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Malignant Hyperthermia as a Cause for Postoperative Rhabdomyolysis

To the Editor:—We read with great interest the article by Dr. Uratsuji concerning a case of rhabdomyolysis after abdominal surgery in the hyperlordotic position.¹ The authors concluded that rhabdomyolysis and the increase of creatine kinase (CK), lactate dehydrogenase, and serum myoglobin were sufficiently explained by lumbar muscle damage. However, malignant hyperthermia (MH) as another possible cause was not ruled out.

First, it is important to know whether this patient was anesthetized before this incident and whether the patient's family members had anesthetic complications or a history of muscle disease. This patient had an elevated CK of 168 U/l at rest, which might be caused by subclinical myopathy. Furthermore, it is well known that MH is characterized by a hypermetabolic response to inhalational anesthetics (e.g., sevoflurane) or depolarizing muscle relaxants, leading to muscle rigidity, metabolic acidosis, hypercapnia, tachycardia, and fever. However, relevant clinical parameters necessary for interpretation of this syndrome, such as temperature, end-tidal carbon dioxide concentration, arterial blood gases, heart rate, and muscle tone (i.e., rigidity or masseter spasm) were not presented. With these clinical parameters, it would be possible to predict the qualitative likelihood of susceptibility to MH using the Clinical Grading Scale (CGS).² In this case, the raw-score rank of the CGS has a minimum of 15 points (CK elevation > 10,000 U/l; MH rank 3, which is defined as somewhat less than likely). However, one might speculate that the use of all clinical indicators of the CGS might produce a higher MH rank.³

The clinical course of MH is highly variable (e.g., fulminant, moderate, and mild forms) and postoperative rhabdomyolysis may be the only symptom of MH. Although the probability of MH susceptibility in patients with anesthesia-induced rhabdomyolysis is only 0.07,⁴ the *in vitro* contracture tests with halothane and caffeine are necessary for diagnosis of MH susceptibility.^{5,6} This view is also emphasized in several case reports that present clinical courses of postoperative rhabdomyolysis after the use of volatile anesthetics.⁷⁻⁹

We recommend that the qualitative likelihood of susceptibility to MH should be assessed using the CGS in all cases with MH-like symptoms. Furthermore, all patients with clinical suspicion of MH should undergo muscle biopsy for *in vitro* contracture tests, histologic examination, and genetic screening.

Frank Wappler, M.D.

Associate Professor
Marko Fiege, M.D.
Staff Anesthesiologist
Department of Anesthesiology
University Hospital Eppendorf
Martinistr. 52
Hamburg, Germany
wappler@uke.uni-hamburg.de

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CORRESPONDENCE

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In Reply:—Thank you for the opportunity to comment on the remarks made by Drs. Wappler and Fiege regarding our case report. We agree that the clinical course of malignant hyperthermia (MH) is variable and that postoperative rhabdomyolysis can be the only symptom of MH.

In response to the questions posed by Drs. Wappler and Fiege, our patient had no history of anesthesia induction, and neither he nor his family members had a history of muscle diseases or anesthetic problems. Except for an increase of creatine kinase (CK) up to 13,409 IU/l, he did not show signs of MH perioperatively (e.g., muscle rigidity, metabolic acidosis, hypercapnia, tachycardia, or fever). The results of arterial blood gas analysis did not show abnormal findings during or after the operative procedure. Other pathologic findings included thoracolumbar paravertebral muscle necrosis, which was confirmed by computed tomography, and ischemic dermal damage on the back. Immediately after emerging from the anesthesia, the patient reported severe back pain. At the involved area, pneumatic support was placed in the hyperlordotic supine position for 11 h; therefore, the cause of elevated CK is due to the ischemic damage by the enforced hyperlordotic position.

According to the Clinical Grading Scale,¹ our patient had a raw score of 15 (i.e., CK elevation), but this scale should be estimated within 24 h after the administration of an anesthetic. The CK level 24 h later was 3,544 IU/l, and increased to a maximum of 13,409 IU/l at 30 h. These data suggest that our patient did not have MH. Further, review of the literature revealed that CK levels after intraoperative-pressure muscle ischemia are lower (< 75,000 U/l),² which is compatible with our data. Our patient's preoperative CK level of 168 IU/l was within the normal range (20–180 IU/l) seen in our hospital. Thirty days later, this patient underwent a second operation for closure of the jejunostomy, which

proceeded uneventfully using the same method and agents of anesthesia as in the first operation.

We still conclude that rhabdomyolysis was induced by the pneumatic device, not by MH.

Yuko Uratsuji, M.D.
Chief Anesthesiologist
Kazuko Ijichi, M.D.
Jun Irie, M.D.
Staff Anesthesiologist
Department of Anesthesia
Kobe Rosai Hospital
Sanji Kitamura, M.D.
Chief Anesthesiologist
National Kobe Hospital
Kagoike-dori
Chuo-ku
Kobe, Japan
yuga.uratsuji@nifty.ne.jp

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Analgesic Effects of Neostigmine in the Periphery

To the Editor:—In recent years, the journal *ANESTHESIOLOGY* has published several reports on the analgesic effectiveness of the cholinesterase inhibitor neostigmine. Although there is good evidence for a spinal action of neostigmine,^{1,2} a rationale for a peripheral mechanism of action is lacking. Intrathecal injection of neostigmine produces analgesic effects in animals,³ including humans,⁴ accompanied by a high incidence of side effects. The inhibition of spinal cholinesterase

results in an increase of endogenous acetylcholine, which is most likely released from intrinsic cholinergic neurons within the dorsal horn of the spinal cord.⁵ These cholinergic neurons terminate in the vicinity of primary afferents,⁵ which express muscarinic receptors.^{6,7} Consistently, analgesic effects of intrathecal neostigmine could be reversed by muscarinic receptor antagonists.⁸ The analgesic effect may be explained by a muscarinic presynaptic inhibition of glutamatergic