Rhabdomyolysis (RM) due to *LPIN1* mutation

Priority patient: must not be kept waiting in A&E

Transport by emergency ambulance to a University Hospital with an A&E, and infusion started at home if there is the slightest clinical sign of RM

If there is fever, vomiting, diarrhoea, muscle pain, or anaesthesia, :
Risk of Acute Rhabdomyolysis rapidly followed by life-threatening hyperkalaemia with cardiac rhythm disorders and renal failure

1 EMERGENCY WORKUP

Blood **CPK, glucose**, electrolytes, **potassium**, calcium, phosphate, urea, creatinine, blood gases, ionic Ca, lactate, AST, ALT, GGT, PT - **Factor V. ECG** on arrival**.** Note the **colour of the urine (myoglobinuria).** Further tests depending on the intercurrent illness triggering the episode.
Do not wait for results of tests before starting infusion.

2 TREATMENT TO BE STARTED URGENTLY, without awaiting test results:

A- Treatment in all cases

- **Corticosteroid therapy** Start at home orally (Cortancyl®) then IV upon arrival: **Methylprednisolone 1 to 2mg/kg/day for 3 to 5 days**
- **Stop Hydroxychloroquine treatment**
- **If signs of hypo-perfusion, rehydrate** with Ringer Lactate or NaCl 0.9% at **10ml/kg** (maximum 500 ml) if no cardiac signs; reassess and continue if necessary.
- **Infusion for hyperhydration**
  - Volume **3L/m²/day**
  - Preparation for 1 litre of fluid: 200 ml of G30% (30% glucose) + 400 ml of Bicarbonate 14 ‰ + 400 ml of NaCl 0.9%
    No potassium or calcium
- **If rhabdomyolysis present, admit to ICU or HDU in all cases (whatever the level of CPK elevation)**
- Start specific treatment for any intercurrent infection

B- Adjustment according to the subsequent evolution of CPK level

- Infusion for **at least 24 hrs** even if CPK is initially normal. If CPK remains normal, it is possible to switch to an infusion of **G10%** (10% glucose) + **NaCl 6g/L** with an intake of **2L/m²/day** (maximum flow rate 150 ml/hr). **Do not use ready-made solutions containing potassium during the first few hours, except if there is secondary hypokalaemia. If there is no RM, reintroduce K+ and in line with the level of serum potassium.**

3 SIGNS OF SEVERITY

Look up the emergency

- **CPK > 20 000 IU/L**
- **Cardiac rhythm disorders**, **ECG signs** of hyperkalaemia, **hyperkalaemia > 7 mmol/L**
- **Oliguria / anuria, port wine-coloured urine, kidney failure**
- **Neurological disorders, exhaustion** (risk of hyperosmolar coma)

- **Consider extra-renal purification** if:
  - blood potassium level > 5mmol/L,
  - any abnormality of any kind in ECG,
  - anuria / oliguria, and with serum electrolyte results contra-indicating continuation of hyperhydration,
  - kidney injury (creatinine levels do not reflect the severity of kidney injury, because it is released by muscle necrosis; urea level is more reliable).

4 Initial MONITORING in HDU / ICU

- Blood glucose, Na, and K every 2 hours for the first 24 hours, adjusting potassium intake in line with potassium level and renal function (if there is no potassium in the infusion, there is also a risk of hypokalaemia if the rhabdomyolysis is not severe).
- Complete electrolyte panel with Ca, P, Mg, urea, creatinine, and CPK every 6 hours.
- Hourly monitoring of urine output > 2ml/kg/hr, urine pH and density < 1005.
- Blood electrolytes every 3 hrs to adjust hyperhydration.
- ECG ordered with a trace per hour. Monitoring of cardiac function (clinical and ultrasound).
- If CPK normal, **keep the patient in hospital** for at least **24 hrs on an infusion** to make sure that there is no secondary CPK elevation

PATHOPHYSIOLOGY:

Mutations of the *LPIN1* gene predispose patients to particularly severe and rapid acute rhabdomyolysis which can be life-threatening. This is mainly due to cardiac rhythm disorders due to hyperkalaemia (ventricular fibrillation or ventricular tachycardia), but also potentially from myocardial damage which can cause rhythm disorders either directly or by lowering the threshold of tolerance to hyperkalaemia. Acute episodes can occur in at-risk situations (e.g. fever, intercurrent infection, vomiting, diarrhoea, unusual physical activity, or in any fasting or catabolic state).

Some patients also suffer from chronic muscle pain or fatigue upon exertion, with moderately elevated CPK levels outside an acute setting. The CPK level may increase secondarily in at-risk situations.

Standard treatment, depending on the patient:

- Low-dose Hydroxychloroquine as maintenance treatment. Treatment must be stopped during acute attacks of rhabdomyolysis
- Short corticosteroid therapy in all at-risk situations, to be started by the patient at home.

SITUATIONS WHERE THERE IS A RISK OF DECOMPENSATION

- Intercurrent infectious disease, fever, anorexia, vomiting or **any fasting or catabolic state** .
- Non-usual physical exercise
- Surgery / anaesthesia

CLINICAL SIGNS OF DECOMPENSATION: Do not wait for these signs!

- Muscle pain (may precede elevation of CPK level)
- Inability to walk, exhaustion
- Cardiac rhythm disorders, heart failure
- Impaired consciousness
- Hypovolaemic shock
- Myoglobinuria (sign of severe rhabdomyolysis)

DRUG CONTRAINDICATIONS / GENERAL ADVICE

- Treatments that are contraindicated during the acute phase of rhabdomyolysis NSAIDs, all drugs which raise serum potassium
- Statins (increased risk of rhabdomyolysis)
- Some anaesthetic agents: see below

- All vaccinations are recommended (particularly influenza).

IF UNDERGOING GENERAL ANAESTHESIA:

- **Contraindicated anaesthetic agents: Halogens (myocardial depression), depolarising neuromuscular blocking drugs (succinylcholine, induce muscle contraction), prolonged administration of propofol**
- **CPK to be monitored pre- and post-operatively.**

NUMBERS AND MEDICAL SPECIALISTS

On-call telephone numbers for metabolic emergencies:

At night, only medical teams can call in emergency situations, and only if the emergency certificate has not been understood or if the clinical state or test results are worrying. As far as possible, make calls before nighttime.

Secretarial issues must be dealt with via the medical secretariat during the week, or by email addressed to the patient's metabolic medicine specialist.

Certificate issued on Dr