Malignant Hyperthermia

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Case Presentation

- CC: 65 year old male with Rectal Cancer
  - Colonoscopy- 2 cm rectal mass, 13 cm from anal verge.
  - Biopsy- infiltrating colonic adenocarcinoma.
- PMH: HTN, DM, a fib, gout, OSA, CRI, dyslipidemia, CAD, GERD
- Meds: lasix, toprol, isosorbide, colchicine, zocor, gabapentin, glimepiride
- PE
  - Obese male (320 lbs), AAO x 3
  - Chest- Clear breath sounds b/l, no murmurs
  - Abdomen non-tender, non-distended.
  - Extremities- mild edema
Case Presentation

- Labs pre-op
  - CBC- 6/13/39/138
  - Chem- 143/5/99/36/53/1.5/80
  - Tprot/alb-6.3/3.7
  - Coags – 13/33/1

- EKG- NSR at 65 bpm

- Imaging
  - Abdominal CT scan- negative for metastasis.
  - TTE- normal left ventricular function and EF 78%.

- The patient was cleared for surgery by cardiology and pulmonary.
Case Presentation

- Exploratory laparotomy.
  - Proctosigmoidoscopy- rectal mass at 5 cm from anal verge.
  - Urology placed bilateral ureteral stents.
- Low Anterior Resection
  - Primary anastomosis between descending colon and distal rectum using an EEA stapler.
  - Transverse loop colostomy.
  - IV antibiotics pre and intraop – Gentamicin and Flagyl.
  - EBL– 500 ml, Crystalloid- 5.5 L
  - He was kept intubated and transferred to ICU.
Post-Op Course

- **POD 1**
  - Onset of 101°F fevers. IV resuscitation continued.

- **POD 2**
  - Fevers as high as 102°F.
  - WBC went from 5 to 16 K.
  - ID consulted - Zosyn was started after cultures were taken.
  - Hypotension requiring pressors.
  - Mild elevation in troponins peaking a 0.68 ng/ml.
    - Cardiology- demand ischemia due to sepsis

- **POD 3**
  - Fevers 104°F.
  - WBC decreased to 8K.
  - Pressors were weaned.
Post-Op Course

- POD 4
  - Pt continued febrile.
  - Blood and urine cultures were negative.
  - Sputum culture
    - P mirabilis sensitive to Zosyn.
  - Vancomycin added as per ID.
  - TTE showed EF of 50% and mild decreased left ventricular systolic function.
  - Abdominal CT- negative for fluid collections.
  - Chest CT scan- bilateral basal atelectasis.
Post- Op Course

- POD 5
  - Fevers as high as 106° F. WBC was 5K.
  - Cooling measures - cooling blankets, ice packs, gastric irrigation.
  - Hypotension, requiring pressors.
  - Neurology consult
    - Possible central fever: intracerebral bleed, acute hypothalamic lesion. Pt unstable for brain imaging.
  - Anesthesia consult
    - Malignant hyperthermia unlikely
      - No acidosis- pH- 7.38, lactate- 1.6
      - No hypercapnia- pCO2- 31
Post- Op Course

- OR for exploratory laparotomy.
  - No necrosis or perforations on the small or large bowel.
  - Peritoneal cavity was irrigated.
- Ventricular tachycardia 35 mins after returning to ICU.
- ACLS protocol was started, including cardioversion.
- The patient was pronounced dead 22 mins later.
- Path from colon resection- pT2, N1, Mo, negative margins.
Malignant Hyperthermia
Normal Body Temperature

- $37 \degree C (98.6 \degree F)$
  - Wunderlich CA, Sequine E (1871)*

Variations

- Site
  - Axillary, Rectal > Oral, Ear canal
  - Thermistor-equipped pulmonary artery or bladder catheter

- Age

- Diurnal variation
  - Early morning vs late afternoon

Fever

- Definition - Body temperature $\geq 38.3 ^\circ C (101 ^\circ F)$
  - Society of Critical Care Medicine (1998)*
- Fever vs Hyperthermia
  - Both indicate an elevated body temperature
  - Hyperthermia
    - abnormal thermoregulatory system
  - Fever
    - normal thermoregulatory system, but operating at a higher set point.

Fever

Tissue injury (infection) → Inflammatory cytokines (endogenous pyrogens) → Hypothalamus → Elevate body temperature → Enhanced Immune Function

Post-Op Fevers

- The classic Ws
  - Wind – atelectasis / pneumonia
  - Water – urinary tract infections
  - Wound – wound infection
  - Walking – DVT/ thrombophlebitis
  - Wonder drugs – drug fever
    - Findings: rigors, myalgia, ↑ WBC, eosinophilia, rash, hypotension
Hyperthermia Syndromes

- Heat stroke
- Neuroleptic Malignant Syndrome
- Malignant Hyperthermia (MH)
  - Described by Denborough (1962)
  - Incidence
    - 1 in 15,000 episodes of general anesthesia *
    - 1 in 50,000 adults
    - 1 in 15,000 children (young males)
  - Autosomal dominant inheritance

Malignant Hyperthermia

Inhalational anesthetics - halothane, isoflurane, servoflurane, and desflurane.

Depolarizing neuromuscular blockers – succinylcholine

Excessive release of calcium from the sarcoplasmic reticulum into cytoplasm of skeletal muscle cells.

Increased metabolic rate
Clinical Manifestations of MH

- Sudden rise in end-tidal $\text{PCO}_2$
  - Hypermetabolism- Acidosis, hypercapnia.
- Followed by generalized muscle rigidity.
  - Rhabdomyolysis
  - Myoglobinuric renal failure (ATN)
  - Rise in body temperature (often above $40^\circ\text{C}$ or $104^\circ\text{F}$).
- Altered mental status
- Autonomic instability
  - Cardiac arrhythmias, fluctuating blood pressure.
- Disseminated intravascular coagulation
- Pulmonary edema
Treatment of MH

- Immediate discontinuation of the offending anesthetic agent.

- Dantrolene sodium (1975)
  - Muscle relaxant
  - Blocks the release of calcium from the sarcoplasmic reticulum.

- Dose regimen
  - 1 - 2 mg/kg as IV bolus, repeat every 15 minutes if needed to a total dose of 10 mg/kg.
  - 1 mg/kg IV or 2 mg/kg orally qid for 3 days to prevent recurrences.

- Side effects
  - Muscle weakness
  - Hepatocellular injury.
    - more common when the daily dose exceeds 10 mg/kg
    - Active hepatitis and cirrhosis are relative contraindications to dantrolene tx

- Supportive treatment and cooling measures.
Malignant Hyperthermia

- Prognosis is poor if not aggressively treated.
  - 1970’s mortality > 80%
  - Now mortality < 5% †

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Malignant Hyperthermia Diagnosis

- In vitro contracture test (IVCT)
  - Caffeine/halothane contracture test (CHCT)
- Genetic testing- confirms diagnosis in about 70%.*
  - **RYR 1** (MHS1 locus)
    - Encodes the type 1 **ryanodine receptor** of skeletal muscle.
    - 70%-80% of individuals with MHS.†
  - **CACNA1S** (MHS5 locus)
    - Encodes the $\alpha_1$-subunit of the skeletal muscle dihydropyridine receptor of L-type calcium channels.
    - 1% of all MHS ^

References