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Susceptibility to Malignant Hyperthermia Manifested as Delayed Return of Increased Serum Creatine Kinase Activity and Episodic Rhabdomyolysis after Exercise

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IT is difficult to definitely predict the occurrence of malignant hyperthermia (MH) and to identify patients at risk before anesthesia. Preoperative increase of serum creatine kinase activity (CK) at rest is considered one of the risk factors for MH susceptibility.[1] However, the use of CK determination as a screening test for malignant hyperthermia susceptibility (MHS) has failed in some patients.[2,3] We present a case of a patients with MHS with normal resting CK level who showed asymptomatic delayed recovery of exercise-induced CK elevation.

Case Report

A 28-yr-old, 79-kg muscular man, who was scheduled for excision of herniated lumbar disc during general anesthesia, demonstrated increased serum CK level of 3,794 U/l (normal, 45-195 U/l) with an MM type of 99% on the day of admission. The CK had been 185 U/l before an uneventful appendectomy with spinal analgesia 9 months earlier. The present surgery was postponed, and serial serum CK values decreased daily, but it took 17 days to return to the normal range. During that period, examinations by the neurologists failed to reveal myositis or apparent neuromuscular diseases. There was neither remarkable medical history nor family history of MH or any muscular disease. However, the patient was sometimes aware of muscle cramps and dark-colored urine after exercise. He ran a 20-km race 23 days before admission to the hospital and had not been exercising since the race because low back pain had developed. This was later diagnosed as one of the symptoms of herniated disc. That race was presumed to be the cause of his high CK values, his delayed recovery of CK, and the episodes of rhabdomyolysis suggested underlying muscular disease. Diagnostic muscle biopsy from the quadriceps femoris muscle was obtained for caffeine-halothane contracture test (CHCT), calcium-induced calcium release (CICR) test, and histopathologic examination.

Histopathologic study showed no specific changes such as central core disease or other neuromuscular diseases, but a mild myopathy was recognized. The patient was diagnosed as having MHS based on CHCT according to the protocol of the European Malignant Hyperthermia Group[4] (the threshold concentrations of caffeine and halothane for a 0.2-g increase of tension were 2 mM and 1%, respectively) and that of the North American Malignant Hyperthermia Group[5] (0.4-g and 1.2-g contracture on exposure to 2 mM caffeine and 3% halothane, respectively). CICR rate was not accelerated.[6] Phosphorus-31 nuclear magnetic resonance (^{31}P NMR) spectroscopy[7] demonstrated a greater decrease and slower recovery in forearm muscle pH after exercise and an early depletion of phosphocreatine during the exercise compared with a control subject confirmed as MH negative by CHCT (fig. 1).

Surgery was uneventfully performed during spinal analgesia 3 months later. The CK levels peaked at 391 U/l on the following day and normalized in 3 days.

Discussion

Even in a healthy person, gross increases in serum CK level after high-intensity or prolonged weight-bearing exercises, such as a marathon, have been reported.[8] However, considering that CK levels generally normalize in 3-7 days, it would be assumed that if serum CK activity exceeds 10,000 U/l after the exercise or 5,000 U/l more than 24 h after the event, subclinical myopathy predisposing the person to the risk of rhabdomyolysis was likely to be present.[8,9] Our patient showed a serum CK level of more than 3,000 U/l 23 days after a 20- km run, suggesting the presence of subclinical myopathy.

Subclinical myopathy is often related to MH. Although the primary defect in MH patients lies in the sarcoplasmic

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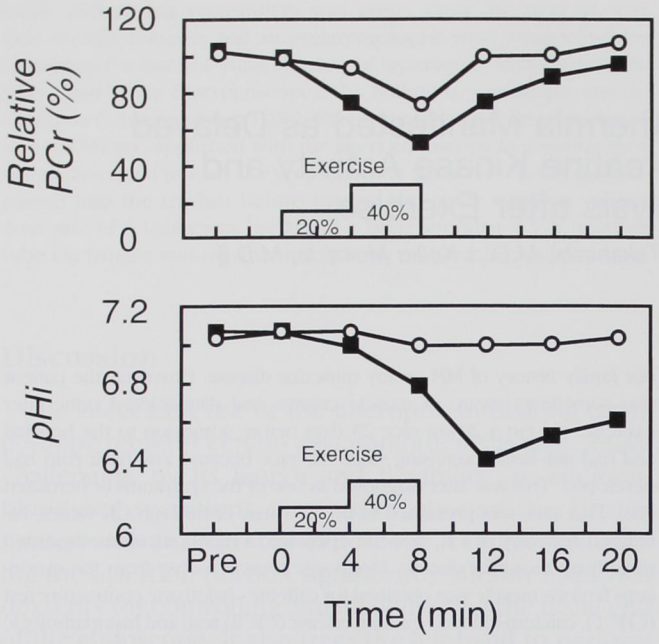

Fig. 1. Serial changes of phosphocreatine peak area (Pcr: shown as the ratio to the preexercise value) and intracellular pH (pHi) in the patient (■) and the control subject (○) assessed by ^{31}P-NMR spectroscopy. The test was performed according to the method reported by Olgin J *et al.*[7]

reticulum of skeletal muscle cells, histologic examination cannot detect any specific findings of MH with a few exceptions, such as patients with central core disease or King-Denborough syndrome.[10] Pathophysiologically, MH may be regarded as a subclinical primary myopathy with secondary systemic changes.[11] Epidemiologic studies show that many MHS patients have episodes of muscular cramps, pain, and pyrexia after exercise,[12] which suggests that these patients are associated with an underlying myopathy. Sporadically reported MHS subjects linked with exercise-induced myolysis[13,14] support this idea. Allsop *et al.* also showed that MHS subjects showed decreased power output and suggested the presence of an underlying myopathy manifested by high-intensity exercise in MHS patients.[15]

This patient was diagnosed as MHS by CHCT. However, a functioning abnormality in the ryanodine receptor of the sarcoplasmic reticulum could not be identified as the cause of MHS because CICR was not accelerated. The mechanism of persistent increased CK values after the semi-marathon suggests increased leakage of CK through the muscle cell membrane caused by the loss of membrane integrity maintained by high energy compounds such as phosphocreatine and ATP, which might be the explanation for the patient's episodic rhabdomyolysis. Early depletion and slow recovery of such high energy compounds during and after muscle-loading exercise, which occurs when the production of ATP *via* metabolic pathway is deteriorated or when the breakdown of ATP is accelerated, might play a role in disturbing the function of the muscle cell membrane.

We conclude that delayed recovery of CK level increase after prolonged weight-bearing exercise in this patient represents an underlying myopathy that might be associated with MHS. We should not overlook the possibility of MHS in an otherwise healthy person showing an abnormal CK increase after exercise.

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Radicular Pain Due to a Retained Fragment of Epidural Catheter

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NERVE root lesions during epidural anesthesia are usually caused by direct trauma (from the needle or catheter) or neurotoxicity of local anesthetics.[1]

Retained fragments of sheared epidural catheter are generally considered not to have any clinical consequences, and most authors therefore recommend leaving such fragments in place.[2] This case report concerns a patient with nerve root pain caused by a fragment of epidural catheter rolled around the L3 root, which resolved after surgical removal of the fragment.

Case Report

A healthy 34-yr-old woman was referred for pain in the distribution of the left third lumbar nerve. This pain was refractory to physical therapy. Lumbar computed tomography also demonstrated a density in the lumbar spine, incompatible with a herniated intervertebral disc. Her history was unremarkable, except that, since delivery of a child 7 months previously, she suffered from a nerve root syndrome with pain radiating to the anterior surface of the thigh. This did not interfere with her everyday activities. The delivery had been by cesarean section during general anesthesia after failure of epidural analgesia. Clinical examination showed a moderate pain in the low lumbar region and sensory loss on the anterior surface of the left thigh in the distribution of the femoral nerve. No motor deficit, sphincter disturbance, or signs of a pyramidal tract lesion were detected, and all deep tendon reflexes were present. The laboratory assessment did not reveal any evidence of systemic inflammation (normal leukocyte count, normal sedimentation rate). Standard radiographs revealed the presence of a coiled fragment of epidural catheter (figs. 1 and 2). The patient was told about the presence of the catheter. She remembered the epidural anesthetic, but was not aware of any incident. The obstetric anesthetic file could not be obtained. Although there appeared to be a correlation between the onset of pain and her obstetric anesthetic, the fragment of catheter was not considered responsible for the clinical features because this material is generally believed to be well tolerated. Medical treatment with non-steroidal antiinflammatory drugs was prescribed. Eleven months later, the patient still suffered from root pain, which now interfered with her everyday activities. Clinical examination was identical. Magnetic resonance imaging visualized the epidural catheter in front of L3, forming a fairly large mass because of its numerous loops. Results of electromyography were normal. However, lumbosacral myelography confirmed the compressive nature of the catheter (fig. 3). It was therefore decided to remove the catheter surgically. Surgery revealed

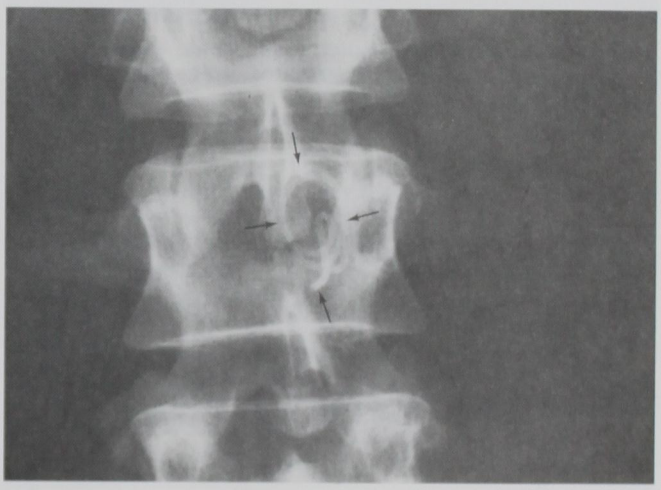

Fig. 1. Plain radiograph of the lumbar spine centered on L3 (anteroposterior view) visualizing the residual fragment of sheared catheter (*arrows*).

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