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# Acute Rhabdomyolysis following Halothane Anesthesia without Succinylcholine

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We report a case of acute rhabdomyolysis with marked elevation of the creatine phosphokinase (CPK) level following anesthesia with halothane and $N_2O$. Myoglobinuria in children has not been described after general anesthesia without succinylcholine. Our case is noteworthy also because the myoglobinuria we observed was the first indication of an underlying muscle disease.

## REPORT OF A CASE

A well-developed, healthy-looking, 13-kg 5-yr-old boy was scheduled for an adenoidectomy. There was no personal or family history of myopathy or myoglobinuria. Preoperative medication was not given, and a smooth inhaled induction of anesthesia resulted. The trachea was intubated easily under deep halothane anesthesia, and no muscle relaxant or atropine was required.The surgical procedure lasted 12 min, and the patient was reactive and breathing spontaneously upon extubation of the trachea. In the postanesthesia recovery room (PAR), he was given 25 μg of fentanyl iv for pain, and he was fully awake and alert when discharged from the PAR.

Over the next 24 h, the child voided seven times. The first urine, approximately 2 h postoperatively, was noted to be grossly red. The second urine, approximately 2 h later, was cola-colored and was sent for microscopic examination and myoglobin determination. The third and fourth urine samples were brownish and turbid, and, thereafter, the specimens were clear and amber.

The serum level of CPK 4 and 8 h postoperatively was 105,088 U/l and 139,246 U/l, respectively (normal, less than 60 U/l). Blood urea nitrogen and creatinine were normal. Urine myoglobin determinations, both by column separation with Sephadex and by ammonium sulfate precipitation, showed strongly positive results. Examination of the urine showed no intact red blood cells. A pediatrician was consulted, and aggressive intravascular fluid administration was initiated. Good urine output continued, and, on the next day, CPK level declined to 66,844 U/l. The child remained afebrile and comfortable, although lethargic, and was discharged home on the second postoperative day. Subsequent evaluation by a pediatric neurologist and a muscle biopsy from the vastus lateralis under local anesthesia both indicated Duchenne's muscular dystrophy.

## DISCUSSION

Rhabdomyolysis in children after the administration of halothane and succinylcholine is a well-recognized entity, but its etiology and pathophysiology are unclear. The reported incidence varies from 0.4% to 45%.[1–3]

Many factors have been implicated as causes of rhabdomyolysis, including the administration of halothane in combination with succinylcholine,[3–6] physical exertion,[6] cold exposure, myopathies,[7,8] trauma associated with drug or alcohol abuse,[9,10] licorice ingestion,[11] the lack of muscle phosphorylase or phosphofructokinase, and the persistence of fetal myoglobin.[2,8] Muscular ischemic injury or a defect in oxygen utilization may be the common denominator in rhabdomyolysis, regardless of the precipitating factor. If muscle cell injury impairs energy production or utilization, as happens in severe ischemia, hypothermia, hypoglycemia, pressure injury, or drug toxicity, the permeability of the cell membrane is increased. Muscle enzymes are then released, along with potassium, phosphorus, and myoglobin.

The normal effect of succinylcholine on the release of enzymes, myoglobin, and potassium from the muscle cell is well established. Succinylcholine is known to be a triggering agent for rhabdomyolysis. Halothane may also play a role in muscle injury,[12] and, thus, may increase CPK activity. In *in vitro* studies, halothane induced an abnormal decrease in the ATP content of muscles in susceptible animals.[13] Succinylcholine and halothane may act synergistically to produce muscle damage.

The appearance of myoglobin in the urine signifies extensive muscle damage. Correlation between the strength of muscle fasciculation and the degree of CPK release, and possibly of myoglobin release, has been reported.[4,12] In patients with an underlying myopathy, however, rhabdomyolysis can occur with minimal insult. Waters *et al.*[6] reported three pediatric patients with postanesthesia myoglobinuria, one after strabismus repair and two after adenoidectomy performed with halothane and succinylcholine anesthesia. In the first pa-

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tient, fever developed during anesthesia and the procedure was cancelled. All three patients had myoglobinuria and markedly elevated CPK levels postoperatively. Myoglobinuria cleared in 24 h, but, in all three patients, Duchenne's muscular dystrophy was later diagnosed.

Patients at high risk for rhabdomyolysis include: patients susceptible to malignant hyperthermia, pediatric patients with latent or evident myopathy, patients with a history of myoglobinuria after exercise, and, possibly, those with a history of drug or alcohol abuse. Death after acute myoglobinuria, although uncommon, has been attributed to respiratory paralysis,[14] cardiac arrest secondary to electrolyte imbalance, malignant hyperthermia,[15] and renal failure. Myoglobin has a low molecular weight (17,000), is minimally bound to haptoglobin, and has a renal threshold of 15 U/l. This muscle protein alone may be toxic to the kidneys, but the specific mechanism has not been established.

The treatment of acute myoglobinuria is purely preventive and supportive. Our patient responded well to aggressive intravascular fluid administration and maintained good urine output. Bennike and Jarnum[16] further recommended alkalinization of the urine to prevent the formation of metmyoglobin, which precipitates more easily in acid urine. Mannitol may be given early if intravascular volume is adequate, to dilate the renal vasculature, as well as to cause osmotic diuresis.[17]

The reported case suggests that acute rhabdomyolysis can be precipitated by halothane in patients with underlying myopathy, such as Duchenne's muscular dystrophy. The severity of the muscle injury seems not to depend on the presence of fasciculation. Thus, we consider it hazardous to use halothane, with or without succinylcholine, in pediatric patients known or suspected to have such a myopathy.

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