Intra-operative presentation of Malignant Hyperthermia (confirmed by RYR1 gene mutation, c.7522C>T; p.R2508C) leads to diagnosis of King-Denborough Syndrome in a child with undiagnosed myopathy

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INTRODUCTION

We present the novel case report of a child with undiagnosed myopathy with physical characteristics of King-Denborough syndrome (KDS), a congenital myopathy associated with dysmorphic features and musculoskeletal abnormalities (1), who developed Malignant Hyperthermia (MH) intra-operatively. Neurology work-up identified the child with KDS, further confirmed by presence of pathological Ryanodine receptor (RYR1) mutation (2).

CASE DESCRIPTION

- Demographics- 2 year old male
- Preoperative diagnosis- non-specific myopathy
- Surgical Procedure—bilateral robotic orchiopexy
- Anesthetic induction—inhalation induction with Sevoflurane and IV Propofol and Rocuronium
- Anesthetic Maintenance—Sevoflurane
- Positioning—steep trendelenberg with full body drape and forced air warmer (43 degrees Centigrade)
- Intraoperative course
  - End tidal carbon dioxide (etCO2) steadily climbed and peaked at 68mm Hg despite increasing minute ventilation (Figure 1)
  - Esophageal temperature increased to 38.9 degrees Centigrade despite discontinuation of the air warmer (Figure 1)
  - Blood pressure and heart rate increased along with a brief period of body rigidity
- MH was suspected and two doses of dantrolene (2.5mg/kg) intravenously were given 15 minutes apart, 2 hours after induction
  - The temperature, heart rate and etCO2 decreased within 15 minutes, by 2 degrees, 40 beats/min, 15 mmHg, respectively
  - Arterial blood gas showed predominantly respiratory acidosis
  - MH hotline was called
  - Creatine phosphokinase (CPK) and myoglobin levels were drawn and neurology consult was obtained.
  - The patient received three more doses of dantrolene 1mg/kg over the next 36 hours to treat rising CPK levels and episodes of rigidity.
  - Pediatric neurologist diagnosed KDS and genetic testing revealed a known pathological mutation on RYR1 gene, c.7522C>T; p.R2508C, which has been proven causative for MH (2).
- Postoperative course
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  - Creatine phosphokinase (CPK) and myoglobin levels were drawn and neurology consult was obtained.
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DISCUSSION

- Presentation of MH was confusing
- Rise in etCO2 due to laparoscopic technique and Trendelenburg positioning is common
- Rise in core temperature is also relatively common from full draping, air warmer, and robotic instrumentation
- Rigidity, a pathognomonic sign of MH, present for a brief duration was recognized by the anesthesia team
- Vigilance and the early administration of dantrolene likely averted a severe presentation of MH
- Dantrolene was administered within 5 minutes of event and was likely the reason for mitigating the severity of the blood gas, CPK, and myoglobin results.
- When MH is suspected, dantrolene administration should not be delayed waiting to draw blood samples (3)
- It is crucial to refer to neurology to diagnose the underlying disease which determines the future care of the patient and the family.

GENETICS

- Patient confirmed to have RYR1 gene mutation, c.7522C>T;p.R2508C
- There are 35 known causative mutations of RYR1 for MH as listed on the European MH website (2)
- MH registry at MHAUS has 3 other known patients with RYR1 mutation to His at 2508 (3). This mutation was also reported by Migita et al.(4)
  - 2/3 patients carried diagnoses of myopathy
  - 2/3 patients died of MH in the operating room
  - 1/3 patients had MH in the operating room but lived
  - 0/3 patients diagnosed with KDS

REFERENCES

1. Dowling: Neuromuscular Disord 2011
2. www.emhg.org/genetics
3. Personal communication BWB, www.mhaus.org/register