencies.

Table 1 biochemical values in mother-infant pairs I and II, before and after riboflavin therapy. AGs: Acylglycines (isobutyrylglycine, isovalerylglycine, 3-oxoalanyl-glycine). EMA: ethylmalonic acid. Pathological values are reported in italics.