A case of neonatal glutaric aciduria type 2 in a context of maternal deficiency

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3 days old boy

EMERGENCY ROOM

- Severe hypoglycemia
- Severe acidosis

- Moderate hyperammonemia
- Hyperlactemia
- Hypotonia
- Cardiogenic choc

- Glucose 4 mg/dL (0,22 mmol/L)
- pH 7,01 Bicar 14 mmol/L
  BE -16,6 mEq/L
- NH3 200 mcg/dL (118 mcmol/L)
- Lactate 5 mcmol/L

- NT-proBNP 70000 ng/L

Medical Background

- Uneventful pregnancy
- Delivery at 40 weeks with vacuum
- CPAP respiratory assistance up to 4 minutes of life
- Exit from the maternity ward at D2 with physiological weight loss

- Familial background
  - Non-consanguineous parents of Moroccan origin
  - Healthy parents
  - Healthy 4 years old sister

Emergency Treatment

- Intensive care management
- Stop proteins and lipids
  - G10% IV, 10 mg/kg/min
- Carnitine 100 mg/kg/d
- Biotine 10 mg/d
- Thiamine 100 mg/d
- Riboflavine 150 mg/d started at D1

Metabolic analysis

Suspicion of MADD

- Acyl carnitine profile

Elevation of C4, C5, C8, C10, C12, C14, C12:1, C14:1, C14:2

- Urinary organic acids

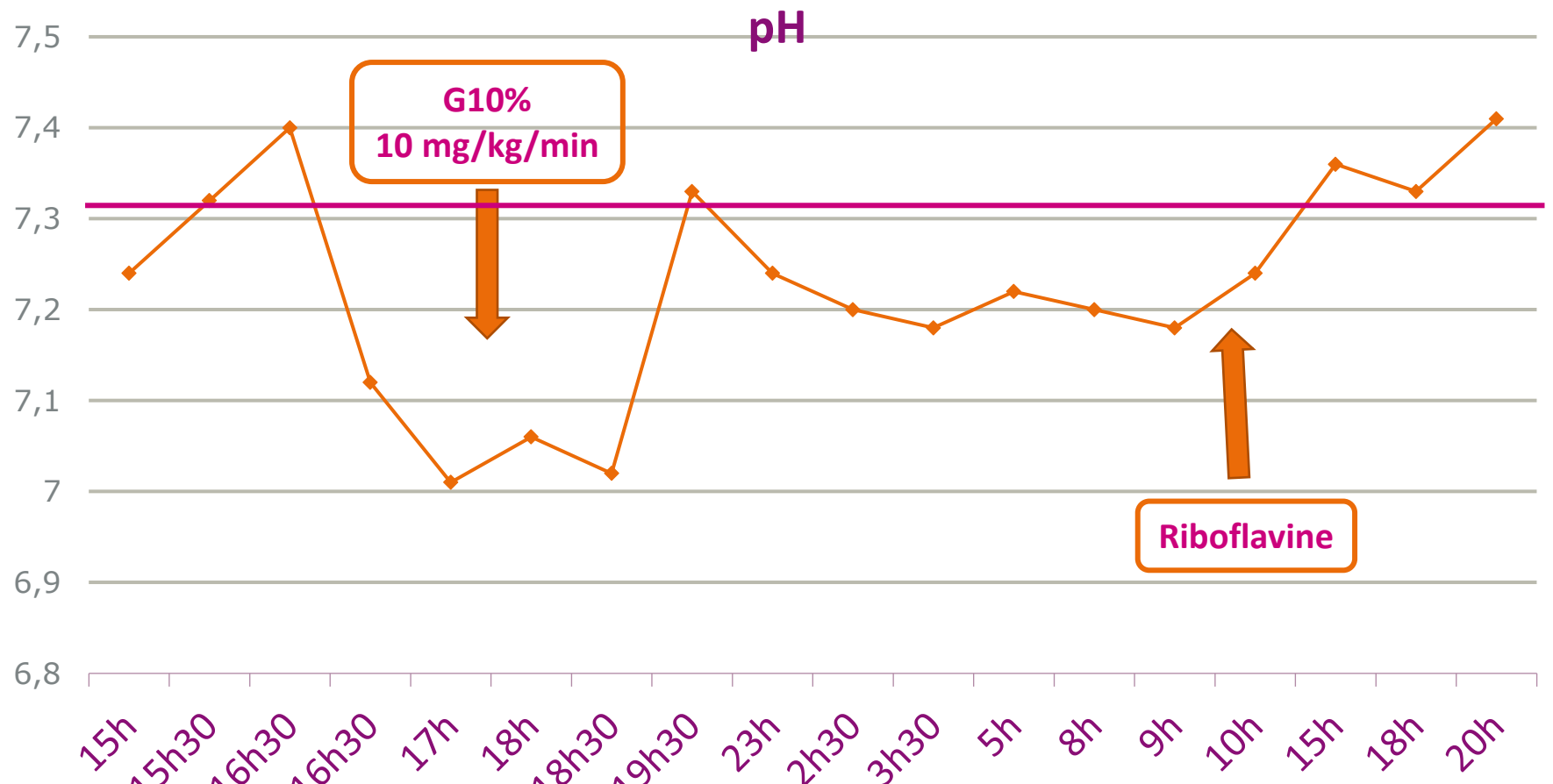
Massive hyperexcrétion of glutarate, adipate, suberate, sebacate, lactate, 5-hydroxyhexanoate, ethylmalonate, 2-hydroxyglutarate,...

- Plasmatic amino acids

Elevation of hydroxyproline, proline, citrulline, valine, isoleucine, leucine, lysine

Clinical evolution

Evolution of the acidosis



Clinical evolution (2)

- Intensive care
  - Extubation at D3
  - Normalization of the cardiac function at D3
- Neurologically
  - Very depressed Visual evoked potentials (VEP) at D3 but normalized at D9
  - Cerebral MRI was normal at D6
- Biologically
  - Normalization of NH3 at D1
  - Normalization of lactate at D2
  - Control of the acyl carnitine profile at D16 : completely normal

Genetic analysis

- Sequencing of the genes encoding ETFA, ETFB, ETFDH → **No mutation**

- Genes encoding for flavin metabolism (SLCA52A1, SLC52A2, SLC52A3, FLAD1, SLC25A32) → **No mutation**

Then … Let’s check the mother !

Mother’s analysis

- B2 vitamin **195** nmol/L (N 240 – 460)

- No mutation in the gene encoding for the riboflavin transporter (SLC52A1)
- Currently waiting for the search of deletions

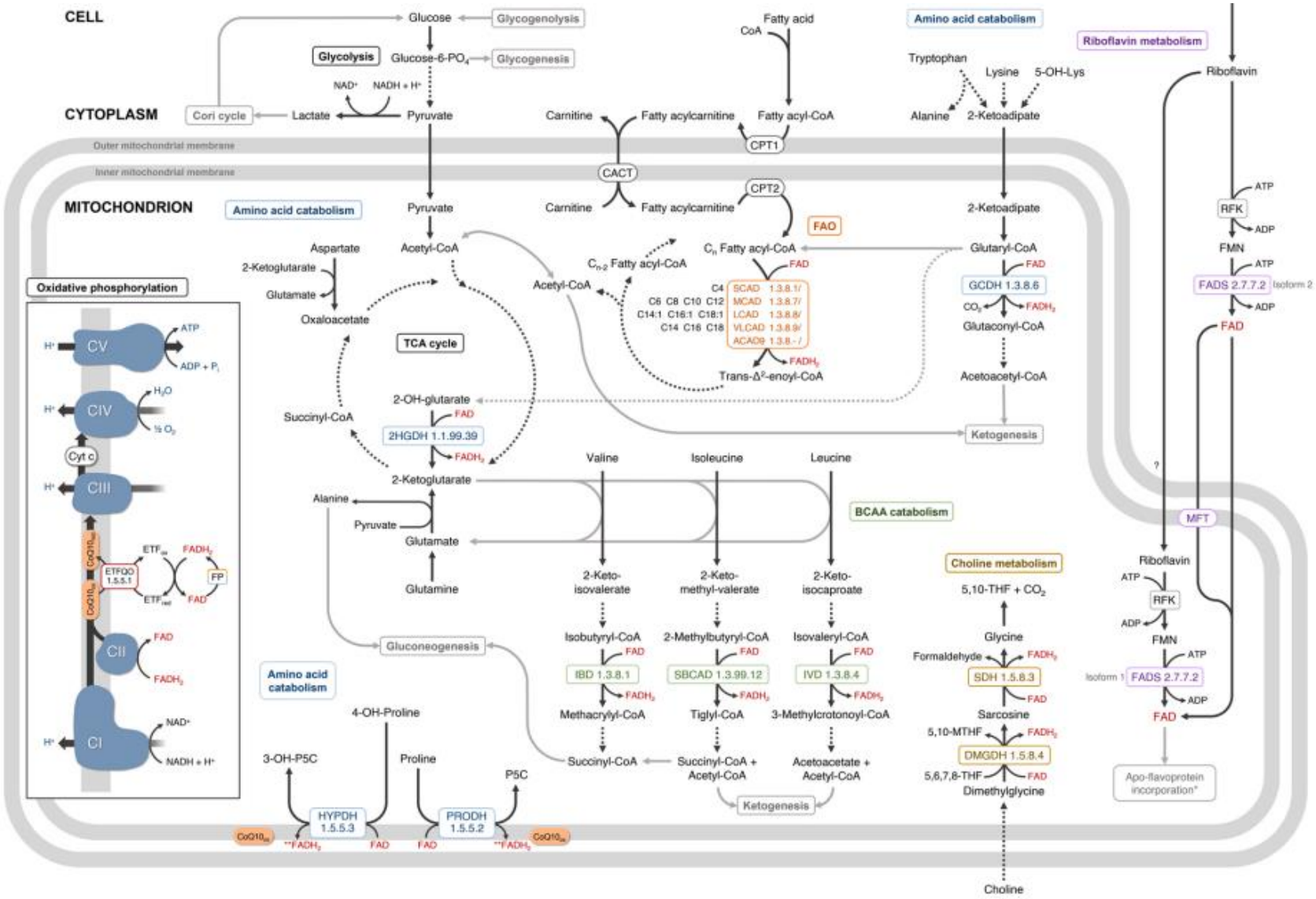
- Low meat consumption during pregnancy and no vitamin supplementation

MATERNAL RIBOFLAVIN DEFICIENCY

Clinical evolution (3)

- No further decompensation even when he had fever or bronchiolitis
- With all this results
  - Progressive enlargement of lipids intake in the diet at 4 and 5 month
  - Night-time fasting of 8 hrs allowed at 6 month
- Remained clinically and biochemically stable
- Normal psychomotor development

MADD and Riboflavin metabolism (2)



M. Mereis et al, 2021

Litterature

- Gramer et al reported 2 cases in 2021 with multiple acyl-coA dehydrogenase deficiency on newborn screening due to maternal vitamin deficiency

  - **Suspicion of MADD with the acylcarnitine profile and the urinary organic acids**
  - **Normal other laboratory tests (ammonia, lactate, blood gas analysis)**
  - **No diet started but treatment with riboflavin**
  - **NBS also showed low Met and elevated tHcy in second tier**
  - **Association with B12 deficiency in mother and child**
  - **First mother had balanced diet but no vitamin supplementation during pregnancy**
  - **Second mother had a vegetarian diet**

Litterature (2)

- Ho et al reported in 2010 a case of transient neonatal-onset glutaric aciduria type 2 due to maternal riboflavin deficiency

  - **Clinical features and urinary organic acids suggestive of MADD at D1 of life**
  - **Oral riboflavin was given within 24hr**
  - **Fast improvement both clinically and biologically**
  - **Genetic and fibroblast study excluded MADD**
  - **No further incident during the 5 years of follow-up**
  - **Mother had low riboflavin level**
  - **Mother's genetic analysis : Deletion in the riboflavin transporter (SLC52A1)**
  - **Dominant disorder with a very mild phenotype**

Take home messages

- Even in neonatal onset of multiple acylcoA deshydrogenase : start riboflavin treatment ASAP
- If we cannot find any mutation in the child → let's check the mother
- Balanced diet and vitamin supplementation during pregnancy and breastfeeding can save lives.

Any questions ?

Merci pour votre attention.

Bedankt voor uw aandacht.

CONTACT

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