Rhabdomyolysis, Myoglobinuria

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- in acute muscle necrosis (rhabdomyolysis), myoglobin escapes into blood → urine (myoglobinuria).

RHABDOMYOLYSIS is synonym for MYOGLOBINURIA

- **serum [myoglobin]** has same diagnostic significance as **serum [CK]**.
- modern techniques can detect minute amounts, so that brown urine discoloration may not be evident.
  If there is no *hematuria*, positive benzidine test result strongly suggests *myoglobinuria*!
  N.B. myoglobinuria itself can induce microhematuria!
- macroscopic myoglobinuria indicates massive rhabdomyolysis (risk of renal failure!).
  N.B. renal failure is more likely if *hypotension (hypovolemia)* and *acidosis* coexist.
- clinically important syndromes are associated with *gross pigmenturia*.

I. *Hereditary Myoglobinuria*
Carnitine palmityl transferase deficiency - most frequent metabolic defect presenting with myoglobinuria!
Glycogenoses type V, VII-XI
Incompletely characterized syndromes: Excess lactate production (Larsson), some mitochondrial myopathies
Uncharacterized:
Familial; biochemical defect unknown: provoked by diarrhea / infection / exercise
Malignant hyperthermia
Repeated attacks in individual; biochemical defect unknown
II. *Sporadic Myoglobinuria*
Exertion in untrained individuals (e.g. military recruits)
"Squat-jump" and related syndromes, anterior tibial syndrome
Convulsions, agitated delirium, restraints, prolonged myoclonus or acute dystonia, status asthmaticus, high-voltage electric shock
Crush syndrome
Ischemia: arterial occlusion, compression and anterior tibial syndromes, DIC
Metabolic abnormalities
Metabolic muscle depression
Barbiturate, carbon monoxide, narcotic coma
Diabetic acidosis
General anesthesia
Hypothermia
Exogenous toxins and drugs
Haff disease
Ethanol (binge drink), heroin, Malayan sea-snake bite poison, plasmocid
Glycyrrhizate, carbenoxolone, amphotericin-B, phenylpropanolamine, lovastatin, succinylcholine
Malignant neuroleptic syndrome
Chronic hypokalemia of any cause
Heat stroke
Toxic shock syndrome
Progressive muscle disease ("polymyositis", "alcoholic myopathy")

CLINICAL SYNDROME

1. Widespread myalgia, muscle swelling and weakness (may persist for weeks!)
2. Renal pain → renal failure (anuria, azotemia, hyperkalemia)
3. Fever

DIAGNOSIS

1. **Serum enzymes**↑ (CK can be > 1000 times normal), **K**↑, **phosphate**↑.
2. **Pigmenturia** (ceases within few days).
3. **EMG** abnormalities (fibrillations and myopathic units) can persist for several months.
4. **Muscle biopsy**:
   – shortly after attack - large numbers of necrotic fibers;
   – later - many regenerating fibers.

TREATMENT

1. Halt **muscle destruction** – bed rest (up to neuromuscular blockade), treat cause.
2. Promote **diuresis** > 2 ml/kg/h (with MANNITOL / dialysis)
3. **Urine alkalinization*** (with SODIUM BICARBONATE).
   *keep urinary pH > 7 - prevents toxic ferrihemate release from myoglobin
4. Control **hyperkalemia**.

TOXIC MYOPATHIES

Inflammatory myopathy: cimetidine, D-penicillamine, procainamide, L-tryptophan, L-dopa
Non-inflammatory necrotizing or vacuolar myopathy: cholesterol-lowering agents, amiodarone, chloroquine, colchicine, emetine, ε-aminocaproic acid, labetalol, cyclosporine and tacrolimus, isotretinoin, vincristine, alcohol.
Rhabdomyolysis and myoglobinuria: cholesterol-lowering drugs, alcohol (due to prolonged obtundation, seizures, hypokalemia, and hypophosphatemia), heroin, amphetamine, phencyclidine, cocaine, ε-aminocaproic acid, pentazocine, toluene.
Myofibrillar myopathy: emetine.
Myosin loss myopathy: glucocorticoids (see p. 2740 >>), non-depolarizing neuromuscular blockers.
Mitochondrial myopathy: zidovudine.

Myotonia: cholesterol-lowering drugs, propranolol, clofibrate, penicillamine, chloroquine, cyclosporine, anthracene-9-carboxycyclic acid, 2,4-d-chlorophenoxyacetic acid.
Malignant hyperthermia → see p. 3910 >>

Focal muscle damage - injection of narcotic analgesics (esp. pentazocine, meperidine, and heroin).

BIBLIOGRAPHY for ch. "Neuromuscular, Muscular Disorders" → follow this LINK >>