Malignant hyperthermia

Malignant hyperthermia (MH) due to hypermetabolism of skeletal muscle due to idiopathic block of Ca++ re-entry into sarcoplasmic reticulum. Transmitted by a multifactorial genetic predisposition. Total body O2 consumption increases × 2–3.

Incidence: 1 in 15,000 anesthetic administrations in peds, 1 in 40,000 adults. 50% had previous anesthesia without MH. Frequently associated with administration of halogenated inhalational agents and the use of succinylcholine (fulminant form: muscle rigidity almost immediately after succinylcholine, may involve masseters → difficulty intubating). Initial attack and recrudescence may also occur post-op. 30% mortality [1)].

Malignant hyperthermia is a hereditary trait characterized by hypercatabolic reactions induced by anesthetic drugs, or physical or emotional stress.

MH is an autosomal dominant disorder characterized by genetic heterogeneity. It was brought to the attention of anesthetists just over 50 years ago when Denborough and Lovell described 10 deaths attributable to general anesthetics in a family living in Melbourne, Australia, although the family was thought to originate from Wales [2)].

Etiology

Trigger substances, such as volatile anesthetic agents and the depolarizing muscle relaxant succinylcholine can induce a potentially fatal metabolic increase in predisposed patients caused by a dysregulation of the myoplasmic calcium (Ca) concentration. Mutations in the dihydropyridine ryanodine receptor complex in combination with the trigger substances are responsible for an uncontrolled release of Ca from the sarcoplasmic reticulum. This leads to activation of the contractile apparatus and a massive increase in cellular energy production. Exhaustion of the cellular energy reserves ultimately results in local muscle cell destruction and subsequent cardiovascular failure [3)].

Malignant hyperthermia following severe traumatic brain injury occurs due to damage to the thermoregulatory centers, occurring within the first three days after head trauma, a time frame less likely for hyperthermia to be attributable to infectious causes [4)].

Sevoflurane is a known trigger agent for MH, with an incidence for MH of 15 per one million sevoflurane anesthesias in Japan [5)].

Clinical features

Malignant hyperthermia clinical features.

Diagnosis

The caffeine/halothane testing of muscle biopsies is currently the most definitive test for malignant hyperthermia susceptibility. The routine use in suspected cases or the immediate family of known cases remains a matter of contention [6].

Treatment

Malignant hyperthermia treatment.

Prevention

1. identification of patients at risk:

a) only reliable test: 4cm viable muscle biopsy for in-vitro tests at a few regional test centers (abnormal contracture to caffeine or halothane)

b) family history: any relative with syndrome puts patient at risk

c) related traits: 50% of MH patients have heavy musculature, Duchenne type muscular dystrophy, or scoliosis

d) patients who exhibit masseter spasm in response to succinylcholine

2. in patients at risk: avoid succinylcholine (nondepolarizing blockers preferred if paralysis essential), may safely have non-halogenated anesthetics (narcotics, barbiturates, benzodiazepines, droperidol, nitrous…)

3. prophylactic oral dantrolene: 4–8 mg/kg/day for 1–2 days (last dose given 2 hrs before anesthesia) is usually effective

Case series

Between June 2003 and June 2013, 110 consecutive patients with malignant hyperthermia following severe traumatic brain injury were treated using mild hypothermia (35-36°C) associated with small doses of sedative and muscle relaxant. Physiological parameters and intracranial pressure were monitored, and the patients slowly rewarmed following the maintenance of mild hypothermia for 3-12 days. Consecutive patients who had undergone normothermia therapy were retrospectively analyzed as the control. In the mild hypothermia group, the recovery rate was 54.5%, the mortality rate was 22.7%, and the severe and mild disability rates were 11.8 and 10.9%, respectively. The mortality rate of the patients, particularly that of patients with a Glasgow Coma Scale (GCS) score of between 3 and 5 differed significantly between the hypothermia group and the normothermia group ($P<0.05$). The mortality of patients with a GCS score of between 6 and 8 was not significantly different between the two groups ($P> 0.05$). The therapy using mild hypothermia with a combination of sedative and muscle relaxant was beneficial in decreasing the mortality of patients with malignant hyperthermia following severe traumatic brain injury, particularly in patients with a GCS score within the range 3-5 on admission. The therapy was found to be safe, effective and convenient. However, rigorous clinical trials are required to provide evidence of the effectiveness of 'cool and quiet' therapy for

hyperthermia [7]

Case report

Itoh et al. report the case of a 16-year-old man who presented with hyperthermia (>40°C), an elevated creatine kinase level (>64,000 IU · l-1), and myoglobinuria one week after undergoing two successive neurosurgeries for a brain hemorrhage under sevoflurane anesthesia. After having been diagnosed with suspicious atypical postoperative malignant hyperthermia, he was treated with dantrolene and his symptoms disappeared on the day of dantrolene administration. Central hyperthermia is defined as hyperthermia associated with thermoregulatory dysfunction after brainstem injury. Postoperative malignant hyperthermia can sometimes be difficult to distinguish from central hyperthermia, especially after neurosurgery. We could not eliminate the possibility of central hyperthermia as a cause of hyperthermia in the present patient If marked postoperative hyperthermia must be addressed immediately and managed appropriately in neurosurgical patients and dantrolene having few serious side effects, we were able to control his symptoms immediately after the infusion of dantrolene. Therefore, the administration of dantrolene should be considered when treating unidentified postoperative hyperthermia after a neurosurgical procedure [8].

1)
Nelson TE, Flewellen EH. The Malignant Hyperthermia Syndrome. N Engl J Med. 1983; 309: 416–418
2)
Denborough MA, Lovell RR. Anaesthetic deaths in a family. Lancet. 1960;276:45
3)
Metterlein T, Schuster F, Graf BM, Anetseder M. [Malignant hyperthermia]. Anaesthesist. 2014 Dec;63(12):908-18. doi: 10.1007/s00101-014-2392-x. German. PubMed PMID: 25384957.
4)
Li J, Jiang JY. Chinese Head Trauma Data Bank: effect of hyperthermia on the outcome of acute head trauma patients. J Neurotrauma. 2012;29:96–100. doi: 10.1089/neu.2011.1753.
5)
Sumitani M, Uchida K, Yasunaga H, Horiguchi H, Kusakabe Y, Matsuda S, et al. Prevalence of malignant hyperthermia and relationship with anesthetics in Japan. Anesthesiology. 2011;114:84–90.
6)
Halliday NJ. Malignant hyperthermia. J Craniofac Surg. 2003 Sep;14(5):800-2. PubMed PMID: 14501352.
7)
Liu YH, Shang ZD, Chen C, Lu N, Liu QF, Liu M, Yan J. 'Cool and quiet' therapy for malignant hyperthermia following severe traumatic brain injury: A preliminary clinical approach. Exp Ther Med. 2015 Feb;9(2):464-468. Epub 2014 Dec 15. PubMed PMID: 25574217; PubMed Central PMCID: PMC4280981.
8)
Itoh K, Nishibe S, Usuda Y, Kitamura A. [Suspected case of postoperative malignant hyperthermia treated with dantrolene one week after neurosurgery]. Masui. 2014 Oct;63(10):1153-5. Japanese. PubMed PMID: 25693350.