Clinical Features, Pathogenesis and Management of Drug-Induced Rhabdomyolysis

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Striated musculature is considered unusually tolerant to all kinds of injuries, and rhabdomyolysis associated with drug overdose or chronic drug intake is a rare event. This may be because striated musculature, in contrast to other tissues such as liver and kidney, shows little affinity for most drugs.

Several different types of drug-induced rhabdomyolysis may be distinguished, and the clinical features of the condition may vary widely, from moderate myalgia to involvement of groups of muscles to involvement of the total skeletal musculature. In clinically asymptomatic rhabdomyolysis, early diagnosis is only made if routine laboratory tests include determination of serum creatine kinase. Determination of myoglobin in serum and urine is more sensitive and allows earlier diagnosis of muscle necrosis. Myoglobinemia may lead to toxin-induced tubular necrosis, and impairment of renal function or even acute renal failure. About 10% of all cases of acute renal failure are due to rhabdomyolysis. Fulminant rhabdomyolysis may be associated with excessive hyperkalaemia and hypocalcaemia which may induce further life-threatening complications. Therefore, early diagnosis of rhabdomyolysis is most important for prevention of its potentially life-threatening sequelae.

Therapy of rhabdomyolysis consists of supportive and specific measures. Early diagnosis may help to prevent life-threatening sequelae like acute renal failure, electrolyte imbalance and shock. Withdrawal of the incriminated drug or detoxification in drug overdose should be followed by supportive measures including infusion therapy and correction of dehydration and electrolyte imbalances. Forced diuresis with sodium bicarbonate may protect the kidney function from acidosis and precipitation of myoglobin in tubules. Elimination of myoglobin from plasma may be enhanced by plasmapheresis. In patients with acute renal failure, hemodialysis is necessary. In malignant hyperthermia, immediate infusion of dantrolene sodium is required. This drug also seems to have a beneficial effect in neuroleptic malignant syndrome.

The repair mechanisms of striated musculature function extremely well. The prognosis of muscular atrophy after the acute stage of rhabdomyolysis is excellent. The same is true for the prognosis of acute renal failure. However, the extent of complications or survival of the acute stage of rhabdomyolysis strongly depend on early diagnosis and start of adequate therapy.

Compared with other tissues like kidney, liver or brain, striated musculature seems to be unusually tolerant to injuries caused by drugs, hypoxia or ischaemia. Therefore, rhabdomyolysis is generally considered a rare event. The same is true for rhabdomyolysis associated with drug intake or drug overdose. However, many different causes of direct or indirect injury to striated musculature have been reported to produce acute or subacute rhabdomyolysis: myotoxic drugs, hypokalaemia, heat, excessive muscular stress, disturbances of muscle metabolism, infectious agents, inadequate blood perfusion, autoimmune disease, and motor neuron or peripheral nerve disease.

The clinical features of drug-induced rhabdomyolysis may vary widely. In many cases, there are no muscular symptoms except in those patients with severe rhabdomyolysis who may develop diffuse swelling of muscles accompanied by moderate myalgia. In many patients with clinically asymptomatic rhabdomyolysis, early diagnosis is only made if routine laboratory tests include determination of plasma creatine kinase (CK). In some cases, the first finding may be a reddish to brown discoloration of the urine due to myoglobin (Penn 1986). Myoglobinemia may lead to toxin-induced tubular necrosis and to impairment of renal function or even acute renal failure. It should be kept in mind that about 10% of all cases of acute renal failure are due to rhabdomyolysis (Rumpf et al. 1983).

In addition to acute renal failure, fulminant rhabdomyolysis may be associated with excessive hyperkalaemia and hypocalcaemia, which may lead