Lesson 248: PreAnesthetic Assessment of the Patient With Malignant Hyperthermia

WRITTEN BY:

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REVIEWED BY:

Lesson 248 was reviewed by Elizabeth A.M. Frost, MD, Department of Anesthesia, Mount Sinai School of Medicine, New York, NY. Date reviewed: July 2005.

DISCLOSURE STATEMENT

Dr. Kaye has disclosed that he is a member of the speakers' bureaus of Baxter and Pfizer. The other author and reviewer have no relationships with pharmaceutical companies or manufacturers of products to disclose. This educational activity may contain discussion of published and/or investigational uses of agents for the treatment of disease. Some uses of these agents have not been approved by the US Food and Drug Administration. Please refer to the official prescribing information for each product for approved indications, contraindications, and warnings.

LEARNING OBJECTIVES

At the end of this activity, the participant should be able to:

1. Define MH.
2. List the anesthetic agents that can trigger MH.
3. Describe the systemic changes caused by MH.
4. Explain the cellular mechanisms involved in MH.
5. Apply appropriate preoperative testing and evaluation of the patient suspected to have MH.
6. Summarize the genetics involved in MH.
7. Outline the comorbid conditions associated with MH.
8. Develop an anesthetic plan for the patient with a previous incident or family history of MH.
9. Anticipate, recognize, and manage likely perioperative complications.
10. Outline a differential diagnosis for patients with a clinical presentation similar to MH.

NEEDS STATEMENT

Malignant hyperthermia (MH) may be identified for the first time during the administration of anesthesia to a patient. It manifests as a hypermetabolic response after exposure to halogenated volatile anesthetics or depolarizing muscle relaxants. Although the disorder is treatable, it can be life-threatening if not managed properly. Newly published information about MH has been reviewed and identified by committee as required learning for anesthesiologists.

TARGET AUDIENCE

Anesthesiologists

CASE HISTORY

A 19-year-old Hispanic woman was a nonrestrained, rear-seat occupant in a car that collided at high speed with a fixed object (a telephone pole). She was ejected from the vehicle, found unconscious, and transported to the hospital emergency room by an ambulance helicopter. She was immobilized on a backboard with a C-collar in place. Intubation was facilitated with succinylcholine. She was then sedated with midazolam. There were obvious deformities of both the left and right humerus, a deformity of the right hand with abrasions, and a fracture of the left lower extremity. Vital signs included: heart rate, 112 beats per minute; blood pressure, 108/58 mm Hg; temperature, 100.2°F. Two 18-gauge peripheral, intravenous (I.V.) cannulae were placed. Evaluation of the patient for trauma revealed a fractured mandible. Information obtained from family members indicated an otherwise healthy person with no significant medical or surgical history, no use of medications, and an allergy to penicillin (rash). On physical examination, the patient's breath sounds were clear, and heart sounds were regular, tachycardic, with no murmurs. Her abdomen was soft and nondistended, with bowel sounds present. Laboratory findings included hemoglobin, 13.4 g/dL; hematocrit, 39.2%; platelet count, 270×10^3/mcL; electrolyte panel, normal; glucose, 198 mg/dL; β-human chorionic gonadotropin, negative; liver enzymes, normal; urinalysis, positive for blood. Arterial blood gas values were: pH, 7.39; Pco_2, 30.6 mm Hg; Po_2, 150 mm Hg; bicarbonate, 18.0 mEq/L; base excess, −5.5 mm Hg. The patient's oxygen saturation was 99.2% on assist control mode; tidal volume, 400 mL; 12 breaths per minute; FiO_2, 0.4; positive end-expiratory pressure, 5 mm Hg. A computed tomography scan ruled out any head injury. The patient was taken to the operating room for emergency orthopedic repairs. Intraoperatively, the patient became progressively tachycardic (>150 beats per minute) and feverish (103°F). End-tidal CO_2 rose significantly to 56 mm Hg.

CALL FOR WRITERS

If you would like to write a CME lesson in *Anesthesiology News*, please send an e-mail to Elizabeth A.M. Frost, MD, at ElzFrost@aol.com.

Malignant hyperthermia (MH) is a potentially fatal clinical syndrome that classically presents during the administration of potent, volatile anesthetic agents and depolarizing muscle relaxants. MH may also occur in susceptible individuals under extreme stress from heat or exercise.[1-5] The syndrome was first described in 1960 by Denborough and colleagues as an inherited disorder of the skeletal muscle. They characterized MH as a hypermetabolic state with skeletal muscle rigidity that occurs after the administration of general anesthetics, and that arises frequently, but not exclusively, in children.[6]

If recognized early, the condition can be treated by administering dantrolene, a muscle relaxant. Additional therapies include cooling and hyperventilation of the patient.[7] If treatment is not given promptly, the patient may suffer from rhabdomyolysis secondary to sustained muscle contraction postoperatively. A disruption of muscle cell membrane allows leakage of myoglobin and creatine kinase into the plasma, which can lead to myoglobinuria. Muscle cell necrosis may occur, causing renal failure and even cardiac arrest. A decreased range of motion, weakness, and severe muscle pain may also be experienced.[8]

MH is a rare disorder with an incidence ranging from 1 in 15,000 children to 1 in 50,000 adults who received triggering agents (eg, succinylcholine and inhalational anesthetics). Older children and adults younger than 30 are the most likely to be affected. Geriatric patients and children younger than 3 have a lower incidence.[9]

The Presentation of MH

Genetics and Triggering Agents

MH normally occurs when susceptible patients are exposed to a triggering agent. MH can be avoided when an extensive personal or family history of the patient has indicated a risk for the disease, a definitive diagnosis has been made, or a high index of suspicion has alerted healthcare workers. Studies indicate that MH displays heterogeneity with autosomal dominant inheritance, reduced penetrance, and variable expressivity.[10] Ryanodine, a plant alkaloid, has been shown to bind calcium release channels in the sarcoplasmic reticulum. The ryanodine receptor is abnormal in patients with MH and results in the inappropriate release of Ca^{2+} in such individuals. Evidence suggests that chromosomes 17 and 19 may play a role in the genetic abnormalities of this heterogeneous, polygenic disorder.[11,12]

Mutations in the ryanodine receptor type 1 (RYR1) gene commonly occur in 3 mutational "hot spots." Recently,

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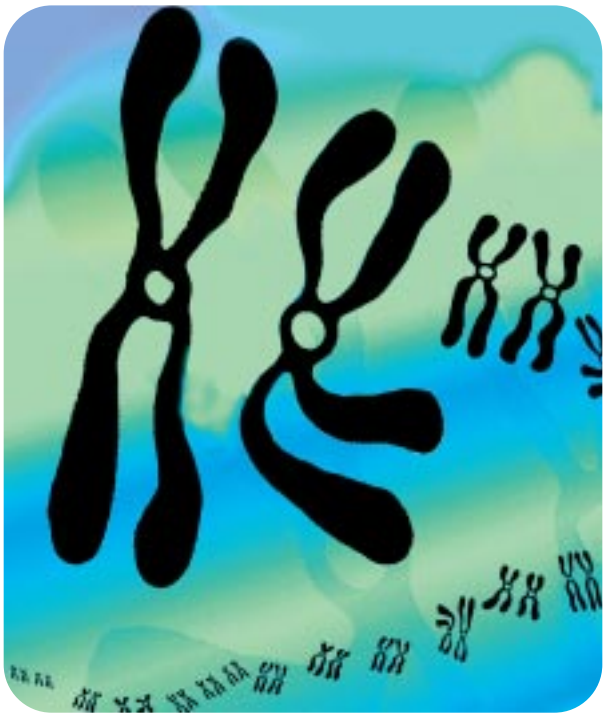

PREANESTHETIC ASSESSMENT

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1) *Read this article, reflect on the information presented, then complete the lesson quiz and course evaluation. Return it to Mount Sinai School of Medicine, Department of Anesthesia, before December 31, 2006. (CME credit is not valid past this date.)*
2) *You must achieve a score of 80% or better to earn CME credit.*
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Table 1. Agents Classified as Triggering And Nontriggering for MH

Triggering	Nontriggering
Potent inhalation agents	Nondepolarizing muscle relaxants
Halothane	Barbiturates
Sevoflurane	Local anesthetics
Desflurane	Propofol
Succinylcholine	Ketamine
Phenothiazines	Benzodiazepines
	Nitrous oxide

Table 2. Signs and Presentation of MH

More specific	Hypercarbia, muscle rigidity, rhabdomyolysis
Less specific	Tachycardia, tachypnea, hyperthermia, hyperkalemia, hypocalcemia

Table 3. Myopathies That Predispose to MH

Central core disease
Hypokalemic periodic paralysis
King-Denborough syndrome
Muscular dystrophy

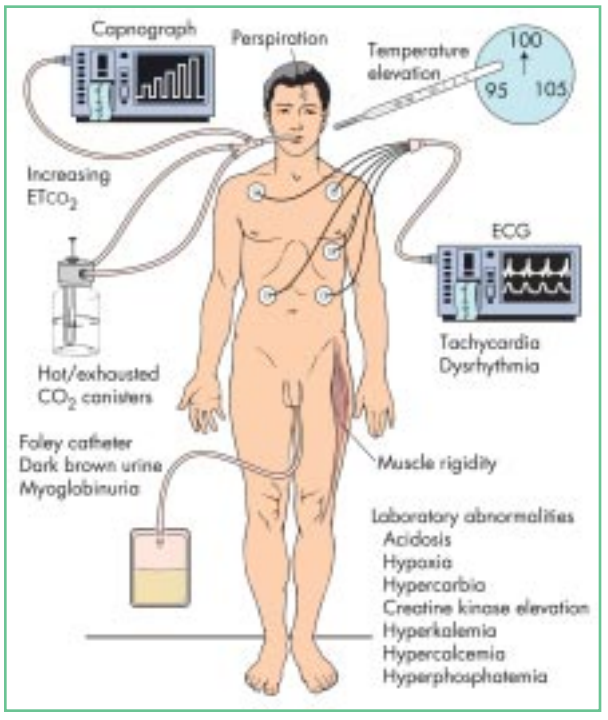

Figure 1. The clinical presentation of the patient with MH.
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however, Sambuughin and colleagues were able to identify 9 previously unknown RYR1 mutations by using denaturing high-performance liquid chromatography (DHPLC) to analyze RNA samples from biopsied skeletal muscles in patients with, and susceptible to, MH. They concluded that their approach increased the rate of detection of mutations up to 70%—significantly higher than the approximately 25% that has been reported. Furthermore, their study suggested that: RYR1 mutations may be present in up to 70% of patients diagnosed with MH or in those with a predisposition to the disease (MH-susceptible); mutations may be found outside the original hot spots; and DHPLC may be useful for future screening.[13]

Common triggering agents for MH include succinylcholine and potent inhalation anesthetics such as halothane, sevoflurane, and desflurane. Drugs that do not trigger MH include nondepolarizing muscle relaxants, barbiturates, local anesthetics, propofol, ketamine, benzodiazepines, and nitrous oxide (Table 1).[14]

Intraoperative Clinical Presentation

Signs of MH include tachycardia, tachypnea, hyperthermia, generalized muscle rigidity, and acidosis. The most sensitive and specific sign, however, is a rising end-tidal carbon dioxide ($ETCO_2$) concentration (Table 2) in the background of hyperventilation or constant minute ventilation.[15] The result is a mixed metabolic and respiratory acidosis as a result of anaerobic and aerobic metabolism. There is an increase in sympathetic tone and heart rate. The combination of sympathetic drive and peripheral vasodilation secondary to tissue acidosis results in a patient who may present with either a raised or lowered arterial pressure.[14]

In 1% of children anesthetized by inhalation agents followed by succinylcholine, spasm of the masseter muscle, jaw rigidity, or trismus occurs.[16] Masseter muscle spasm is approximately 3 times greater in children with a history of strabismus, which is consistent with the notion that MH is linked with mild myopathies. Clinically, the spasm may not occur for up to 30 minutes in patients with MH or in those who are MH-susceptible. Laboratory contracture testing (discussed below) is positive in up to 50% of such patients. Furthermore, 20% to 30% of patients manifesting masseter muscle rigidity develop other signs of MH, such as elevated creatine kinase.[17,18] Because the development of rigidity or spasm may signify MH, some clinicians advise the immediate discontinuation of all anesthetics[19]; others disagree. Rosenberg has advised that elective surgery be postponed to prevent the progression of MH, but that urgent surgery be continued after replacing the triggering anesthetics with nontriggering agents.[14] Patient gender has not been shown to affect decision making about proceeding with surgery.

Myoglobinuria occurs with all episodes of MH, and therefore a 24-hour observation of the patient is advised, in addition to a determination of myoglobin and creatine kinase levels.[14] In rare cases, as a result of the introduction of dantrolene, hyperkalemia and sympathetic stimulation may occur early as adverse metabolic reactions, and can lead to arrhythmias and intraoperative death if management is inadequate.[20]

Hyperthermia is actually a late indicator of hypermetabolism and sometimes is completely absent. The production and metabolism of adenosine triphosphate produce heat that overwhelms the body's physiologic dissipation mechanisms. Moreover, the hyperthermia can be so intense that a 5-fold increase in oxygen consumption and carbon dioxide production may result. Severe acidosis, shock, and ventricular fibrillation can occur in as little as 20 minutes (Figure 1).[14]

Postoperative Clinical Presentation

MH reactions may present postoperatively with the same features seen intraoperatively. The anesthesiologist must be aware of this fact, because the combination of hyperthermia without a hypermetabolic state does not suggest MH.[15,21] On rare occasions, a patient may present 2 to 4 days postoperatively with acute renal failure secondary to rhabdomyolysis, without hypermetabolic activity.[15,22] Other postoperative complications of MH include hyperkalemia, necrosis, pulmonary edema, muscle edema, consumptive coagulopathy, neurologic sequelae, and a recurrence of MH.[23]

Pathophysiology and Molecular Biology

Advances in molecular genetics have shed light on understanding the pathophysiologic mechanism of MH.[15] Studies indicate that triggering agents lead to an uninhibited release of free calcium from the sarcoplasmic reticulum of skeletal muscle. The critical initial event is a sudden rise in myoplasmic calcium, with a peak rate of intracellular calcium release that is up to 3 times greater than normal individuals.

Ultimately, the release of extra calcium results in a sustained muscle contracture and the increased use of adenosine triphosphate. In addition, the increase in aerobic metabolism elevates carbon dioxide levels, so that both respiratory and metabolic acidosis are common findings. Intracellular high-energy phosphate degradation is hypothesized to result in the leakage of potassium, calcium, myoglobin, and creatine kinase into the circulation, secondary to a loss of sarcolemmal integrity.[14] Furthermore, biochemical studies have revealed that muscles of patients with MH have a lower threshold for excitation—known as a potassium ion shift.[14,24] As a result of these findings, the pathophysiology of MH is now regarded as an exaggerated muscular response to calcium, rather than an exceptional pathology.[25]

Predisposing Disorders

Central core disease, hypokalemic periodic paralysis, and King-Denborough syndrome are myopathies associated with MH susceptibility.[14] Central core disease, characterized by hypotonia and progressive muscle weakness, is inherited via either autosomal dominant or autosomal recessive mechanisms. Microscopically, the muscle cells exhibit a central area of necrosis, giving the appearance of a cell with a "cored out" center. Causal mutations associated with this disorder—found on the ryanodine receptor gene—result in abnormal Ca^{2+} homeostasis in skeletal muscle.[26]

Hypokalemic periodic paralysis (hypoPP) results from an abnormality of the sodium channels in muscle, and leads to electrical instability of the muscle membrane. Paralysis develops as potassium levels decrease. In most cases, hypoPP stems from mutations in the dihydropyridine receptor gene. Because hypoPP is linked to a mutation on the same gene associated with MH susceptibility, further studies on hypoPP may help elucidate the genetic mechanisms behind MH and the coupling theory involving ryanodine and dihydropyridine receptors.[27]

Patients with King-Denborough syndrome present with congenital hypotonia, joint hyperextensibility, proximal muscle weakness, and slightly delayed motor development. Other features include multiple facial and skeletal deformities, epicanthic folds, palmar simian lines, pectus excavatum, and winged scapulae. Patients who experience hyperthermic events under anesthesia have been reported to respond to dantrolene,[28] and thus King-Denborough syndrome may be included in the spectrum of myopathies for predisposition to MH (Table 3).[29]

Differential Diagnosis

Multiple conditions mimic MH in presentation (Table 4). A careful examination of the patient can help differentiate these. For example, postsurgery sepsis in the patient presenting with fever, tachycardia, tachypnea, and acidosis resembles the presentation of MH. In postsurgery sepsis, the increase in $ETCO_2$ is caused by hypermetabolism, as is seen in MH. To distinguish sepsis from MH, the clinical setting must be examined, as well as the patient's response to antipyretics.[13]

Another cause of hypermetabolism is thyrotoxicosis. Although rare, the patient with elevated thyroid hormone can present with tachycardia, tachypnea, and hyperthermia, although muscle rigidity is absent.[30] Myopathies such as Duchenne's dystrophy and Becker's muscular dystrophy are characterized by an absence or alteration of the dystrophin protein. The administration of succinylcholine or other MH-triggering drugs can lead to life-threatening hyperkalemia and muscle rigidity in this population, and result in sudden cardiac arrest. Hyperkalemia must be considered in such patients if they abruptly experience cardiac arrest; proper treatment with I.V. calcium, glucose, and insulin should follow. The administration of dantrolene does not relieve these

symptoms in this group of patients.[31]

Myotonia, characterized by prolonged muscle contraction, can mimic MH. Patients with the classic form, myotonic dystrophy—characterized by extended and intense muscle rigidity, may respond to succinylcholine administration. The hypermetabolism associated with MH, however, is not observed in these patients.[14]

In patients suffering from neuroleptic malignant syndrome, tachycardia, fever, muscle rigidity, acidosis, and elevated creatine kinase levels are found. In such patients, however, a history of the ingestion of neuroleptic medication (eg, phenothiazines, haloperidol, or antipsychotics) is established. The administration of benzodiazepines or bromocriptine is efficacious in these patients.[14,32]

In cases involving lengthy surgery of peripheral, localized parts of the body, such as of the hand or foot, aggressive warming may be used to prevent hypothermia. Unfortunately, this treatment can lead to severe iatrogenic hyperthermia. Ineffective vasodilation in these patients results from draping, and heat dissipation becomes suboptimal. Body temperature may rise considerably, and therefore temperature should be monitored in all patients undergoing surgery that lasts a significant length of time.[14]

Head trauma cases may present with similarities to MH. Injury to the brain can cause hyperthermia, hypermetabolism, and tachycardia via several mechanisms, including increased metabolic demand, catecholamine release, hypothalamic injury, inflammatory changes, lipid peroxidation, and cell death. Other signs and symptoms of brain injury are an altered level of consciousness, dystonia, hypertension, tachypnea, agitation, and diaphoresis.[33]

Laboratory Diagnosis

In 1977, Kalow et al exposed biopsied muscle tissue to gradual increments of caffeine. They observed a leftward shift of the dose-response curve when using muscle taken from patients who had reported episodes of MH. Earlier, Ellis and colleagues had described how muscle contracted in response to different concentrations of halothane in vitro. Today, the in vitro contracture test (IVCT) is the gold standard for diagnosing MH.[34-36]

Patients with a family history of MH, or who develop unexplained hypercarbia or exhibit perioperative rhabdomyolysis, are suitable candidates for biopsy. The IVCT requires approximately 2 g of muscle excised from either the vastus lateralis or vastus medialis muscle. Subsequently, the muscle is dissected into longitudinal strips, sutured at both ends, and placed into baths. One end of the strip is attached to a force transducer while the other is attached to an immobilized hook. The contractile response of the muscle is measured against incremental doses of caffeine and halothane. A contracture of 0.7 g or greater with halothane or 0.3 g with caffeine is considered an abnormal (positive) response and is diagnostic for MH. Presently, this standardized test approaches 99% sensitivity and up to 90% specificity. European, Japanese, and North American protocols differ by varying caffeine and halothane concentrations, and, in addition, use different diagnostic thresholds.[14,37]

To enhance the specificity of the IVCT, new diagnostic agents such as ryanodine (a potent ligand of the ryanodine receptor) have been used. Another compound, 4-chloro-m-cresol, is a substitute or supplement for caffeine in the IVCT. 4-Chloro-m-cresol acts similarly to caffeine by releasing Ca^{2+} through the ryanodine receptor, but shows a higher potency than caffeine. 4-Chloro-m-cresol may exert its effect via a different binding site than does caffeine.

Patients are diagnosed as either MH-susceptible (muscle reacts to halothane and caffeine challenge) or MH-normal (muscle demonstrates no reaction to halothane and caffeine challenge) according to the standardized protocols developed by the European Malignant Hyperthermia Group. Although 4-chloro-m-cresol is used to increase the accuracy of the IVCT, recent research suggests that the compound is not superior to caffeine in discriminating between MH-normal and MH-susceptible cells in other minimally invasive experiments, such as calcium imaging tests.[38]

Contracture-inducing substances that have been studied in swine may direct future research on MH. In a recent study by Fiege and colleagues, enoximone, a type-III phosphodiesterase (PDE-III) inhibitor, stimulated marked contracture in MH-susceptible humans as well as swine. To determine whether the contraction was caused by PDE-III inhibition or by a substance-specific effect, studies on swine were also performed with inamrinone, another PDE-III inhibitor. The administration of inamrinone resulted in marked contractures, suggesting that PDE-III and the cyclic adenosine monophosphate system may be involved in MH pathophysiology; these findings may lead to additional test protocols in the future.[39]

According to the Web site for the Malignant Hyperthermia Association of the United States (MHAUS), www.mhaus.org, there are currently 6 centers in the United States and 2 in Canada that comply with the standardized protocols for muscle biopsy testing for MH. Presently, muscle biopsy centers do not pay for patients' travel expenses, and reimbursement for travel and expenses varies from one insurance company to the next.

In the future, molecular genetic diagnostics might become the standard methodology for MH testing. Such tests are specific, highly reproducible, and minimally invasive. Furthermore, only a small amount of biologic material is required, although currently these tests are relatively expensive.[14] Molecular genetic testing may also eliminate false-negative diagnoses of MH, which will help prevent unnecessary complications and surprises in the operating room during anesthesia. European guidelines for genetic testing have already been incorporated as a supplement to the IVCT protocol (Figure 2).[36,40]

Other tests for MH that have been developed involve the measurement of creatine kinase, creatine phosphate, adenosine triphosphate, and pH; nuclear magnetic resonance spectroscopy; lymphocyte tests; and cultured muscle cells.[14,37]

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Table 4. Differential Diagnosis

Diagnosis	Characteristics
Postsurgery sepsis	Fever, tachycardia, tachypnea, acidosis, increased $ETCO_2$, atypical setting for MH
Thyrotoxicosis	Tachycardia, tachypnea, hyperthermia; muscle rigidity is absent
Duchenne's dystrophy and Becker's musculodystrophy	Hyperkalemia and muscle rigidity
Myotonic dystrophy	May respond to succinylcholine administration with extended and intense muscle rigidity; no signs of hypermetabolism
Neuroleptic malignant syndrome	Tachycardia, fever, muscle rigidity, acidosis, elevated CK, history of neuroleptic medications
Iatrogenic hyperthermia	Hyperthermia without muscle rigidity or acidosis
Head trauma	Tachycardia, hypermetabolism, occasional hyperthermia; also alterations in level of consciousness, dystonia, hypertension, tachypnea, agitation, and diaphoresis

CK, creatine kinase

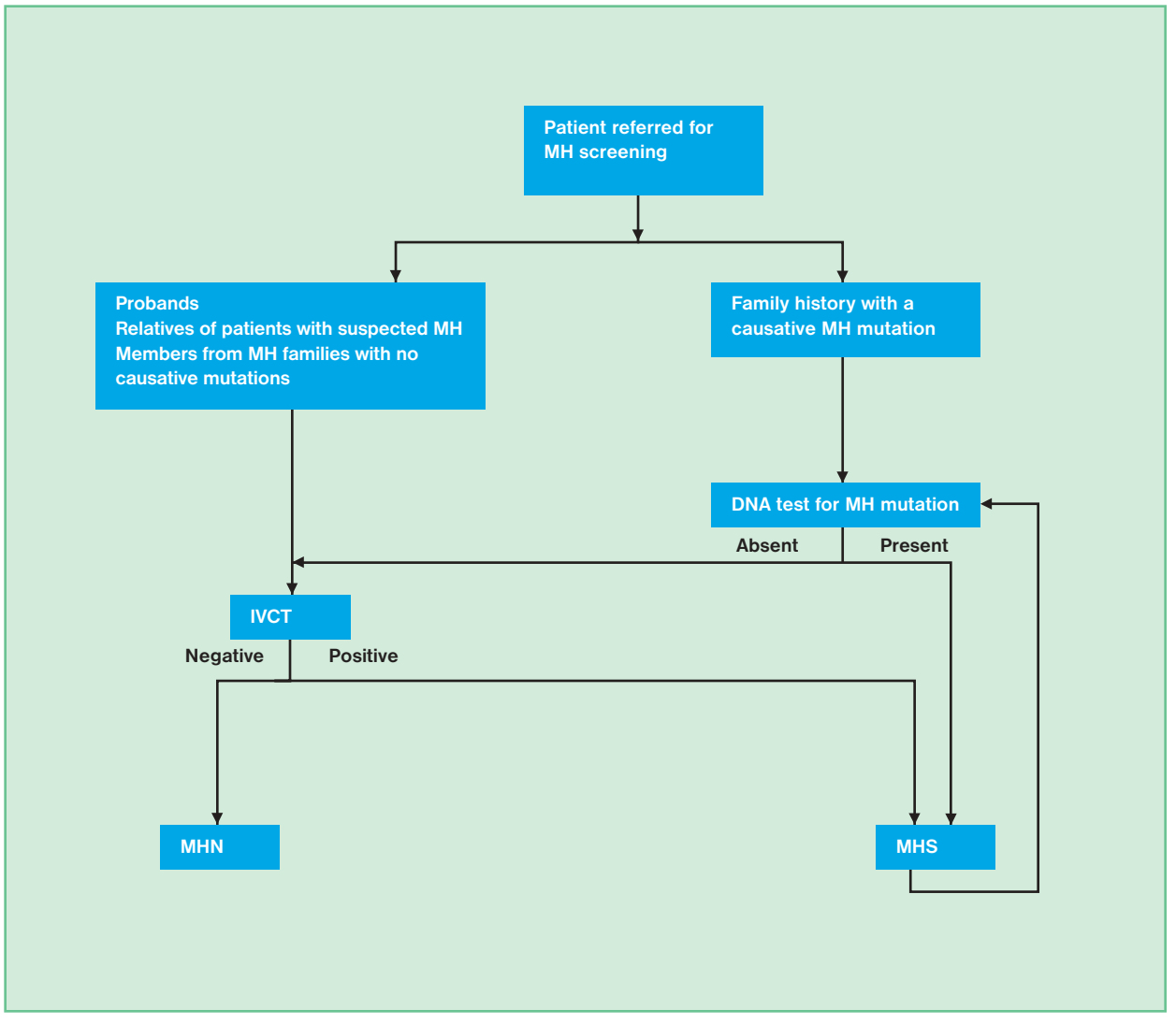

Figure 2. Protocol for genetic testing.[39]
IVCT, in vitro contracture test; **MH**, malignant hyperthermia; **MHN**, malignant hyperthermia–normal; **MHS**, malignant hyperthermia–susceptible

Table 5. Treatment of the Patient With MH[13]

Acute Period
- Stop triggering agent
- Hyperventilate with 100% oxygen
- Administer bicarbonate, 1-2 mg/kg prn for hyperkalemia
- Administer 2.5 mg dantrolene I.V.; repeat if necessary
- Use gastric lavage and/or cold I.V.s to cool patient
- Treat any arrhythmias (calcium channel blockers contraindicated)
- Obtain arterial blood gas values
- Draw blood for electrolyte, coagulation and myoglobin levels

Postacute Period
- Monitor patient for 24 hours in intensive care unit
- Administer 1 mg/kg dantrolene I.V. q4-6 h for 24-36 h
- Maintain adequate urine output with I.V. fluids, mannitol, and furosemide
- Counsel family members about muscle biopsy testing
- Report episode to North American Malignant Hyperthermia Registry

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Treatment and Management of MH

Although MH is a life-threatening disease, swift and proper treatment can prevent complications. The first step in preventing complications is the availability of an MH kit. MHAUS recommends that each kit contain 36 vials of dantrolene, sterile water without bacteriostatic agent for injection, and bicarbonate. Each 70-mL vial contains 20 mg of dantrolene and 3 g of mannitol. By directly affecting the contractile response of muscle and excitation-contraction coupling, the mixture results in skeletal muscle relaxation. Side effects may include nausea and vomiting, pain at the injection site, and weakness.

Dantrolene sodium is specific to skeletal muscle and, therefore, does not create problems with smooth or cardiac muscle. It reverses the hypermetabolic state by dissociating the excitation-contraction coupling by blocking calcium release from the sarcoplasmic reticulum. With I.V. administration, the effects of dantrolene are noticed within 2 to 3 minutes; its average half-life is between 5 and 8 hours, but can extend to 12 hours in some patients with MH.

MHAUS has developed a management protocol that recommends a loading dose of 2.5 mg/kg of dantrolene via a large-bore needle. If needed, incremental doses of up to 10 mg/kg may be administered. Dantrolene is continued at 1 mg/kg intravenously every 6 hours for the next 48 to 72 hours after the episode. Because the dantrolene preparation contains 3 g of the osmotic diuretic mannitol, urinary output must be monitored by means of a urinary catheter. In order to prevent renal failure, urinary output should be >2 mL/kg per hour. Although dantrolene is not recommended for prophylaxis, if the anesthesiologist chooses to use it for this purpose, 2.5 mg/kg intravenously, 30 minutes before anesthesia, is suggested.

As soon as an episode of MH is recognized, the administration of all volatile inhalational anesthetics and succinylcholine should be discontinued immediately. Management of the patient should include hyperventilation with high-flow 100% oxygen as dantrolene is prepared and dispensed. Cooling blankets or ice packs should be used concurrently to help control hyperthermia. MHAUS provides consultation to clinicians via a hotline telephone number: (800) MH-HYPER [(800) 644-9737].

Although cardiac arrhythmia generally abates when acidosis and hyperkalemia are brought under control, it may persist. In such cases, standard antiarrhythmic agents can be used, but calcium channel blockers are contraindicated because they can worsen the hyperkalemic condition and lead to cardiac collapse. Agents for the treatment of hyperkalemia include bicarbonate, I.V. glucose, and insulin. In addition, $ETCO_2$, arterial blood gases, potassium, calcium, urine output, and blood clotting values must be strictly monitored.

After an episode of MH, the patient should be carefully observed postoperatively for recurrence. A minimum of 36 hours of surveillance in the intensive care unit is recommended. The I.V. administration of 1 mg/kg dantrolene every 6 hours for 24 to 48 hours may also help prevent a recurrence. Arterial blood gases, creatine kinase, potassium, calcium, and myoglobin levels, in addition to body temperature and blood clotting, should all be monitored until normal values are obtained (Table 5).[16]

Prevention

Taking preventive measures against MH should be emphasized because the onset of hyperthermia is usually unexpected and potentially catastrophic. Obtaining a thorough anesthetic history from the patient, which takes into account family members who have had MH, is the first step. Family relatives identified as MH-susceptible should not be given triggering agents. For these individuals, testing for MH is recommended. Obtaining medical records for relatives is often possible if the patient is seen in an outpatient facility before surgery.

Myotonia in a patient is a strong indication against the use of succinylcholine. Moreover, patients with predisposing disorders such as central core disease and muscular dystrophy should not be given triggering agents (Table 3). Intraoperative monitoring of the patient's core temperature may help detect an ensuing episode of MH.[14]

Management of the Case

The intubated patient arrived in the operating room and monitors for vital signs were applied. The patient's vital signs were stable: heart rate, 85 beats per minute; blood pressure, 110/60 mm Hg; SpO_2, 100%; and temperature, 100.4°F. The patient was administered 5 mcg/kg of fentanyl, isoflurane 1.1%, 1.0 L per minute of oxygen, and 1.0 L per minute of air, then paralyzed with additional vecuronium, 0.04 mg/kg. The ventilator was set at 400 mL (8 mL/kg); a rate of 12; I:E, 1:2; and inspired O_2, approximately 0.55.

Approximately 15 to 20 minutes into the case, the patient's heart rate began to increase. Fluid administration and the concentration of the volatile agent were increased. The patient's blood pressure was maintained at about 110/60 mm Hg, and additional fentanyl was administered. For the next 10 to 15 minutes, tachycardia gradually became more pronounced (115-125 beats per minute) and blood pressure decreased slightly. The patient received 2 additional liters of lactated Ringer's fluid—delivered through both peripheral lines with a pressure bag. Her heart rate continued to climb (135-155 beats per minute), her temperature rose to 103.8°F, her blood pressure continued to fall, and at that time, it was first noticed that CO_2 concentration was rising (45-55). The ventilator was adjusted by initially increasing the rate, and then increasing the rate and volume. For 5 to 10 minutes, other causes of the patient's intraoperative tachycardia were investigated and ruled out: light anesthesia, hypovolemia, hypoxia, hypercarbia, pneumothorax, acidosis, cardiac tamponade, anemia, pulmonary embolism, and sepsis/fever. The $ETCO_2$ value did not decrease in response to the increased ventilator settings, but persistently rose.

The surgeons were notified to finish the procedure as soon as possible, and the anesthetic agent was turned off. Over the next 20 to 30 minutes, the ventilator rate was increased to 40 respirations per minute, and delivery of 100% O_2 was initiated. The circuit was flushed and an MH cart was obtained. The patient was packed in ice from groin to axillae and behind the neck. Central and arterial cannulae were placed and a total of 140 mg of dantrolene, 25 g of mannitol, and 20 mg of furosemide were administered. Propofol and fentanyl infusions were started and a bolus dose of scopolamine delivered. The tachycardia continued but at a slower rate (100-110 bpm), and then normalized 1 hour after the dantrolene was administered. The patient's blood pressure returned to normal 20 to 30 minutes after treatment began and her temperature fell to 96.8°F after 1 hour. The patient was transferred to the surgical intensive care unit on a dantrolene regimen of 1 mg/kg every 6 hours for 24 hours.

The patient's family was informed in detail of the complication and the implications of the diagnosis. A letter was sent to the family after discharge of the patient on day 10. Subsequent surgeries on the patient were performed with a total I.V. anesthetic technique and there were no further complications.

Conclusion

Although MH is potentially fatal, morbidity and mortality can be reduced when it is recognized early. A thorough medical and family history is at the core of prevention, with laboratory findings being confirmatory of the disease. Many clinical anesthesiologists will simply decide to avoid the use of triggering agents after hearing a family history described in the preoperative holding area. Researchers are developing newer testing modalities that stem from the gold-standard IVCT. In a situation where MH presents unexpectedly, dantrolene should be administered immediately, and the triggering anesthetic discontinued. A national MH hotline is available 24 hours per day to provide experienced advice should a case arise. Increased awareness and early recognition of MH have helped decrease the mortality and morbidity of this disease over the last 20 years. With new improvements in laboratory diagnostics, it may decline further.

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Lesson 248: PreAnesthetic Assessment of the Patient With Malignant Hyperthermia

Post-test

1. Within what time period are the effects of dantrolene noticed after I.V. administration?
a. 30 seconds
b. 2 to 3 minutes
c. It depends on the triggering agent
d. >10 minutes

2. Which of the following is *not* a trigger for malignant hyperthermia (MH)?
a. Propofol
b. Desflurane
c. Halothane
d. Succinylcholine

3. MH in humans:
a. may be inherited as an X-linked trait
b. can be caused by an abnormality of chromosome 16
c. causes fever and rigidity by definition
d. can present with spasm of the masseter muscle

4. The administration of dantrolene:
a. blocks potassium uptake
b. blocks calcium release from the sarcoplasmic reticulum
c. is commonly used in the prevention of MH
d. all of the above

5. Characteristics of MH include all of the following *except*:
a. autosomal dominant transmission
b. triggering by local anesthetic agents
c. an association with central core myopathy
d. improved survival after administration of dantrolene

6. Which of the following is true regarding MH?
a. Unexplained tachycardia is common.
b. Metabolic acidosis is seen on examination of blood gas values.
c. The earliest sign is increased end-tidal CO_2.
d. All of the above.

7. Which of the following is *not* part of a differential diagnosis for MH?
a. Hyperthyroidism
b. Neuroleptic malignant syndrome
c. Myotonia
d. Heroin intoxication

8. Which of the following is most clearly associated with MH?
a. Myotonia congenita
b. Bilateral strabismus
c. Central core disease
d. History of heat stroke

9. Which of the following is *not* a sign of MH?
a. Hypercarbia
b. Rhabdomyolysis (elevated creatine kinase)
c. Muscle rigidity
d. Decreased oxygen saturation

10. In vitro contracture testing is enhanced by the addition of:
a. 4-chloro-m-cresol
b. caffeine
c. dantrolene
d. succinylcholine