Malignant Hyperthermia in a Two-Month Old Child with Holt-Oram Syndrome Undergoing Cardiac Surgery

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CASE PRESENTATION

- A two month old female patient with Holt Oram Syndrome (HOS) presented for operative repair of a perimembranous ventricular septal defect (VSD), secundum atrial septal defect (ASD) and patent ductus arteriosus (PDA).

- Patch closure of the VSD and ASD with sevoflurane followed by IM pancuronium and IV fentanyl was uneventful. Anesthesia was maintained with inhaled isoflurane, fentanyl, and rocuronium. The surgical procedure was completed and the patient was paced due to third degree atioventricular block.

- Approximately 1 1/2 hours after heparin reversal and discontinuation of CPB, she developed rapid hyperthermia, hypercarbia, and hypoxia. Transthoracic echocardiogram revealed no residual shunt.

- The patient was ventilated with 100% oxygen via ambu bag, isoflurane was discontinued, labs were drawn, ice packs were placed, and dantrolene (2.5mg/kg) was administered.

- The patient was extubated on post operative day 1. Extensive discussion was held with the family who opted to not have the child tested for MH.

- The patient was ventilated with 100% oxygen via ambu bag, isoflurane was discontinued, labs were drawn, ice packs were placed, and dantrolene (2.5mg/kg) was administered. Labs revealed a metabolic and respiratory acidosis despite adequate ventilatory support. The Malignant Hyperthermia hotline was called and confirmed a high suspicion for malignant hyperthermia (MH).

- The pediatric intensive care unit was notified of the patient's condition and upon arrival, additional dantrolene (1.5mg/kg) was administered. The patient's condition stabilized in the intensive care unit, labs were monitored and no additional dantrolene was administered.

- The patient was extubated on post operative day 1. Extensive discussion was held with the family who opted to not have the child tested for MH.

- The child has subsequently undergone several non-triggering anesthetics without complication.

- Holt-Oram Syndrome (HOS) is an autosomal dominant disorder associated with musculoskeletal deformities, congenital heart malformation, and cardiac conduction disorders.

- Both HOS and MH may manifest clinically with a wide variety of cardiac arrhythmias.

- HOS is a result of T-box transcription factor 5 (TBX5) with over 37 mutations described. Very little is known about the mechanism by which defects in the TBX family lead to arrhythmias.

- Genetic defects in the ryanodine receptor, which regulates calcium release from the sarcoplasmic reticulum, is well reported to be the genetic basis of malignant hyperthermia.

- TBX5 transcription factor may have an association with the ryanodine family of receptors, or other ion channel proteins, with genetic alterations manifesting as MH.

- Holt-Oram Syndrome (HOS) is an autosomal dominant disorder associated with musculoskeletal deformities, congenital heart malformation, and cardiac conduction disorders.

- We present the first reported case of MH in a patient with HOS.

- Though this may be an isolated case in a single patient, the genetic basis of HOS may warrant consideration of a susceptibility to MH.

- Certain forms of HOS may render a child susceptible to MH, as we have reported.

- No clear association between HOS and MH may be made as we currently have an incomplete understanding of the molecular basis of HOS.

- Following strict MH precautions on all patients with HOS is likely not indicated.

- Vigilance about the development of MH in anesthetized patients with HOS is warranted, particularly when alterations in cardiac rhythm, temperature, or hemodynamics are seen.

- Children with HOS present frequently for operations due to upper extremity and cardiac deformities.

- Though this may be an isolated case in a single patient, the genetic basis of HOS may warrant consideration of a susceptibility to MH.

- Variability in the manifestation of symptoms depends on the location of the defect in the TBX5 gene, and so certain variants of HOS may be more susceptible to MH than others.

REFERENCES