WHEN TO CONSIDER FATTY ACID BETA-OXIDATION DEFICIENCY

Neonatal screening in France for MCAD, LCHAD, PCD deficiencies [1]: clinical pictures for these deficiencies should no longer be seen in children who have been screened [2]

Discovered most frequently by an acute episode or repeated acute episodes in high-risk situations:
unusual fasting or increase in energy requirements (intercurrent infection, vomiting, anaesthesia, surgery, intense physical effort), pregnancy, alcohol

Clinical signs

Neonates, Infants, Children, Adolescents, Adults

Variable association of 4 types of acute disorder, with risk of multiorgan failure

Hypoglycaemia
on unusual or long fasting time

Assess concomitant ketosis

Acute or rapidly progressing**altered consciousness** which can lead to **coma,** possible convulsions

Additional tests

Hypoketotic hypoglycaemia
Metabolic acidosis
Hyperlactataemia
Hyperammonaemia[3]

Liver damage
Hepatomegaly
Hepatocellular insufficiency (Reye Syndrome)

Additional tests

Elevated liver enzymes (transaminases)
Possible hepatocellular insufficiency (decrease in PT, V)
Hyperammonaemia[3]

Abdominal ultrasound: hyperechogenic liver (steatosis)

Cardiac impairment
Cardiomyopathy with heart failure
Ventricular arrhythmias

Additional tests

Cardiac ultrasound: hypertrophic or dilated cardiomyopathy, heart failure

ECG: Tachycardia, ventricular fibrillation, atrioventricular block, long QT

Muscle damage
Rhabdomyolysis attacks (myalgia, muscle weakness) brought on by prolonged effort, the cold or intercurrent infections
Exercise intolerance

Additional tests

Elevated CPK muscle enzymes (often > 10,000 IU/l)

Risk of kidney failure

Infants, Children, Adolescents, Adults

Other possible signs
Retinopathy and / or peripheral neuropathy
Chronic **muscle weakness**
Malformations (rare) (polycystic kidneys, brain)
Lung damage (rare)
Acute fatty liver of pregnancy(in mothers of affected foetuses)

Specialist workup

Mitochondrial fatty acid β-oxidation disorder?

Specialist workup to guide the diagnosis[4]
in collaboration with the centre of excellence, and at the same time as looking for other potential differential diagnoses

Plasma: Acylcarnitine profile during an acute episode (otherwise before breakfast), measurement of free and total carnitine

Urine: Urinary organic acid chromatography, and if PCD is suspected: measurement of free carnitine

Telltale abnormalities

Confirmatory genetic study to be carried out subsequently by a specialist centre
+/- enzyme / functional analysis (flow)

Specialist medical opinion and reference laboratory

Urgent specialist advice from Centre of Excellence: Rare Disease Centre of Reference / Competence: https://www.filiere-g2m.fr/annuaire/
Start the parallel treatment urgently
Refer to the emergency protocols for each symptom and/or disease: https://www.filiere-g2m.fr/urgences

Specialist treatment coordinated by a Centre of Excellence

Genetic counselling, family screening in a specialist centre

For more information: PNDS French National Authority for Health - MCAD deficiency and other Mitochondrial fatty acid β-oxidation disorders (has-sante.fr)

[1] MCAD: Medium Chain Acyl-coA Dehydrogenase, LCHAD: Long Chain Hydroxy-Acyl-coA Dehydrogenase, PCD: Primary Carnitine Deficiency. Fatty acid beta-oxidation deficiencies are genetic deficiencies of the various enzymes that play a role in this metabolic pathway.

[2] Neonatal screening (https://depistage-neonatal.fr) exists for some fatty acid beta-oxidation deficiencies: MCAD deficiencies (December 2020), LCHAD and PCD (January 2023), which makes it possible to identify affected neonates and initiate treatment at an early stage to prevent the onset of clinical symptoms.

[3] Pay attention to sample-taking conditions. Always check but do not necessarily wait for the test results to initiate treatment (see emergency protocol for hyperammoniaemia: https://filiere-g2m.fr/urgences). Standard norms (may vary depending on the laboratories): Neonate: ammonia < 100 µmol/L, Non-neonate ammonia < 50 µmol/L

[4] To be collected in the acute phase, freeze the urine taken closest to the hypoglycaemia/episode if the specialist laboratory is not accessible.

See: Help sheet for hypoglycaemia diagnosis: https://www.filiere-g2m.fr/banque-nationale-de-donnees-maladies-rares.

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