Chapter

12

Malignant Hyperthermia

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A three-year-old, 18 kg male presents for tonsillectomy and adenoidectomy. No other pertinent past medical history or family history was reported. Inhalational induction and intubation without muscle relaxation was safely performed. Fifteen minutes after intubation and initiation of adequate controlled ventilation, generalized muscle rigidity is noted. Vital signs at that time include: $EtCO_2$ 110 mmHg, BP 140/80, HR 160 bpm, and T 38ºC.

How Will You Approach This Constellation of Clinical Findings?

The most likely diagnosis for increased end tidal carbon dioxide, fever, and muscle rigidity in this age group is malignant hyperthermia (MH). Other possible diagnoses that are usually considered include serotonin syndrome, sepsis, pheochromocytoma, neuroleptic malignant syndrome, thyroid storm, and adverse drug reactions, but none of these alternatives have been reported in this type of patient and should not be considered.

MH is a hypermetabolic response to inhalational anesthetics or succinylcholine. Acute signs include hypercarbia, tachycardia, master muscle or generalized muscle rigidity, arrhythmia resulting from hyperkalemia, or hyperthermia as an early or later sign. A rapid elevation of temperature is associated with increased severity of disease. Arterial blood gas sampling demonstrates a respiratory acidosis and possibly metabolic acidosis. Complications from MH include disseminated intravascular coagulation (DIC) from prolonged severe hyperthermia, rhabdomyolysis and myoglobinuria, end-stage organ failure, cardiopulmonary collapse, and death.

How Is MH Diagnosed?

Acute MH is diagnosed only by clinical characteristics and index of suspicion. After the event, a diagnosis of MH susceptibility can be confirmed by a positive result of a caffeine-halothane contracture test (CHCT) from a skeletal muscle biopsy, or finding a known MH-causative mutation on genetic screening. However, only a negative CHCT can rule out MH susceptibility; a negative mutation analysis is not sufficient to rule out MH susceptibility. Most MH-causative mutations are located on the gene that encodes for the skeletal muscle ryanodine receptor (RYR1), and rarely on the *CACNA1S* gene that encodes for the dihydropyridine receptor. In very rare cases, MH has been associated with a mutation in the *STAC3* gene, which also contributes to the excitation-contraction complex in skeletal muscle.

What Is the Incidence of MH?

The approximate incidence of acute MH during general anesthesia with triggering agents has been estimated to be between 1/10,000 and 1/25,000 cases. The estimated prevalence of MH susceptibility is thought to be between 1/3,000 and 1/8,500 people. Historically, half of the diagnosed cases of MH have been found in the pediatric population. However, in recent years, studies have found that only 17–18% of patients diagnosed with MH in the United States are under the age of 18. This may be due to better detection of MH susceptibility and anesthetic preparation for MH susceptible patients by anesthesiologists. Male sex is also predominant in pediatric patients diagnosed with MH.

What Diseases Are Associated with MH Susceptibility?

Diseases that are associated with or caused by mutations in *RYR1*, *CACNA1S*, or *STAC3* should be presumed to be associated with MH susceptibility. They are summarized in Table 12.1.

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What Is the Treatment for Acute MH?

Once the anesthesia provider suspects MH, the inhalational agent should be discontinued and dantrolene administered. The initial dose of dantrolene is 2.5 mg/kg and it should be continued until signs of MH begin to abate. In some reported cases, doses up to 10 mg/kg have been required. Hyperventilation with 100% oxygen is helpful to counteract rising blood CO_2 levels. The surgical procedure should be aborted or finished rapidly, and total intravenous anesthesia administered until the patient's condition has stabilized.

Additional priorities include treatment of hyperkalemia with calcium, bicarbonate, or glucose/insulin, and aggressive lowering of hyperthermia to maintain core body temperature below 38.5 °C. The effects of rhabdomyolysis may be minimized by increasing crystalloid administration. An indwelling urinary catheter may be necessary to monitor urine output postoperatively. After the clinical signs of MH have abated, the patient may be weaned off intravenous anesthesia, and the endotracheal tube removed. Dantrolene 1 mg/kg every 6 hours should be continued for at least 24 hours past the point that MH signs have abated and the creatine kinase is trending down.

Table 12.1 Mutations associated with malignant hyperthermia

RYR1	*CACNA1S*	*STAC3*
Normal phenotype	Normal phenotype	Native American myopathy
Central core disease	Multiminicore disease	
Multiminicore disease	Congenital fiber type disproportion	
King–Denborough syndrome	Potassium-related periodic paralysis	
Congenital myopathy with cores and rods		
Centronuclear myopathy		
Congenital fiber type disproportion		
Potassium-related periodic paralysis		
Idiopathic hyperkalemia		

How Would You Approach the Anesthetic Management of a Patient with a Personal or Family History of MH?

For such patients, premedication with dantrolene is not indicated; however, it should be easily available for the operative procedure. Total intravenous anesthesia (TIVA) and/or regional anesthesia should be used, avoiding inhalation agents and succinylcholine. The anesthesia machine can be prepared by replacing the CO_2 absorbent, removing or taping over the vaporizers, removing succinylcholine from the work area, and replacing the anesthesia breathing circuit. The anesthesia machine and circuit should be flushed free of residual anesthetic vapors. The use of charcoal filters will greatly shorten and facilitate this process (Figure 12.1). Although there is no known safe

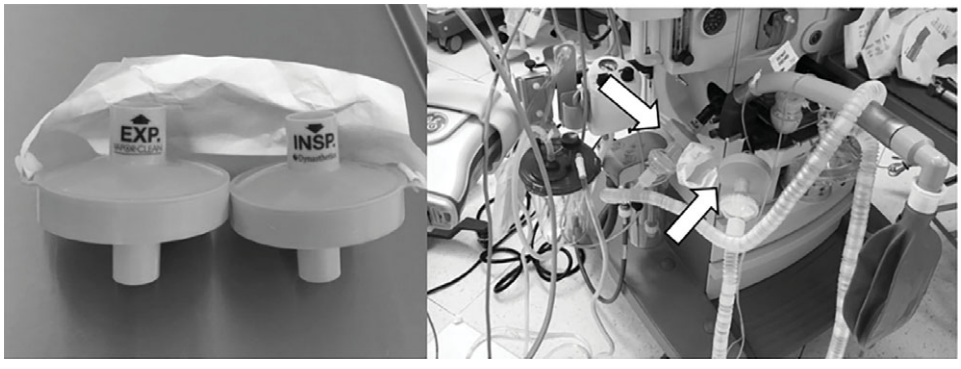

Figure 12.1 Charcoal filters in situ on the anesthesia machine circuit.

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exposure level for MH-susceptible patients, the goal of these measures is to decrease the amount of inhalation anesthetic exposure to less than 5 ppm.

Patients with a history of malignant hyperthermia can be treated safely in an ambulatory care setting where dantrolene is easily accessible.

Suggested Reading

Birgenheier N, Stoker R, Westenskow D, et al. Activated charcoal effectively removes inhaled anesthetics from modern anesthesia machines. *Anesth Analg*. 2011;112 (6):1363–70. PMID: 21543783.

Kim TW, Nemergut ME. Preparation of modern anesthesia workstations for malignant hyperthermia-susceptible patients: a review of past and present practice. *Anesthesiology*. 2011;114(1):205–12. PMID: 21169802.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010 Feb 1;110(2):498–507. PMID: 20081135.

Nelson P, Litman RS. Malignant hyperthermia in children: an analysis of the North American malignant hyperthermia registry. *Anesth Analg*. 2014;118(2):369–74. PMID: 24299931.

Rosero EB, Adesanya AO, Timaran CH, et al. Trends and outcomes of malignant hyperthermia in the United States, 2000 to 2005. *Anesthesiology*. 2009;110(1):89–94. PMID: 19104175.

Salazar JH, Yang J, Shen L, et al. Pediatric malignant hyperthermia: risk factors, morbidity, and mortality identified from the Nationwide Inpatient Sample and Kids' Inpatient Database. *Paediatr Anaesth*. 2014;24(12):1212–6. PMID: 24974921.

Wappler F. Anesthesia for patients with a history of malignant hyperthermia. *Curr Opin Anaesthesiol*. 2010;23(3):417–22. PMID: 20173632.

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