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Clinical Characteristics and Time Course Associated with Malignant Hyperthermia Presenting in the Postoperative Period

Introduction: The Malignant Hyperthermia (MH) hotline of the Malignant Hyperthermia Association of the United States (MHAUS) receives a large volume of calls from physicians reporting symptoms from patients suspected of suffering from MH during the postoperative period. The most commonly reported signs include fever, acidosis, hypercarbia, tachycardia, and rhabdomyolysis. On further investigation it is found that very few, if any, of these cases represent true MH. Cases of MH presenting in the postoperative period are rarely reported.^{1,2} Therefore, we searched the North American MH Registry in an attempt to determine the relative incidence of MH occurring postoperatively as well as to describe its clinical characteristics.

Methods: Following IRB approval, we obtained cases reported to the North American MH Registry (NAMHR). Of the 528 cases which were screened, we found 215 in which MH may have occurred after the completion of the surgical procedure. Since the MH Registry contains many different types of adverse metabolic events that may not have been MH, we subjected these cases to the Larach MH score. We then excluded from our analysis any case with a score less than 20, which indicates a low likelihood of MH.³ This analysis resulted in 64 cases of potential postoperative MH. The records of these 64 cases were then subjected to further review by three MH Hotline consultants and one senior anesthesiology resident. Each of these reviewers

characterized each case as Likely, Not Likely, Not Enough Information (to determine whether or not a case was MH), or Not Applicable (where MH was not the final definitive diagnosis). A presumptive diagnosis of postoperative MH was made when two of the four reviewers agreed that MH was likely.

Results: Seven patients were classified to have had a likely episode of postoperative MH (Table 1). All of these patients were reported as receiving treatment with dantrolene and surviving the event.. One of these patients (#5) had a history of an undefined myopathy.

Conclusion: Postoperative MH is infrequent and occurs within forty minutes of receiving an anesthetic agent. None of the cases in this series of postoperative MH presented with an isolated elevated temperature.

Introduction

The Malignant Hyperthermia hotline has anesthesiologists who are experts on Malignant Hyperthermia on call twenty-four hours a day, seven days a week to answer questions and assist in the treatment and diagnosis of MH. Some of the calls they receive are inquiries regarding patients who are having MH-like symptoms, most commonly post operative fever, after the completion of their anesthetic. Other signs which these experts are called for include acidosis, hypercarbia, tachypnea, tachycardia, rigidity, or observations consistent with rhabdomyolysis. On further investigation, most of these patients' findings are found to be due to another pathologic process such as sepsis.

There have been few cases of post operative MH reported in the literature. Most of those that have been reported as "possible MH" on further review have seemed to be due to another

pathologic process. Such patients include a 48 year old man s/p a general anesthetic without incident who returned to the hospital 3 days later with rhabdomyolysis,¹ a patient who may have developed delirium tremens s/p carpal tunnel release, a patient with fever to 38.3, muscle swelling and acidosis four hours postoperatively, another with fever and hypertension three hours s/p thyroid surgery,^{2,3} and an 18 yo s/p appendectomy who developed post operative fever which responded to active cooling.⁴ However, some cases of postoperative MH reported in the literature do sound genuine such as a 28 year old female s/p removal of a right ovarian cyst who developed muscle rigidity, tachycardia, cyanosis, and a sudden elevated temperature less than one minute after emergence,⁵ and an 18 yo male with a strong family history of MH and who was MH susceptible who developed symptoms and signs consistent with MH about 30 minutes after his ORIF of his right tibial fracture.⁶ Thus far there has not been any studies to analyze the risk factors or time course of MH occurring post operatively.

We sought to establish the clinical characteristics and onset of MH which occurred post operatively by searching and analyzing data from the North American Malignant Hyperthermia Registry.

Methods

Approval for our study was obtained from our health system's Institutional Review Board and data from current cases on file with the North American MH Registry (NAMHR) were obtained through 2004. This yielded 528 of possible MH reported to this registry. These cases were then screened to find 215 incidents in which MH may have occurred outside of the operating room. These remaining cases were then subjected to a Larach MH score.⁷ This score is a tool developed by Marilyn Green Larach in 1994 using the Delphi method and an

international panel of 11 malignant hyperthermia experts. Using this scale any score less than 20 was felt to be either “almost never”, “unlikely”, or “somewhat less than likely” to be MH (Table 2 and 3).⁷ We decided to exclude from our analysis any case with a score less than 20, indicating a low likelihood of MH.³ Using this method resulted in 64 cases of potential postoperative MH. The individual reports for these 64 cases were then subjected to further review by three MH Hotline consultants and one senior anesthesiology resident. Each of these cases were further characterized as Likely, Not Likely, Not Enough Information (to determine whether or not a case was MH), or Not Applicable (where MH was not the final definitive diagnosis) by three MH hotline consultants and one senior anesthesiology resident. A presumptive diagnosis of postoperative MH was made when two of the four reviewers agreed that MH was likely.

Results

Eleven patients were classified to have had a likely episode of postoperative MH (Table 1). All of these patients were reported as receiving treatment with dantrolene and surviving the event.. One of these patients (#5) had a history of an undefined myopathy. The time course for the onset of symptoms ranged from five to forty minutes after the discontinuation of the suspected triggering agent.

Discussion:

Although there have been some cases of postoperative Malignant Hyperthermia reported in the literature, such events are fortunately very rare. Many of the incidents, both in the literature and reported to the MH Registry, appeared to be vaguely consistent with the diagnosis

of MH and were may well have been due to other causes (with sepsis being consistent with the signs and symptoms in the majority of cases). In all of our identified cases an inhalational anesthetic was administered with the onset of sign within 16 minutes in the majority of cases (the longest being 40 minutes).

Unfortunately, further data using genetic analysis or halothane-caffeine contracture testing data could not be obtained for our cases. Due to patient confidentiality issues there does not seem to be a method in the registry of linking reporting forms completed by patients and physicians to the muscle biopsy testing results. Despite this lack of additional data we felt that, since the diagnosis of MH depends on clinical signs using the Larach score in addition to opinions from other malignant hyperthermia experts (a total of 14 including the 11 used to construct the score) served as an adequate measure to confirm the diagnosis of MH.

This analysis is especially relevant from a clinical standpoint since it allows further classification of MH to include a time constant in the likelihood of the diagnosis of this rare disorder.

Conclusion: Postoperative MH is an infrequent event and occurs within forty minutes of the discontinuation of an anesthetic agent. None of the cases in this series of postoperative MH presented with an isolated elevated temperature.

| Patient | Age (yrs) | Gender | Triggering Agent(s) | Signs at Presentation | Time Interval after Discontinuation of Anesthetic (min) |
|---------|--------------|--------|------------------------|--------------------------|---|
| 1 | 19 | M | Isoflurane | Hypercarbia, generalized | 5 |

| | | | | | |
|----|-------------|---|--------------------------------|---|------|
| | | | | rigidity | |
| 2 | 75 | M | Isoflurane | Tachycardia, cyanosis, generalized rigidity | 10 |
| 3 | Unkn own | M | Isoflurane, succinylcholine | Tachycardia, rapid temperature increase, hypercarbia | 5 |
| 4 | 26 | M | Isoflurane, succinylcholine | Tachypnea, cyanosis, tachycardia | 7 |
| 5 | 19 | M | Isoflurane | Ventricular tachycardia | 2 |
| 6 | 12 | M | Isoflurane | Generalized rigidity, tachycardia, tachypnea | 10 |
| 7 | 44 | M | Isoflurane, succinylcholine | Generalized rigidity, hypercarbia, tachypnea | < 10 |
| 8 | 6 | M | Halothane | Generalized rigidity, tachypnea, skin mottling, tachycardia | 5 |
| 9 | Unkn own | M | Isoflurane, succinylcholine | Tachycardia, generalized muscle rigidity, tachypnea, hypertension | 15 |
| 10 | 36 | F | Isoflurane, succinylcholine | Tachycardia, tachypnea, rapid temperature increase | < 40 |
| 11 | 25 | M | Isoflurane, succinylcholine | Tachycardia, tachypnea, hypercarbia | 16 |

Table 1: Clinical characteristics of the 11 patients felt to have post operative Malignant Hyperthermia.

| Process | Indicator | Points |
|-----------------------------------|---|--------|
| Process I: Muscle Rigidity | Generalized muscle rigidity (in absence of shivering due to hypothermia, or during or immediately following emergence from inhalational general anesthesia) | 15 |
| | Masseter spasm shortly following succinylcholine administration | 15 |
| Process II: Muscle Breakdown | Elevated creatinine kinase > 20,000 IU after anesthetic that includes succinylcholine | 15 |
| | Elevated creatinine kinase > 10,000 IU after anesthetic that did not include succinylcholine | 15 |
| | Cola colored urine in perioperative period | 10 |
| | Myoglobin in urine > 60 microg/L | 5 |
| | Myoglobin in serum > 170 microg/L | 5 |
| | Blood/plasma/serum K > 6 meq/L (in absence of renal failure) | 3 |
| Process III: Respiratory Acidosis | P_{ETCO_2} > 55 mmHg with appropriately controlled ventilation | 15 |
| | Arterial P_{aCO_2} > 60 mmHg with appropriately controlled | 15 |

| | | |
|----------------------------------|---|----|
| | ventilation | |
| | $P_{ETCO_2} > 60$ mmHg with spontaneous ventilation | 15 |
| | Arterial $Pa_{CO_2} > 65$ mmHg with spontaneous ventilation | 15 |
| | Inappropriate hypercarbia (in anesthesiologist's judgment) | 15 |
| | Inappropriate tachypnea | 10 |
| Process IV: Temperature Increase | Inappropriately rapid increase in temperature (in anesthesiologists judgment) | 15 |
| | Inappropriately increased temperature > 38.8 C (101.8 F) in the perioperative period (in anesthesiologist's judgment) | 10 |
| Process V: Cardiac Involvement | Inappropriate sinus tachycardia | 3 |
| | Ventricular tachycardia or ventricular fibrillation | 3 |

Table 2: Clinical indicators used in the determination of the Larach score.

MH Indicators

Review the list of clinical indicators. If any indicator is present, add the points applicable for each indicator while observing the double-counting rule below, which applies to multiple indicators representing a single process

If no indicator is present, the patient's MH score is zero.

Double-counting

If more than one indicator represents a single process, count only the indicator with the highest score.

Application of this rule prevents double-counting when one clinical process has more than one clinical manifestation.

Exception: the score for any relevant indicators in the final category of Table 2 (other indicators) should be added to the total score without regard to double counting.

Table 3: Scoring rules for the Larach score.

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